CADTH OPTIMAL USE REPORT

Point-of-Care Troponin Testing in Patients With Symptoms Suggestive of Acute Coronary Syndrome: A Health Technology Assessment

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Fiona Clement contributed to the protocol development, contributed to the review of the economic literature, conducted economic analyses, and assisted with revisions of the report.

Mohammed Jabr contributed to the economic protocol development, contributed to the review of the economic literature, and contributed to the economic evaluation.

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Conflicts of Interest

No authors declared conflicts of interest.

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Abbreviations

ACS	acute coronary syndrome
AMI	acute myocardial infarction
CABG	coronary artery bypass grafting
CI	confidence interval
cTn	cardiac troponin
cTnI	cardiac troponin I
cTnT	cardiac troponin T
CV	coefficient of variation
ECG	electrocardiogram
ED	emergency department
HTA	health technology assessment
LOS	length of stay
MI	myocardial infarction
NACB	National Academy of Clinical Biochemistry
NSTEMI	non-ST segment elevation myocardial infarction
OCC	Ontario case costing initiative
PCI	percutaneous coronary intervention
POC	point of care
PPV	positive predictive value
QALY	quality-adjusted life-year
RCT	randomized controlled trial
ROC	receiver operator characteristic
STEMI	ST segment elevation myocardial infarction
TAT	turnaround time
TCD	time to clinical decision
TTD	time to discharge
UA	unstable angina

Executive Summary

The Issue

Testing of cardiac biomarkers, such as cardiac troponin I or cardiac troponin T, has an important role in the diagnostic workup for acute coronary syndrome (ACS) (including acute myocardial infarction [AMI] and unstable angina), and in patients presenting with acute chest pain and a non-diagnostic electrocardiogram (ECG). Bedside testing of cardiac troponins (cTn) using point-of-care (POC) assays was developed to reduce the turnaround time of the standard tests performed in a central laboratory, and to expedite treatment. Given the introduction and increasing diffusion of POC cTn use**,** a review of its clinical and economic evidence is needed to inform decisions about its acquisition and use in emergency rooms and other in-hospital settings, as well as in rural health care centres and remote settings.

Objectives

The aim of this health technology assessment (HTA) is to inform decision-making about the appropriate use of POC cardiac cTn testing. The policy question of whether to adopt POC troponin testing in specific settings (rural health care centres, remote locations, in hospital, in emergency settings) has been raised in Canadian jurisdictions. This HTA will address these questions by evaluating the diagnostic accuracy, clinical utility, and cost-effectiveness of POC cTn testing in patients presenting with ACS. The economic evaluation will determine the cost per quality-adjusted life-year (QALY) gained with POC troponin compared with central laboratory troponin testing (context 1) or no POC troponin testing (context 2). This HTA will address the following research questions:

1. Using POC cTn devices approved by Health Canada, what is the diagnostic accuracy of POC cTn testing compared with central laboratory methods in patients presenting with symptoms of ACS?

2. What is the clinical utility of POC cTn testing in altering the treatment and outcomes of patients presenting with symptoms of ACS compared with:
   a. standard care in settings where a central laboratory is not available (pre-hospital settings, rural settings, or remote locations)
   b. central laboratory methods in settings where a central laboratory is available (in hospitals and emergency departments)?

3. What is the cost-effectiveness of POC cTn testing in patients presenting with symptoms of ACS compared with:
   a) standard care in settings where a central laboratory is not available (pre-hospital setting, rural setting, remote locations)
   b) central laboratory methods in settings where a central laboratory is available (in hospitals and emergency departments)?

Methods

A peer-reviewed literature search strategy was employed to identify published literature in the following bibliographic databases: MEDLINE (1946–) with in-process records and daily updates via Ovid; Embase (1974–) via Ovid; The Cochrane Library (2015, Issue 1) via Wiley; and PubMed. No filters were applied to limit the retrieval by study type. Retrieval was not limited by publication year or language. The initial search was completed on January 14, 2015 and regular alerts were conducted up to February 12, 2016. Grey literature (literature that is not commercially published) was identified by searching the Grey Matters checklist (www.cadth.ca/resources/grey-matters). Google and other Internet search engines were used to search for additional Web-based materials.

Studies were included if they met the selection criteria detailed in the text. Data were extracted independently by one reviewer and checked for accuracy by another reviewer, and any disagreements were resolved through discussion until consensus was reached. A quality assessment of included diagnostic-accuracy studies was conducted using the QUADAS-2 tool, and studies on clinical utility were assessed using the Downs and Black checklist. Quality was appraised by one reviewer and the assessments verified by a second reviewer, with disagreements resolved through discussion.

The original search identified 1,434 citations. From these, 322 potentially relevant reports were retrieved for further scrutiny, and six reports were retrieved from search updates (alerts) and grey literature. Forty-one original publications, five companion reports, and two guidelines were selected for inclusion. Nine studies and one companion report on the diagnostic performance of POC in patients with chest pain were included. Thirty studies, three companion reports, and two guidelines on the clinical utility of POC cTn testing in patients with symptoms suggestive of ACS were included. Two additional studies and one companion report[1] were included for both diagnostic-accuracy and clinical-utility outcomes.

The diagnostic accuracy of POC troponin testing was assessed based on the ability of POC troponin testing to predict AMI. The review on diagnostic accuracy was limited to POC cTn devices that are available in Canada and approved by Health Canada, and to studies where an elevated troponin level was based on a result above the 99th percentile cut-off threshold. Meta-analysis of diagnostic-accuracy outcomes was not possible due to heterogeneity among the included studies, such as differences in devices used. A review that includes a narrative synthesis was conducted, with results reported in tables with ranges.

The clinical utility of POC troponin testing was based on findings about the benefits and risks resulting from test use. Recommendations from evidence-based guidelines were also reported. The review on clinical utility was not limited to POC cTn devices approved for use in Canada. Meta-analysis was not possible due to clinical and methodological heterogeneity among trials, such as difference in definitions of outcomes and inconsistencies in reporting. A review that includes a narrative synthesis and summary of study findings was conducted, with results reported in tables with ranges.

For diagnostic-accuracy and clinical-utility outcomes, subgroup analyses were performed based on study design, clinical setting (e.g., emergency department, rural health care centres, or remote locations), the level of sensitivity of the central laboratory method, type of cardiac troponin test (cardiac troponin I [cTnI], cardiac troponin T [cTnT]), and study funding status (private and public).

Diagnostic Accuracy

Compared with central laboratory methods, POC tests tended to provide lower sensitivity, lower negative predictive value, higher specificity, and higher positive predictive value (PPV). Both positive and negative-likelihood ratios tended to be higher with POC testing compared with central laboratory testing, although only one study was available for the central laboratory comparison. This trend was maintained across different POC devices, and with blood samples taken at admission, three hours and six hours after admission, and between six to nine hours after admission. Subgroup analyses of studies based on the study design, setting, sensitivity levels of the central laboratory methods, the types of cTn (I or T), and the funding status did not show any systematic differences in findings.

Clinical Utility

In Settings Where a Central Laboratory is Available

POC cTn testing tended to shorten turnaround time (TAT), length of hospital stay, and time to discharge. The use of POC cTn did not statistically change mortality rates or severe adverse events compared with a central laboratory in most studies, in up to one year of follow-up. There was no difference in quality of life among patients who were tested using POC or central laboratory within up to three months' follow-up. Subgroup analyses of clinical-utility studies based on study design, setting, the level of sensitivity of the central laboratory methods, the types of cTn (I or T), and funding status did not show any differences in findings.

The majority of physicians and nurses who participated in related survey studies agreed that they were satisfied with POC testing, and that cTn testing shortened TAT, was easy to use, and led to better patient management.

The National Academy of Clinical Biochemistry (NACB) and the European Society of Cardiology (ESC) guidelines recommend that, based on sufficient and fair evidence, POC tests for cardiac troponins should be implemented when a central laboratory cannot consistently provide test results within 60 minutes.

In Settings Where No Central Laboratory is Available

In pre-hospital or ambulance settings, limited evidence points to the potential use of POC cTn tests for the diagnosis and management of patients. POC cTn testing may reduce the percentage of patients referred to the emergency department from a primary health care centre. POC cTn testing was shown to be feasible and reliable for patients transported by ambulance, and can shorten the time from first medical contact to patient disposition. The majority of physicians and nurses who participated in related surveys in rural health care centres or remote locations agreed they were satisfied with POC testing, and that cTn testing shortened TAT, was easy to use, and led to better patient management.

Economic Evaluation

An economic evaluation was conducted in which standard of care was compared with POC cardiac troponin (cTn) testing in two settings: where a central laboratory is available, either alone or in addition to POC cTn (context 1), and in settings where a central laboratory is not available (context 2). The target population was adult patients presenting with chest pain or other symptoms suggestive of ACS identified by ECG testing as having non-ST elevation. For each context, a decision-tree model was developed to simulate what could happen to patients from the chest pain presentation at the emergency department or doctor's office until one year after their episode. The analysis assumed a payer's perspective. A one-year time horizon was used for the economic analysis. The proportion of patients in each of the potential diagnostic categories (true-positives, false-positives, true-negatives, false-negatives) was determined by both the underlying prevalence of non-ST elevation myocardial infarction (NSTEMI) and the diagnostic accuracy of the cTn test strategy being evaluated. The primary outcome was the cost per QALY gained. Different utility estimates were included for the general population, NSTEMIs, and missed NSTEMIs. Secondary measures for context 1 include the length of stay in the emergency department and the probability of readmission due to misdiagnosis of NSTEMI, and were accounted for and expressed as costs. No secondary measures were available for context 2. All outcomes were considered for one year. The analysis considered test costs, emergency room costs, in-patient costs, and physician fees for services that are covered in provincial fee schedules. Indirect costs, such as productivity losses, out-of-pocket patient costs, and time costs were not included in the first setting. However, in the second setting, where the patient may be transferred to the hospital from either a rural emergency room or primary care practice, limited patient-borne costs were included. A cost-effectiveness analysis was conducted in which costs were measured in dollars and the outcome was measured in QALYs.

Discussion

Our findings concur with observations from other systematic reviews that an ideal POC assay for the diagnosis of AMI does not yet exist and, despite improvement in TAT and length of hospital stay, there is no strong evidence of improvement of clinical outcomes compared with cTn testing by a central laboratory. In the absence of a central laboratory, POC cTn testing may be of additional benefit compared with standard care without troponin testing. In rural centres and remote locations, the use of POC cTn testing may lead to improved patient care, as cTn results, in addition to clinical assessment of the patient, may help prevent unnecessary transfers to hospital, thereby allowing patients to remain in their communities for follow-up and care. This may result in other benefits, such as reduced out-of-pocket costs and familial disruptions, and ensuring the transfer of only those patients who require it. The results from our clinical review must be interpreted with caution, given the limited quality of the included studies, and the outcomes analyzed are reflective of short-term follow-up times.

Generally, POC cTn testing strategies were found to be less effective and less expensive compared with standard of care, regardless of context. However, there are plausible variations in diagnostic accuracy that change the cost-effectiveness from cost-saving to cost-incurring. Generally, the weak evidence base for effectiveness and costs limited the scope of this economic evaluation.

Conclusions

Overall, given the limitations with the data and the inconsistency in diagnostic test accuracy estimates, the usefulness of POC cTn testing in settings with access to central laboratories may be limited. However, in settings with no access to a central laboratory, such as in rural health care centres or remote settings, POC cTn testing may be useful due to the potential to help reduce unnecessary transfer of patients to larger centres.

1. Introduction

1.1 Chest Pain and Acute Coronary Syndrome

Chest pain can be the result of a wide variety of causes, including acute coronary syndrome (ACS) and non-cardiac conditions, such as gastro-esophageal reflux, anxiety, and muscular pain.[2,3] Individuals who present with chest pain or other symptoms suggestive of ACS undergo investigations such as clinical assessment and electrocardiogram (ECG) to rule out or rule in a potential acute myocardial infarction (AMI).[4] However, clinical assessment and ECG findings are often inconclusive and further investigation may be required to rule out or rule in the possibility of an AMI.

ACS is a term for a group of conditions that result from a decrease of blood flow in the coronary arteries, leading to reduced blood supply to the heart muscle (myocardial ischemia) and, if severe and prolonged, to heart muscle necrosis (myocardial infarction). The most common symptom of ACS is pressure-like chest pain radiating to the left arm or jaw associated with shortness of breath, nausea, and sweating. ACS includes ST segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina.[2]

STEMI results from complete and prolonged occlusion of a coronary artery and is defined as ACS with an ST segment elevation on ECG, and an increase in cardiac biomarkers such as creatine kinase isoenzyme MB, cardiac troponin I (cTnI), or cardiac troponin T (cTnT). NSTEMI results from partial and transient occlusion of a coronary artery and is defined as ACS without an ST-segment elevation but with an elevation of cardiac biomarkers. Unstable angina results from myocardial ischemia that, unlike STEMI and NSTEMI, is not severe enough to cause myocardial damage and the release of detectable quantities of cardiac biomarkers, and is defined as ACS without an ST elevation and without an elevation of cardiac biomarkers.[2]

A 2013 CADTH report cited that in Canada, there were an estimated 818,847 emergency visits for suspected ACS, and an estimated 109,109 hospitalizations for ACS in 2009.[5,6] In Canada, AMI requiring in-patient acute care has been listed as one of the top 15 most expensive medical conditions.[7] Given the broad range of causes of chest pain, approximately 75% to 85% of patients who present to emergency departments with chest pain are not diagnosed with ACS.[8]

1.2 Cardiac Troponin Testing

Because of the similarity of the symptoms and the transient or non-specific ECG findings,[2] a 2012 universal definition of AMI was published by several leading international cardiac associations using cardiac troponin (cTn) as a diagnostic determinant. For a diagnosis of AMI, there must be a “detection of a rise and/or fall of cardiac-biomarker values (preferably cardiac troponin) with at least one value above the 99th percentile upper reference limit” along with at least one other criterion, such as pathological Q waves in the electrocardiogram or symptoms of ischemia.[2]

The conventional method of assessing cTn concentrations is via central laboratory testing. High-sensitivity cTn laboratory tests have recently emerged. Testing for cTn via a central laboratory can provide evidence of AMI[9] with a one-hour recommended turnaround time.[10] Due to the development of the higher-sensitivity cTn assays, the thresholds of positive cTn values have decreased approximately 40 fold since 1995.[11] The increase in sensitivity of cardiac-biomarker tests may result in an increase in false-positive diagnoses of NSTEMI and a corresponding decrease in diagnoses of unstable angina. Blood cTn concentrations can also be increased in non-cardiac conditions such as renal failure or neuromuscular diseases, again leading to an increased potential for false-positives.[12]

A CADTH report[5] generated a one-year economic model and found that, from time of presentation at the emergency department to one year later, the costs, after undergoing standard laboratory testing of cTn, ranged from $2,018 to $2,186 per patient per year, which includes the costs of false-positive hospitalizations. Multiplying the total number of emergency visits by $2,018 equals an estimated annual cost of C$1,652,433,246 to care for patients presenting with suspected ACS to emergency departments and who undergo laboratory testing for cTn. This model also assumed that each patient would receive two laboratory tests at either $3.00 (for cTnT testing) or $6.75 (for troponin I tests) per test.

1.3 Point-of-Care Cardiac Troponin Testing

Central laboratories are not always on-site, nor available for use 24 hours a day, seven days a week. Point-of-care (POC) testing is a care model that moves the assay to the patient and is now available to measure cTn levels. POC cTn tests offer a significantly shorter turnaround time for biomarker detection, typically providing results within 10 to 20 minutes.[4] POC cTn testing has been used with the goal to expedite patient care both in hospital emergency departments and in various settings where central laboratory testing is not available, including use by paramedics aboard a land or air ambulance, and by health personnel in rural health care centres or remote locations. Use of POC cTn testing could potentially speed up therapeutic decisions and decisions around patient transfers, hospital admissions, and discharge for patients presenting with ACS. Theoretically, the result could be less congested emergency departments and fewer transfers of patients to larger hospitals for further assessment. Improved patient flow may result in cost reductions from fewer unnecessary hospital admissions and laboratory costs.[9]

POC cTn testing is more expensive than laboratory testing, with one manufacturer citing $12.50 per test. However, a cost-per-test approach is not an informative cost comparison with laboratory testing; rather, the question is how POC testing compares with laboratory testing when examining factors beyond the costs of reagents to include the costs of running the POC program (for example, training, quality assurance and quality control, maintenance, data management) and savings from avoiding the costs of patient transfers and hospital admissions.

There are several POC troponin devices available in Canada produced by various manufacturers that test for one or both types of cTn (cTnI and cTnT). A list of POC troponin devices approved in Canada is provided in Appendix 1.

1.4 Decision-Making About Point-of-Care Troponin Testing

It is unknown whether health outcomes can be improved and if cost savings can be realized with POC cTn testing in various Canadian health care settings (such as hospitals with a central laboratory, community hospitals, remote locations, hospitals without a central laboratory, remote nursing stations, medical clinics, long-term care settings, and emergency medical services). To answer these questions, a review of the clinical and economic evidence on POC troponin testing is needed to inform decisions about its acquisition and use. As such, CADTH has undertaken a health technology assessment (HTA) on POC cTn testing. For the purpose of this HTA, we have categorized relevant health care settings as those where a central laboratory is available, such as in emergency departments and other hospital units, and those settings where central laboratory testing is not available full-time, such as in rural, remote, or other settings.

2. Objectives

The aim of this HTA is to inform decision-making about the appropriate use of POC cTn testing. Policy questions such as whether to adopt POC cTn testing in specific settings, including those with and without access to a central laboratory, have been raised in Canadian jurisdictions. This HTA will address these questions by evaluating the diagnostic accuracy, clinical utility, and cost-effectiveness of POC cTn testing in patients presenting with ACS. The economic evaluation will determine the cost per quality-adjusted life-year (QALY) gained with POC cTn testing compared with central laboratory testing (context 1), or no troponin testing (context 2).

2.1 Research Questions

1. What is the diagnostic accuracy of POC cTn testing, using POC cTn devices approved by Health Canada, compared with central laboratory methods in patients presenting with symptoms of ACS?

2. What is the clinical utility of POC cTn testing in altering the treatment and outcomes of patients presenting with symptoms of ACS compared with:
    a. standard care in settings where a central laboratory is not available (pre-hospital settings, rural settings, or remote locations)
    b. central laboratory methods in settings where a central laboratory is available (in hospitals and emergency departments)?

3. What is the cost-effectiveness of POC cTn testing in patients presenting with symptoms of ACS compared with:
    a) standard care in settings where a central laboratory is not available (pre-hospital setting; rural setting, or remote location)
    b) central laboratory methods in settings where a central laboratory is available (in hospitals and emergency departments)?

3. Clinical Review

3.1 Clinical Review Methods

A systematic review of the literature on the diagnostic accuracy and clinical utility of POC cTn testing for patients with symptoms suggestive of ACS was conducted.

3.1.1 Literature search strategy

The literature search was performed by an information specialist using a peer-reviewed search strategy.

Published literature was identified by searching the following bibliographic databases: MEDLINE (1946–) with in-process records and daily updates via Ovid; Embase (1974–) via Ovid; The Cochrane Library via Wiley; and PubMed. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were POC and troponin.

No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. Retrieval was not limited by publication year or language. Conference abstracts were excluded from the search results. See Appendix 2 for the detailed search strategies.

The initial search was completed on January 14, 2015. Regular alerts were established to update the search until the final draft was completed (February 12, 2016). Regular search updates were performed on databases that do not provide alert services.

Grey literature (literature that is not commercially published) was identified by searching the *Grey Matters* checklist (www.cadth.ca/resources/grey-matters), which includes the websites of HTA agencies, clinical practice guidelines, advisories and warnings, drug and device regulatory approvals, and databases (free). Google and other Internet search engines were used to search for additional Web-based materials. These searches were supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry. See Appendix 2 for more information on the grey literature search strategy.

3.1.2 Selection criteria and methods

Two reviewers (CH, KC) independently screened the titles and abstracts of all citations retrieved from the literature search and, based on the selection criteria (Table 1), ordered the full text of any articles that appeared to meet those criteria. The reviewers independently reviewed the full text of the selected articles, applied the selection criteria to the articles, and compared the independently chosen studies. Disagreements were resolved through discussion until consensus was reached. Multiple publications of the same trial were excluded, unless they provided additional information about outcomes of interest.

Table 1: Clinical Report Selection Criteria

	Diagnostic Accuracy (Question 1)	Clinical Utility (Question 2)
Settings	Medical centres where central laboratory testing is available (such as hospital emergency departments)	• Medical centres where central laboratory testing is available (such as hospital emergency departments) • Medical centres or settings where central laboratory testing is not available (such as pre-hospital settings, rural health care centres or remote locations)
Population	Adults presenting with chest pain or other symptoms suggestive of ACS	Adults presenting with chest pain or other symptoms suggestive of ACS
Intervention/ Index Tests	POC cTn assays/tests approved for use in Canada by Health Canada that use the 99th percentile cut-off threshold[a] Central laboratory methods for measuring cTn	• Any POC cTn test
Comparator/Reference Standard	Clinical adjudication	• For settings where a central laboratory is available: central laboratory methods either alone or in addition to POC cTn • For settings where central laboratory is not available: standard care (e.g., transfer to facility with testing capabilities)
Outcomes	Clinical validity of POC cTn tests, including: sensitivity, specificity, positive predictive value, negative predictive value, positive-likelihood ratio, and negative-likelihood ratio of POC cTn testing in the detection of AMI	• Benefits and risks of POC cTn testing such as: turnaround time, time to clinical decision-making, time to discharge or transfer (length of hospital stay, length of emergency department stay), number of hospital admissions, adverse events rate, mortality rate, repeat emergency department visit • Behaviour/treatment patterns of health care professionals • Availability of the test, acceptability of and interest in the test for patients • Ethical, legal, social implications of POC cTn testing • Recommendations from evidence-based guidelines
Study design	RCTs, cohort studies, case-control studies	RCTs, cohort studies, evidence-based guidelines, surveys (for outcomes related to behaviour/treatment patterns, and availability and acceptability of tests)

ACS = acute coronary syndrome; AMI = acute myocardial infarction; cTn = cardiac troponin; CV = coefficient of variation; POC = point of care; RCT = randomized controlled trial.
[a] Studies on diagnostic accuracy were included if, in addition to other inclusion criteria, they used the 99th percentile at 10% of the normal population, or the 99th percentile suggested by the manufacturer (which may be higher than 10% CV).

Studies were excluded when they did not meet the selection criteria or presented preliminary results in abstract form. Duplicate publications, narrative reviews, case studies, and editorials were excluded.

3.1.3 Data extraction

A data-extraction form for the reviews of diagnostic accuracy and clinical utility was designed a priori to document and tabulate relevant study characteristics (e.g., study design, inclusion criteria, patient characteristics, setting, and other such factors and measures of clinical utility, as outlined in Table 1) in the selected studies. Recommendations on the use of POC cTn were extracted from the included guidelines. Data were extracted independently by one reviewer and verified by another reviewer; any disagreements were resolved through discussion until consensus was reached.

3.1.4 Critical appraisal of individual studies

The quality of the included studies on diagnostic accuracy was assessed using QUADAS-2;[13] the Downs and Black checklist was used to assess the quality of the studies on clinical utility.[14] One reviewer appraised each study using the appropriate tool, and the assessments were then checked by a second reviewer. Disagreements were resolved through discussion. The quality of the included guidelines was assessed by one reviewer, using the AGREE II[15] checklist, then checked by a second reviewer. Numeric scores were not calculated; instead, the strengths and limitations of the included studies were described narratively.

3.1.5 Data analysis and synthesis methods

The diagnostic accuracy of POC troponin testing was assessed based on the ability of POC troponin testing to predict AMI (clinical validity) compared with central laboratory assessments. Clinical assessment and adjudication of POC and clinical laboratory results were used to determine diagnostic accuracy of both central laboratory and POC tests. Findings were reported on: those patients who were identified as having AMI (sensitivity); those who did not have AMI (specificity); those who truly had AMI from among those who tested positive (positive predictive value), those who did not truly have AMI from among those who tested negative (negative predictive value), and the likelihood that a positive or negative test result would be expected in a patient with AMI compared with the likelihood that the same test result would be expected in a patient without AMI (positive and negative-likelihood ratio). Due to the heterogeneity of the included studies (for example, due to varying reference standards, types of central laboratory cTn test, patient characteristics, and inclusion of POC devices from different manufacturers), pooling via meta-analysis was not appropriate. Rather, study results are reported narratively in tables with ranges, with special attention paid to issues that could contribute to heterogeneity.

The clinical utility of POC troponin testing was assessed based on findings about the benefits — how testing influences management of ACS or AMI, and whether or not testing results alter clinical outcomes — and risks resulting from test use.

Meta-analysis for the clinical-utility outcomes was not possible due to clinical and methodological heterogeneity among trials, such as differences in definitions of outcomes (for example, definitions of turnaround time) and inconsistencies in reporting (such as values reported as mean or median). A review was conducted that included a narrative synthesis and summary of study findings with the goal of describing both the direction and size of any observed effects, and results were reported in tables with ranges.

For diagnostic-accuracy and clinical-utility outcomes, subgroup analyses were planned and performed based on clinical setting (emergency department, rural health care centre, or remote location), the level of sensitivity of the central laboratory method, type of cTn test (cTnI, cTnT), and study funding status. A subgroup analysis based on study design was conducted for clinical-utility outcomes. Subgroup analyses in the absence of meta-analysis involved inspection of the results for any systematic patterns between groups.

Recommendations on the use of POC cTn testing from evidence-based guidelines were also reported. Further, relevant results within included studies regarding behaviour and treatment patterns of health care professionals for POC troponin testing, availability of testing, interest and acceptability of testing to the patient, and ethical, legal, and social implications of POC troponin testing are summarized descriptively by topic, when they were available.

4. Clinical Results

4.1 Literature Search Results

The original search identified 1,434 citations. From these, 322 potentially relevant reports were retrieved for further scrutiny, and six reports were retrieved from search updates (alerts) and grey literature. Forty-one original publications, five companion reports, and two guidelines were selected for inclusion. Nine studies[16-24] and one companion report[25] on the diagnostic performance of POC in patients with chest pain were included. Thirty studies,[26-55] three companion reports,[56-58] and two guidelines[59,60] on the clinical utility of POC cTn testing in patients with symptoms suggestive of ACS were included. Two additional studies[61,62] and one companion report[1] were included for both diagnostic-accuracy and clinical-utility outcomes. The PRISMA flow chart is presented in Appendix 3. The lists of included and excluded studies are provided in Appendix 4 and Appendix 5, respectively.

4.2 Study and Patient Characteristics

Seven randomized controlled trials (RCTs),[26,29,39-41,50,55] 22 prospective observational studies,[16-18,20,22-24,28,32-36,43-48,51,61,62] 10 retrospective observational studies,[19,21,27,30,31,37,38,42,49,52] two surveys,[53,54] and two evidence-based guidelines[59,60] are included in this review. Twelve studies were from the United States;[18-20,26,27,30,32,36-38,42,49] five were from Australia;[28,40,41,44,52] four were from Sweden;[43,45,46,61] four were from Italy;[23,24,31,33] three were from Denmark;[21,48,62] three were from the United Kingdom (UK);[39,50,53] two were from the Netherlands;[22,34] one each was from Canada,[55] New Zealand,[16] Germany,[17] Finland,[54] Slovenia,[35] France,[29] and China;[51] and one study was from multiple countries (Spain, the UK, Germany, Austria, Ireland, and Sweden).[47] The European Society of Cardiology (ESC) guidelines[59] were developed and published in 2011 by the ESC Task Force for the Management of ACS in Patients Presenting Without Persistent ST-Segment Elevation. The *Laboratory Medicine Practice Guidelines*[60] were developed and published in 2007 by the National Academy of Clinical Biochemistry for POC testing. In both guidelines, the level of evidence and the strength of a recommendation were graded according to pre-defined scales.

Sixteen different POC devices of interest were examined in the included studies: Stratus CS,[23,24,29,30,32,33,39,45,49,53] i-STAT,[18,20,26,27,38,40,43,46,52,53] AQT90 FLEX,[17,18,21,22,41,44] Cardiac Reader,[34,36,47,51,53] PATHFAST,[18,35] Triage,[31,53] Cobas h232,[61,62] Triage Cardiac Panel,[33] Triage Profiler SOB,[42] Triage Cardio3,[19,55] Triage Meter Pro,[28] Spectra Status,[37] GEM Immuno,[18] TropT,[48] Cardiac T,[50] and Cardio3.[16] One survey[54] did not specify what devices were used. Most study settings were hospital, medical centre, or community centre emergency department.[16-20,22-24,26-44,46,47] Additional settings utilized by some studies were: cardiology service or coronary care unit;[49-51] both emergency department and coronary care unit;[21,45] pre-hospital (ambulance);[48] both ambulance and emergency department;[55,62] primary health care;[61] remote health centre;[52] and heath trust or health care unit.[53,54]

Full or partial funding by industry or author conflicts of interest were present in 22 studies,[16-18,20-22,26-29,35,36,38,43-49,55,62] 16 studies did not report information on funding and/or author conflicts of interest,[19,23,24,30-34,37,40,42,50-54] and three studies stated they were not funded by industry and had no author conflicts of interest.[39,41,61]

The included studies varied in size, from 31[35] to 4,905[48] patients. The study patients were adults with chest pain or symptoms suggestive of ACS, and there was variability in the reporting of patient comorbidities by the study authors, with many not including those characteristics in the reports.

Further details on study and patient characteristics are provided in Appendix 6 and Appendix 7, respectively.

4.3 Results of Critical Appraisal

The majority of the diagnostic-accuracy studies had appropriate exclusion of patients, although in some cases[16,19-23,61] it was unclear whether a consecutive sample of patients was enrolled. In two studies,[22,23] it was unclear whether all patients were included in the analysis and, in four studies,[16,19,20,62] not all patients were included. It was unclear in many studies whether the POC cTn test results were interpreted without knowledge of the results of the central laboratory cTn test and vice versa.[1,16-23,61,62] The time interval between the POC cTn test and the central laboratory cTn test was not indicated in many studies,[1,17,19,23,61,62] while the remaining studies reported an appropriate time interval. An additional limitation is the potential knowledge of the results of the cTn test during clinical adjudication, which may lead to confirmation bias. Concerns about the applicability of the included studies to the research questions were generally low. In all studies, the concern that the included patients did not match the review question was low. In four studies,[16,18,19,21] it was unclear whether the index test, its conduct, or its interpretation differed from the review questions.

Seven out of 32 studies on clinical utility were RCTs with an appropriate randomization process and allocation concealment,26,29,39-41,50,55 with the remaining studies being observational or pre–post studies. In all studies, the hypothesis, aim, objective, and main outcomes were clearly described. Subjects asked to participate in the study were representative of the entire population from which they were recruited in 11 studies,[29,30,32,33,38,41,42,47,49,50,55] and may not be representative in the remaining, as characteristics of all patients at admission were not clearly described. About half of the studies reported having sufficient power to detect a clinically important effect for the primary outcomes,[26,28-31,33-40,42,50] and the remaining studies did not report power. For six studies,[29,37,39,44,55,62] it was made explicit that an attempt was made to blind patients, outcome assessors, or both, to treatment allocation. For the remaining studies, it was not possible to make an assessment of blinding. Data relevant to staff satisfaction were collected in various studies[27,35,37,38,52,54,56,58] using reliable Web-based software programs designed to determine satisfaction and usage among device operators according to a 5-point scale.

The guidelines[59,60] had clear scope and purpose, clear methods for searching for and selecting the evidence, and rigorous methods for formulating the recommendations based on well-conducted systematic reviews of the evidence. They provided specific and unambiguous recommendations, with health benefits, side effects, and risks stated in the recommendations, and the target users of the guidelines clearly defined. It was unclear whether patients' views and preferences were sought, or whether the guidelines were piloted among target users. Procedures for updating the guidelines were not provided, and the potential cost implications of applying the recommendations were not considered.

Details of the critical appraisal of the included studies and guidelines are provided in Appendix 8.

4.4 Diagnostic Accuracy

4.4.1 Results

Eleven studies[16-24,61,62] and two companion reports[1,25] were included that assessed diagnostic-accuracy outcomes. In the following discussion of results, the article reporting the specific data (either the original study or the companion report) is referenced. Details on the diagnostic accuracy of different POC cTn tests reported at admission (Table 19 and Table 20), three hours, six hours, and six to nine hours post-admission compared with a central laboratory (Table 21) are provided in Appendix 9. The final diagnosis of myocardial infarction (MI) was based on the available biochemical laboratory data, cardiac-imaging data, electrocardiographic results, and clinical findings.

Sensitivity

POC tests tended to provide lower sensitivity compared with central laboratory methods, ranging from a low estimate of 26.0% in one study,[18] to a high of 87.7% in another.[16] Despite variability in the sensitivity estimates, the trend for lower sensitivity compared with a central laboratory was maintained across different POC devices, as variability was observed in sensitivity estimates for the same device in different studies. The trend was also maintained with blood samples taken at three hours, six hours, and between six to nine hours after admission (Table 21), although limited data (i.e., one study each) were available for post-admission data.

Specificity

POC tests tended to provide higher specificity compared with central laboratory methods, ranging from a low estimate of 87.0% in one study to a high of 98.0% in another. This trend was maintained across different POC devices, and with blood samples taken at admission and three hours, six hours, and between six to nine hours after admission, although limited data (i.e., one study each) were available for post-admission data.

Positive predictive value

POC tests tended to provide higher positive predictive value (PPV) compared with central laboratory methods, ranging from a low estimate of 31.0% in one study (central laboratory 31.0%), to a high of 85.0% in another (central laboratory 60.0%). In one study[19] the estimated PPV was higher with central laboratory methods compared with the POC test (66% for the POC test versus 82% for central laboratory). The trend for higher PPV with POC tests was maintained across different POC devices, and with blood samples taken at admission and three hours, six hours, and between six to nine hours after admission, although limited data (i.e., one study each) were available for post-admission data.

Negative predictive value

POC tests tended to provide lower negative predictive value compared with central laboratory methods, ranging from a low estimate of 90.0% in one study (central laboratory 95%), to a high estimate of 99.0% in another (central laboratory 100%). This trend was maintained across different POC devices, and with blood samples taken at admission and three hours, six hours, and between six to nine hours after admission, although limited data (i.e., one study each) were available for post-admission measurements.

Positive-likelihood ratio

POC tests tended to provide higher positive-likelihood ratios compared with central laboratory methods, although only one study reported a positive-likelihood ratio as calculated from central laboratory data.[22] Positive-likelihood ratios ranged from 4.83[25] to 16.2[19] at admission with POC tests and was reported as 3.63 (95% confidence interval [CI], 2.83 to 4.65) in the one study that reported central laboratory data.[22] One study reported positive-likelihood ratios for POC tests at three hours and six hours post-admission, and reported values of 12.9 (95% CI, 9.4 to 17.6), and 11.8 (95% CI, 8.8 to 15.9), respectively (values for central laboratory not available).[19]

Negative-likelihood ratio

POC tests tended to provide higher negative-likelihood ratios compared with central library methods, although only one study reported a negative-likelihood ratio as calculated from central laboratory data.[22] Negative-likelihood ratios ranged from 0.26[17] to 0.37[22] at admission with POC tests and was reported as 0.12 (0.04 to 0.35) in the one study that reported central laboratory data.[22] One study reported negative-likelihood ratios at three hours and six hours post-admission and reported values of 0.16 (95% CI, 0.09 to 0.28) and 0.14 (95% CI, 0.07 to 0.25), respectively (values for central laboratory not available).[19]

4.4.2 Subgroup analyses for diagnostic accuracy

Settings

Except for one study that included patients at primary health care centres[1] and one study in the pre-hospital or paramedic setting,[62] all studies included patients who presented to the emergency department.[16-23,25]

Subgroup analyses based on settings did not reveal any differences by setting, with diagnostic accuracy similar in both settings. Findings from the one study at primary health care centres[1] and the study in the pre-hospital or paramedic setting[62] agreed with those in emergency departments for the reported diagnostic-accuracy outcomes.

High-sensitivity assays

Three studies had central laboratory assays that were high-sensitivity assays.[16,22,61] Subgroup analyses based on high-sensitivity assays did not reveal any systematic pattern for the reported outcomes. Similar results were reported in studies using high-sensitivity central laboratory assays compared with other assays.

Types of cardiac troponin test

Eight studies measured cTnI,[16-21,23,25] and three studies measured cTnT.[1,22,62] Subgroup analyses based on types of cTn found no difference in the outcomes with cTnI or cTnT.

Study funding status

Eight of the 11 included studies reported funding by industry (total or in part), or the author(s) received lecture fees from industry;[16-22,62] one study was not funded by industry,[61] and two studies did not report the funding status.[23,25] Subgroup analyses based on study funding status did not reveal any systematic pattern for the reported outcomes.

Diagnostic accuracy results summary

In general, compared with central laboratory methods, POC tests tended to provide lower sensitivity, lower negative predictive value, higher specificity, and higher PPV. Both positive and negative-likelihood ratios tended to be higher with POC testing compared with a central laboratory, although only one study was available for the central laboratory comparison. This trend was maintained across different POC devices and with blood samples taken at admission, and three hours, six hours, and between six and nine hours after admission. Subgroup analyses of studies based on the study setting, sensitivity levels of the central laboratory methods (high sensitivity or not), the type of cTn (I or T), and the funding status did not show any systematic patterns.

4.5 Clinical-Utility Results

4.5.1 Settings where a central laboratory is available

Thirty-two studies reported on clinical-utility outcomes, and 25 were in a setting with a central laboratory.[26-47,49-51] Clinical utility outcomes of POC testing such as turnaround time (TAT), length of hospital stay (LOS), time to clinical decision (TCD), time to discharge (TTD), mortality rates, adverse event rates, staff satisfaction, and patient quality of life were reported in studies where central labs exist, such as emergency departments and coronary care units. Clinical-utility outcomes are provided in Appendix 10.

Turnaround time

Fifteen studies reported TAT with various definitions, with the majority defining TAT as time from blood draw to result.[26-38,49,50] Thirteen studies measured TAT in the emergency department (ED) and two studies in cardiology services or coronary care units.[49,50] Data suggest that POC cTn testing consistently reduced TAT compared with central library methods. Using a definition of turnaround time as from blood draw to result, the reported time saved in the ED ranges from 18 minutes to 93 minutes and, in cardiology services or coronary care units, two studies reported time saved as 56.5 minutes and 59 minutes. Based on other varied definitions of turnaround time, reported time saved ranged from a low of 54 minutes based on “door to result,” to a high of 147 minutes saved when defined as “time from presentation to anti-ischemic therapy.” Results are summarized in Table 22.

Length of stay

Eight studies reported LOS.[28-30,39-41,49,50] Five studies determined LOS in the (length of ED stay),[28-30,40,41] and three studies in cardiology services or coronary care units (length of hospital stay).[39,49,50] Data suggest that POC cTn testing consistently reduced LOS compared with central library methods. In all but one study, length of ED stay was reduced, with a range between 0.2 hours to 2.7 hours. In the one study[29] where length of ED stay was increased, it was lengthened by six minutes. LOS in hospital was reduced with POC cTn testing compared with central laboratory testing, with hospital stays being reduced between 2.2 hours and 15.7 hours in the studies (Table 23).

Time to clinical decision (time to disposition)

Two studies reported TCD (defined as the conclusion of disposition decision-making) in an ED setting.[26,42] Data suggest that POC cTn testing reduced TCD compared with central library methods, with nine minutes saved in one study, and 26 minutes saved in the other (Table 24).

Time to discharge

Three studies reported TTD from an ED.[26,41,57] Data suggest that POC cTn testing reduced TTD compared with central library methods, with time saved ranging from five minutes to 26 minutes (Table 25).

Mortality and major adverse events

Seven studies reported mortality or major adverse events such as non-fatal AMI, life-threatening arrhythmia, and emergency revascularization.[39,41,43,44,46,47,50] Six studies[39,41,44,46,47,63] reported mortality and major adverse events in the ED, and one study reported such events in a cardiology services or coronary care unit.[50] Data from the majority of studies suggest the use of POC cTn did not statistically change mortality rates or severe adverse events compared with a central laboratory in up to a one-year follow-up. Similar adverse events occurred in both groups, except for one study that reported significantly fewer deaths with POC testing than with central laboratory methods (Table 26).[46]

Patients' quality of life

One study reported patients' quality of life in an ED setting, using the EuroQoL 5-Dimensions Questionnaire.[39] During three months of follow-up, there was no statistically significant difference in quality of life for patients who had been tested for troponin by POC or central laboratory (Table 27).

Staff satisfaction

Four studies reported staff satisfaction in the ED; the majority of physicians and nurses agreed they were satisfied with POC testing, that cTn testing shortened TAT, was easy to use, and led to better management.[27,33,37,38] In one study,[37] participating staff rated the perceived accuracy of central laboratory testing as higher than POC testing (4.33 versus 3.68 on a five-point scale), although they reported higher overall satisfaction with POC testing compared with a central laboratory (4.00 versus 2.06 on a five-point scale) (Table 28).

4.6 Clinical-Utility Results

4.6.1 Settings where a central laboratory is not available

Thirty-two studies reported on clinical-utility outcomes, and seven included results from a setting with no central laboratory.[48,52-55,61,62]

Percentage of patients referred to emergency department

One study, from Sweden, reported the percentage of patients referred to an ED from three primary health care centres using POC cTnT, and four primary health care centres not using POC cTnT.[61] Data suggest that primary health care centres using POC cTn tests reduced the number of patients referred to an ED by 18% compared with centres that did not use POC cTn tests (32 of 128 patients [25%] from primary health care centres with POC cTnT, and 29 of 68 patients [43%] from centres without POC cTnT).

Staff satisfaction

One study reported staff satisfaction with the use of POC testing in a remote setting, with 33 remote health centres from the Northern Territory in Australia participating.[52] A questionnaire was implemented using an online survey provider, and results were analyzed descriptively. Questionnaire feedback showed the implementation of POC testing increased staff satisfaction with cTn testing. Ninety-five per cent of 39 respondents stated that POC testing was more convenient than transporting patients to central laboratory services. A separate survey of 100 health professionals in an unspecified setting found that 47% of staff strongly agreed that POC usage increased patient convenience, while 13% disagreed.[53] A further survey from 406 health care units found the primary reason for staff using POC was shortening of TAT or lack of availability of clinical laboratory testing.[54]

In pre-hospital or ambulance settings

Limited evidence[48,55] reported the use of POC cTn tests for the diagnosis and management of patients in pre-hospital or ambulance settings. In one study, a pre-hospital POC cTnT test was performed by paramedics in 928 patients with suspected AMI. The median time from symptom onset to blood sampling was 83 minutes (46 minutes to 167 minutes).[48] In another study, 601 patients with chest pain were randomized to usual care or pre-hospital POC cTnI testing in ambulance.[55] The time from first medical contact to discharge from ED or admission to hospital was shorter in patients in the POC testing group (median 8.8 hours [range 6.2 hours to 10.8 hours]) compared with usual care (median 9.1 hours [range 6.7 hours to 11.2 hours]; $P = 0.05$). There was no difference among the groups in repeat ED visits, hospitalizations, or death in the next 30 days.

4.6.2 Subgroup analyses for clinical-utility studies

Study design

Seven studies were RCTs,[26,29,39-41,50,55] and 25 studies were observational. Subgroup analyses based on study design did not show a difference between data from RCTs and observational studies for any of the reported clinical-utility outcomes, acknowledging that, for most outcomes, few studies were available to assess meaningful differences.

Study setting

Settings were the ED in 21 studies,[26-44,46,47] primary health care centres in one study,[61] pre-hospital or ambulance in three studies,[48,55,62] cardiac or coronary care units in four studies,[45,49-51] remote centres in one study,[52] and not specified in two surveys on staff satisfaction and patients' quality of life.[54,58] Subgroup analyses based on settings did not show a systematic difference between studies conducted in different settings, acknowledging that for most outcomes, few studies were available to assess meaningful differences.

High-sensitivity central laboratory method

One study used high-sensitivity central laboratory methods as a comparator.[41] The results of this study for the reported clinical-utility outcomes were not meaningfully different from studies using other central laboratory assays.

Type of cardiac troponin

Twenty studies measured cTnI,[26,28-33,35,37-40,43-46,49,55,56,64] 10 studies measured cTnT,[27,34,36,41,47,48,50,51,61,62] one measured both cTnI and cTnT,[54] and one did not specify the type of cTn.[53] Subgroup analyses based on the type of cTn measured did not show a difference in the clinical-utility outcomes in studies that used cTnI or cTnT for the reported outcomes, acknowledging that, for most outcomes, few studies were available to assess meaningful differences.

Funding status

Fourteen of the included studies reported being funded by industry either totally or in part, or the author(s) received lecture fees from industry.[26-29,35,36,43-47,49,55,62] Ten studies were not funded by industry[30,39-41,48,50-52,58,61] and eight studies did not report the funding.[31-34,37,38,42,54] Subgroup analyses based on the funding status did not show a systematic difference between data from the studies funded by industry and the studies not funded by industry for the reported outcomes, acknowledging that, for most outcomes, few studies were available to assess meaningful differences.

4.7 Guidelines

The European Society of Cardiology guidelines (page 3,006) for the management of ACS in patients presenting without persistent ST segment elevation,[59] recommend that “point-of-care tests for troponins should be implemented when a central laboratory cannot consistently provide test results within 60 min.”

The National Academy of Clinical Biochemistry (NACB) Laboratory Medicine Practice Guideline on POC testing[60] states that:

> Institutions that cannot consistently deliver cardiac marker TATs of approximately 1 h should implement POCT devices. (Strength B, Level II)
>
> While it is recognized that qualitative systems do provide useful information, it is recommended that point-of-care systems provide quantitative results. (Strength C, Level II) (page 17)
>
> Strength B: The NACB recommends adoption; there is at least fair evidence that it improves important health outcomes and concludes that benefits outweigh harms.
>
> Strength C: The NACB recommends against adoption; there is evidence that it is ineffective or that it harms outweigh benefits.
>
> Level II: Evidence is sufficient to determine effects, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of the evidence.

5. Clinical Discussion

5.1 Diagnostic Test Accuracy

This systematic review on the diagnostic accuracy of POC cTn tests in patients with symptoms suggestive of ACS shows that currently available POC tests have lower sensitivity and negative predictive value, and higher specificity and PPV than central laboratory methods. Both positive- and negative-likelihood ratios tended to be higher with POC testing compared with central laboratory testing, although only one study was available for the central laboratory comparison. This trend was maintained across different POC devices and with blood samples taken at admission, and at three hours, six hours, and between six and nine hours after admission.

Subgroup analyses of the results of diagnostic-accuracy studies based on the study setting, sensitivity levels of the central laboratory methods (high sensitivity or not), the types of cTn (I or T), and the funding status did not show any systematic patterns for any of the reported diagnostic outcomes.

A reason for the wide variability of the reported data on the diagnostic performance for the POC devices is unclear, although several factors likely contribute. It is possible that some of the variability can be attributed to different methodological aspects of POC assays performed from studies that used different generations of POC assays, using fresh blood or frozen plasma, different clinical staff or technicians, and different reference-standard tests. Patient selection, including the proportion of participants included with prior AMI, or the exclusion of participants with STEMI, may also be factors that could contribute to variability. Given the limited amount of reported information on these variables, we were unable to explore these issues systematically. The time of the patients' presentation to the health care centre was variable across the studies included in this review and, likewise, also could have contributed to the observed variation in results. It is expected that test sensitivity would increase with later presentation time. In addition, the different troponin cut-offs used in different studies would affect the diagnostic test accuracy results, although we controlled for this possibility by including only studies that used the 99th percentile cut-off threshold. Due to the observed variability and the many factors that may have attributed to the heterogeneity in diagnostic-accuracy outcomes across studies, only some studies were used to develop the economic model. Specifically, studies with a high detection rate of AMI were excluded,[16,21] as the patient selection may have been biased, and studies that appeared to be an outlier or lacked sufficient details to determine the reason for the possibly skewed results were also excluded.[18]

5.2 Clinical Utility in Settings With a Central Laboratory

The clinical utility of POC cTn testing in patients with symptoms suggestive of ACS was assessed within two settings for this review: settings where central laboratory tests are available (hospital EDs and other hospital units), and settings where central laboratory tests are not available (primary health care centres, remote stations, rural hospitals or clinics, and ambulance settings). In general, in settings where central laboratories are available, POC cTn testing tends to shorten TAT, LOS, and TTD compared with central laboratory settings. Given the studies that reported adverse event outcomes were not sufficiently powered to detect a difference in adverse events, including mortality, clinical significance of potential differences is likely a more relevant assessment than statistical significance. Overall, reported differences in mortality rates and severe adverse events were not statistically significant between POC testing and central laboratory testing in up to one year of follow-up, although observed numerical differences might be clinically significant. It could be argued that saving time in the ED and shortening TCD is an important effect to balance the potential differences in adverse events. Patient quality of life was assessed in one study, and was found to be similar in those who were tested using POC and those who were tested using central laboratory testing.

In those studies that assessed staff satisfaction, the majority of physicians and nurses in settings with a central laboratory were satisfied with POC testing and agreed that POC cTn testing shortened TAT, was easy to use, and led to better patient management.

Our findings concur with observations from other systematic reviews on POC testing in suspected AMI in EDs[65-67] that POC cTn assays are accurate and improve TAT and LOS, although there was no reported statistical change in clinical outcomes, such as mortality. Subgroup analyses of clinical-utility studies in our review based on study setting, the level of sensitivity of the central laboratory methods (high sensitivity or not), the types of cTn (I or T), and funding status did not show any systematic patterns.

The NACB[60] and the European Society of Cardiology guidelines[59] recommend that, based on sufficient and fair evidence, POC tests for cTn should be implemented when a central laboratory cannot consistently provide test results within 60 minutes. This recommendation was not adopted by the Centers for Medicare & Medicaid Services due to a recall of the POC cTn device.[68]

5.3 Clinical Utility in Settings With No Central Laboratory

Although the evidence identified from primary studies on the clinical utility of POC cTn testing in settings without a central laboratory was limited, the data suggest that referrals to an ED can be reduced by use of POC cTn testing, and that use in ambulance settings may be beneficial. In one study, primary health care centres using POC cTn tests reduced by 18% the number of patients referred to an ED compared with centres that did not use of POC cTn tests.[61] This reduction of emergency referrals may come at the cost of an increased risk of missing patients with AMI, although no such data were available for this review.

In pre-hospital or ambulance settings, a limited quantity of evidence points to the potential of implementation of POC cTn tests for the diagnosis and management of patients with symptoms suggestive of ACS.[48,62] In one study, quantitative POC cTn testing was shown to be feasible and reliable for patients transported by ambulance.[48] Further, POC devices may shorten the time from first medical contact to clinical disposition.[55] Additional equipment and training of staff are required for the implementation of POC testing in pre-hospital setting. The distance and time to a hospital may also be a consideration.

Other published information about the use of POC testing in rural areas indicates that POC troponin devices are being implemented to facilitate AMI diagnosis in areas with challenging geographic settings.[69] An opinion paper suggested that implementation of POC cTn in rural hospitals in Australia reduced the 30-day readmission rate.[70] In our review for remote health care centres where central labs were not available, the implementation of POC testing increased the volume of patients tested for cTn and increased staff satisfaction. In one study, 95% of staff believed POC testing was more convenient than transporting patients to settings with a central laboratory.[52,56] Therefore, use of POC troponin testing in rural Canadian settings may be a feasible option. The information on the use of POC testing in remote areas would be most valuable from a Canadian perspective, but the evidence is limited to one Australian study.[52]

6. Economic Review

6.1 Economic Methods

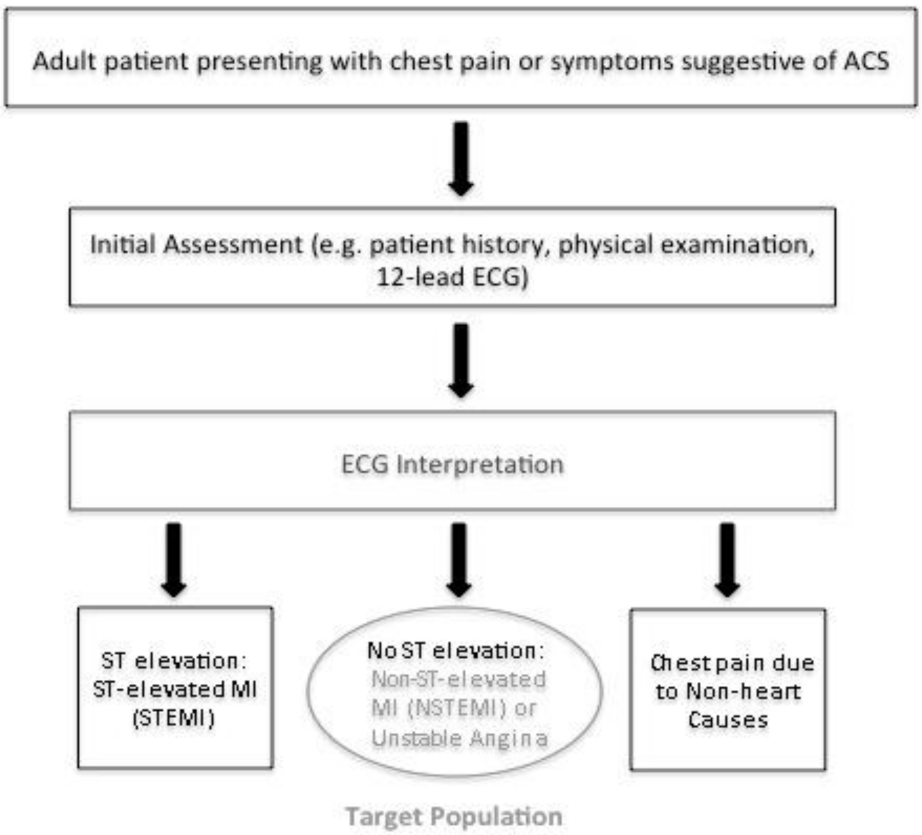
6.1.1 Type of economic evaluation

A cost-utility analysis was conducted. A cost-utility analysis incorporates both mortality and quality-of-life impacts of disease and treatment. The primary outcome was a cost per QALY gained. A cost per QALY allows for comparison across a wide spectrum of interventions and populations with a standardized measure of benefit (i.e., QALY).

6.1.2 Target population

The target population for the economic evaluation is adult patients presenting with chest pain or other symptoms suggestive of ACS identified as having non-ST elevation from ECG testing. These include patients suspected of having NSTEMI or unstable angina (Figure 1).

Figure 1: Patient Population for the Economic Evaluation of Point-of-Care Troponin Testing



ACS = acute coronary syndrome; ECG = electrocardiogram; MI = myocardial infarction; NSTEMI = non-ST segment elevation myocardial infarction; STEMI = ST segment elevation myocardial infarction.

6.2 Strategies

a) Comparators: The comparators are dependent on the contexts reported in Table 2.
b) Intervention: POC cTn testing devices approved by Health Canada.

Table 2: Strategies for Context 1 and Context 2

	Context 1	Context 2
Comparator	**Central laboratory testing of cTn available** E.g., emergency department settings of large, urban (academic or non-academic) hospitals	**Standard care (no cTn testing available via a central laboratory)** E.g., non-hospital settings, small or rural hospitals or remote settings without a central laboratory
Intervention	**POC cTn testing**	**POC cTn testing**

cTn = cardiac troponin; POC = point of care.

6.3 Perspective

The perspective of a publicly funded health care system was adopted. The costs in the analysis included test costs, emergency room costs, in-patient costs, and physician fees for services that are covered in provincial fee schedules. Indirect costs, such as productivity losses, out-of-pocket patient costs, and time costs were not included in context 1. These costs are not expected to vary significantly between treatment strategies, as both POC and central laboratory troponin are completed while the patient remains in the emergency room. However, in context 2, where the patient may be transferred to the hospital from either a rural emergency room or primary care practice, limited patient-borne costs were included as availability in reported literature allowed.

6.4 Time Horizon

A one-year time horizon was used in the model. Although best-practice guidelines suggest a lifetime horizon, it is unlikely that the decision to use a POC device or central laboratory for cTn testing would have an impact on a patient over a lifetime. As such, extrapolating the analysis over the course of a patient's lifetime was deemed to increase the uncertainty in the model and could lead to inappropriate attribution of the strategies to the resulting clinical outcomes. Given that the longest time of reported follow-up in the clinical literature was one year, a one-year time horizon was deemed to be the most appropriate selection.

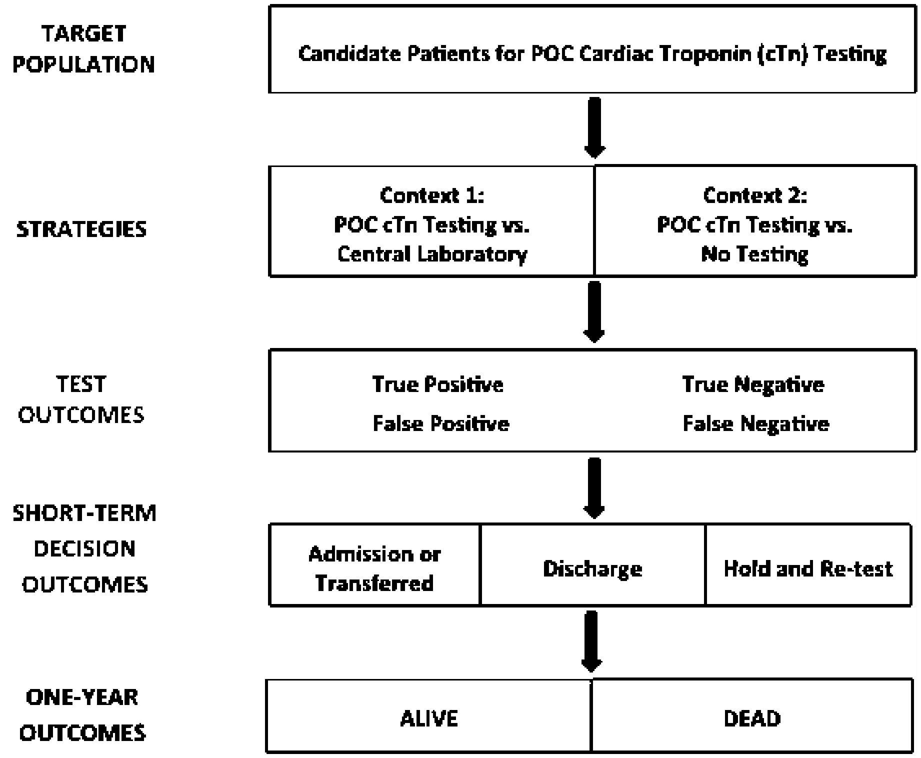
6.5 Effectiveness

The primary outcome was the cost per QALY gained. The measure of effectiveness was the QALY measured using the Health Utilities Index Mark 3. Different utility estimates were included for the general population, NSTEMIs and missed NSTEMIs (see section on utility values for more details). Secondary measures for context 1 include the LOS in the ED and the probability of readmission due to misdiagnosis of NSTEMI and were accounted for and expressed as costs. No secondary measures were available for context 2. All outcomes were considered for one year.

6.6 Decision Analytic Model

For each context, a decision-tree model was developed to simulate what could happen to patients from chest pain presentation at the ED or doctor's office to one year after their episode. A basic graphical representation of the economic model is provided in Figure 2. For the detailed depictions of the decision-tree models in contexts 1 and 2, please see Appendix 11.

Figure 2: Basic Schematic of the Economic Model for Cardiac Troponin Testing



cTn = cardiac troponin; POC = point of care; vs. = versus.

As shown in Figure 2, candidate patients can undergo one of two strategies in each context and the basic pathway and decisions for each patient are assumed to be the same following either strategy. Among those who test positive, there will be a proportion who have NSTEMI (true-positive) and a proportion who do not have NSTEMI (false-positive). Among those who test negative, there will be a proportion who have NSTEMI (false-negative) and those who do not have NSTEMI (true-negative). The proportion of patients in each of the potential diagnostic categories (true-positives, false-positives, true-negatives, false-negatives) was determined by both the underlying prevalence of NSTEMI and the diagnostic accuracy of the cTn test strategy being evaluated.

Four kinds of outcomes were incorporated into the model: true-positives, false-positives, true-negatives, and false-negatives. For all strategies, patients with a positive cTn test at presentation were assumed to be admitted to hospital (context 1) or transferred (context 2) and received treatment. This included both true- and false-positives. Patients with a negative cTn test at presentation could be either discharged and not receive treatment, or held in the ED and retested (serial test) after four to six hours. Patients with a positive serial cTn test were assumed to have been admitted to hospital and to have received treatment, whereas those with a negative serial cTn test were assumed to have been discharged and to have not received treatment. For true-negatives (patients without NSTEMI who test negative), no additional health or cost consequences are accrued. For false-negatives (patients with NSTEMI who test negative), patients are likely to continue to experience chest pain and re-present at the emergency room. The costs of a subsequent emergency room visit and hospitalization, as well as the decrement to their quality of life from continued chest pain, are incorporated.

All patients are followed for up to one year following their presentation of chest pain with an ongoing risk of death. The proportions of NSTEMI patients who died differed, depending on whether or not NSTEMI was diagnosed and treated. For example, patients who have a positive cTn test and are treated are assumed to have a lower mortality rate than NSTEMI patients who are not diagnosed and, thus, untreated. Patients who do not have NSTEMI have one-year mortality rates similar to the general population. Finally, patients who are alive after one year are assigned utility values for their health state; these values are dependent on whether they had NSTEMI or not.

6.7 Valuing Outcomes

A number of clinical variables were used to populate the model and estimate the number of expected QALYs for each cTn test strategy. Studies identified from the clinical systematic review were used as the primary source for the clinical inputs. Additionally, targeted literature searches were used to identify sources for parameters that were not available from the clinical systematic review. Details of the value and sources of the clinical variables used in the economic model are provided in Table 3 and Table 4.

6.7.1 Diagnostic accuracy

Given the observed heterogeneity in study quality and designs, POC cTn devices, and reported outcome measures, the clinical review team did not pool across studies. Diagnostic accuracy was drawn from three high-quality studies[19,20,25,61] that were selected based on quality, perceived validity, and reporting by the clinical review team. Three devices were assessed (i-STAT (Abbott), Stratus CS (Siemens), and Cardio3 Panel (Alere). The sensitivity and specificity for the POC cTn, by device, were provided by the clinical systematic review team. The diagnostic accuracy for central laboratory cTn testing was derived from a meta-analysis of conventional cTn tests (Lipinski et al., 2015).[71] The diagnostic accuracy for the no–cTn testing strategy (context 2) was derived from a study reporting the diagnostic accuracy of primary care practitioners to identify heart-related chest pain at presentation.[72] The values for sensitivity and specificity for each cTn testing strategy, stratified by context, are provided in Table 3.

Table 3: Diagnostic Accuracy Inputs

Strategy	Sensitivity, Presentation (95% CI)	Specificity, Presentation (95% CI)	Sensitivity, Serial Test (4 to 6 hours) (95% CI)	Specificity, Serial Test (4 to 6 hours) (95% CI)	Source
Context 1					
Conventional cTn Central Laboratory	74.9 (72.8 to 76.9)	93.8 (93.2 to 94.3)	89.5 (86.7 to 91.9)	95.2 (94.4 to 95.9)	Lipinski (2015)[71]
Desktop POC (Stratus CS), % (95% CI)	63.6 (53.9 to 72.6)	93.1 (90.2 to 95.4)	87.5[a] (77.9 to 93.3)	92.6[a] (90.2 to 94.4)	Amodio (2007)[25]
Hand-held POC (Cardio3 Panel), % (95% CI)	66.7 (55.2 to 76.5)	95.9 (94.0 to 97.2)	87.5[a] (77.9 to 93.3)	92.6[a] (90.2 to 94.4)	Diercks (2012)[19]
Desktop POC (i-STAT)	63.0	94.0	87.5[a] (77.9 to 93.3)	92.6[a] (90.2 to 94.4)	Lee-Lewandrowski (2011)[20]
Context 2					
No cTn testing, % (95% CI)	93.3	22.7	93.3[b]	22.7[b]	Bruins Slot (2011)[72]

CI = confidence interval; cTn = cardiac troponin; POC = point of care.
[a] Serial values assumed to be the same as Diercks (2012).[19]
[b] Serial values assumed to be the same as presentation values.

6.7.2 Prevalence of non-ST segment elevation myocardial infarction

Based on a high-quality meta-analysis,[5] the estimate of the underlying prevalence of NSTEMI among those who present with chest pain was 16.0% (95% CI, 9.0 to 24.0%).[5] This was used as the base-case prevalence of NSTEMI in both context 1 and 2.

6.7.3 Mortality

The one-year mortality rate after NSTEMI was assumed to be 16.26% and was applied to patients with NSTEMI and who were assumed to receive treatment. This was a pooled estimate of one-year mortality among included studies in a previous meta-analysis conducted by CADTH (2013).[5] The estimated relative risk of one-year mortality of patients with NSTEMI and who were discharged, relative to those who received treatment, was obtained from an RCT that compared central laboratory testing with a panel of POC troponin tests and followed the patients for three months to ascertain diagnostic accuracy and mortality (Goodacre et al., 2011).[39] Thus, the ratio of one-year mortality of untreated MI (21%) to treated MI (11%) patients is equivalent to a relative risk.[39] Lastly, for patients without NSTEMI, the annual mortality risk was based on unadjusted mortality data reported for Canada by Statistics Canada (2014).[73]

6.7.4 Emergency department length of stay

Estimates of the ED LOS for patients that underwent POC cTn testing and central laboratory cTn testing were obtained from a study identified from the clinical systematic review.[41,57] These estimates were applied to all patients in their respective testing strategies and expressed as costs.

6.7.5 Utility values

To calculate QALYs for each strategy, utility values were applied to patients who were alive one year after presenting to the ED. The general population utility value, based on data published by Mittmann (1999),[74] was applied to patients who did not have NSTEMI (utility estimate = 0.93). For patients who had NSTEMI, a utility decrement was applied to general population utility values if the patient received treatment (admitted or transferred, utility decrement = 0.0627) or did not (discharged, utility decrement = 0.08). The decrement for those who were admitted was based on an RCT of 18,624 patients with AMI who received treatment and who had survived an MI after one year (Nikolic et al., 2013).[75] The decrement for those who did not receive treatment was based on annual utility decrements for those with AMI in the community (Ward et al., 2007).[76]

Table 4: Clinical Inputs for Contexts 1 and 2

	Central Laboratory or No cTn Testing	POC cTn Testing	Source
Prevalence of NSTEMI, % (95% CI)	16.0 (9.0 to 24.0)		Pooled estimate, CADTH Optimal Use Report (2013)[5]
Probability of discharge if cTn test negative, %	12.0	28.0	Goodacre (2011)[39]
ED LOS, mean hours	4.52	4.32	Asha (2014)[57]
1-year mortality, NSTEMI, admitted, %	16.26		Pooled estimate, CADTH Optimal Use Report (2013)[5]
Relative risk of one-year mortality, NSTEMI, discharged	1.91		Thokala (2012)[77]
One-year mortality no NSTEMI, %	0.489		Statistics Canada Life Tables (2014)[73]
One-year utility decrement, NSTEMI, admitted	0.0627		Nikolic (2013)[75]

	Central Laboratory or No cTn Testing	POC cTn Testing	Source
One-year utility decrement, NSTEMI, discharged	0.08		Ward (2007)[76]
One-year utility, no NSTEMI	0.933		Mittmann (1999)[74]

CI = confidence interval; cTn = cardiac troponin; ED = emergency department; LOS = length of stay;
NSTEMI = Non-ST elevation myocardial infarction; POC = point of care.

6.8 Cost Estimates and Resource Utilization

Various costs were used to populate the model and estimate the expected cost per cTn test strategy. Details of the value and sources of the included costing data for the testing strategies and resource utilization are provided in Table 4 and Table 5, respectively. Whenever possible, the most current cost estimates were used. All cost estimates were adjusted to 2014 Canadian dollars using the Bank of Canada's Consumer Price Index inflation calculator.[78]

6.8.1 Point-of-care cardiac troponin test and program

Manufacturers were contacted regarding the costs of POC cTn devices, the average lifetime of the device, and the cost of materials (e.g., testing strips). Specifically, the costs of the three POC cTn testing strategies (i.e., Stratus CS, Cardio3 Panel, i-STAT) were applied to the POC cost per test in the respective device-specific analyses. All remaining costs, including the cost for staffing the POC program and quality control, were obtained from laboratory experts in the provinces of Ontario and Alberta. It was assumed that the average annual number of POC cTn tests performed was 1,000 based on expert opinion and, based on this information, a cost of $23.21, $31.31, $26.20 per test was assigned to the Stratus CS, Cardio3 Panel, and i-STAT POC testing strategies, respectively.

6.8.2 Standard practice

In context 1, the cost of central laboratory cTn testing, including the capital costs of the equipment, costs of the reagents and materials, and staffing costs, as well as specimen-procurement costs, were obtained from laboratory experts in the provinces of Ontario and Alberta. A cost of $22 per test was assigned for the central laboratory cTn testing strategy. In context 2, it was assumed that no additional assay or device costs would apply in the no–cTn testing strategy.

Table 5: Costs of Cardiac Troponin Testing Strategies

	Device	Testing Materials (e.g., Strips), per Test	Average Lifetime of Device	Source
POC cTn testing strategies				
Stratus CS (Siemens)	$35,000	$8.50	8.5 years	Siemens
Cardio3 Panel (Alere)	$5,000	$20	7 years	Alere
i-STAT (Abbott)	$8,000	$14	5 years	Expert input (Ontario laboratory estimate)
Cost of staff for POC program (per annum)	$10,000			Expert Input (Ontario laboratory estimates)
Cost of calibration and quality control of POC cTn testing (per annum)	$600			
Number of annual POC tests	1,000			
Standard care				
Conventional cTn central laboratory testing, e.g., device, materials, staff (per test)	$10			Expert input (Alberta laboratory estimates)
Specimen procurement by central laboratory	$12			Expert input (Alberta laboratory estimates)

POC = point of care; cTn = cardiac troponin.

6.8.3 In-hospital costs

Table 5 outlines all of the costs related to resource utilization. The cost of true-positive NSTEMI and false-positive NSTEMI hospital admissions was obtained from estimates derived in previous work[5] and adjusted to 2014 Canadian dollars. These previous estimates were derived using data from the Ontario Case Costing Initiative (OCCI) database,[79] the Ontario Schedule of Benefits for Physician Services,[80] and the literature.[5]

In this previous work, a multi-step process was used to estimate the cost of a true-positive NSTEMI hospitalization.[5] Briefly, the average hospital costs for the following case mix groups were obtained: MI with coronary artery bypass grafting (CABG), MI with percutaneous coronary intervention (PCI), and MI without CABG or PCI.[5] Physician fees for treating each of the case mix groups were added to the respective hospital costs.[5] The average cost of treating all MI was then derived by weighting each of the in-patient costs by assumed proportions of NSTEMI patients who would receive a CABG, PCI, or neither procedure.[5,81]

The estimate for the daily hospital cost for false-positive hospitalization was based on the average in-patient cost and a 3.9-day stay in hospital for unstable angina,[5] one initial consultation, and one subsequent visit by an internal medicine physician.[5] The total cost of a false-positive hospitalization was then based on a two-day in-patient LOS, which was an assumption provided from expert opinion received in the previous work.[5]

6.8.4 Emergency department costs

For patients who have a negative cTn test at presentation and are held and retested, additional ED costs were applied to account for a repeat ECG and an additional six hours of wait time in the ED. These estimates were adjusted to 2014 Canadian dollars and derived from previous work[5] that drew upon Ontario costing data from the published literature[82,83] and the Ontario Schedule of Benefits.[80] For patients who were initially discharged following a negative cTn test and readmitted, an additional cost — accounting for the cost of an ED visit and the cost of a true-positive NSTEMI hospitalization — was applied; this estimate was also drawn from previous work.[5]

Table 6: Costs of Resource Utilization (in 2014 Canadian Dollars)

	Estimate	Source
Cost of true-positive hospitalization for NSTEMI	$11,741	CADTH 2013 Optimal Use Report[5]
Cost of false-positive hospitalizations	$2,203	CADTH 2013 Optimal Use Report[5]
Cost of death	$14,368	Shrive (2005)[84]
Cost of ground ambulance transfer with patient	$928	CADTH expert input
Cost of holding and retesting in ED (i.e., serial testing)	$149.20	CADTH 2013 Optimal Use Report[5]
Cost of false-negatives (readmission for missed diagnosis of NSTEMI)	$11,894	Derived from costs estimates provided in the CADTH 2013 Optimal Use Report[5]

ED = emergency department; NSTEMI = Non-ST elevation myocardial infarction.

6.9 Variability and Uncertainty

The variability in the model was assessed primarily through deterministic sensitivity analysis. Specifically, all model parameters were varied in one-way sensitivity analysis. Probabilities such as the prevalence of NSTEMI, discharge following a negative cTn test and one-year mortality, as well as the relative risk of mortality and utility values, were varied within their respective 95% CIs. Costs of testing strategies and resource utilization were varied within ± 50% of the average calculated estimate. Key scenario analysis — excluding POC cTn device costs, varying the staff costs, varying the quality-control costs, and excluding the costs of POC testing all together — were also performed to inform contexts where the device might already have been purchased or might operate with variable workflow. A similar analysis was completed with the capital cost for central laboratory testing excluded, as the infrastructure to complete cTn tests may already be acquired. In addition, recognizing that high-sensitivity cTn assays are commonly used, a scenario analysis was completed using the diagnostic-accuracy assays and cost of high-sensitivity assays for the central laboratory (sensitivity: 88.4%; specificity: 81.6%; cost: $15 total per test [$3/test, $12/specimen]).[5,71] Lastly, for context 2, a scenario analysis was completed that included the indirect costs. Specifically, the costs of lost productivity for NSTEMI patients transferred (170 hours)[85] and for false-positives transferred (i.e., misdiagnosed as NSTEMI [6.5 hours]).[86]

To assess the impact of uncertainty in the diagnostic accuracy of all POC devices and central laboratory testing, various scenario analyses were completed. Using a pooled receiver operator characteristic (ROC) curve using all studies identified, a range of sensitivity and specificity estimates were applied in the models (Appendix 12). Threshold analyses were completed to document the POC diagnostic accuracy when the costs were equal between central laboratory and POC, and when the effectiveness was equal between central laboratory and POC. The diagnostic accuracy of the central laboratory was similarly varied to establish the same thresholds.

6.10 Cost-Consequence Table

Based on the diagnostic accuracy and target population size, the number of people with each testing outcome was calculated. The total cost per first test was included. The costs associated with each test outcome were also included. In context 2, the costs of serial testing were also included. The same diagnostic accuracy was assumed for the serial test and the same cost as in context 1 was assumed for true positives.

7. Economic Results

7.1 Base-Case Results

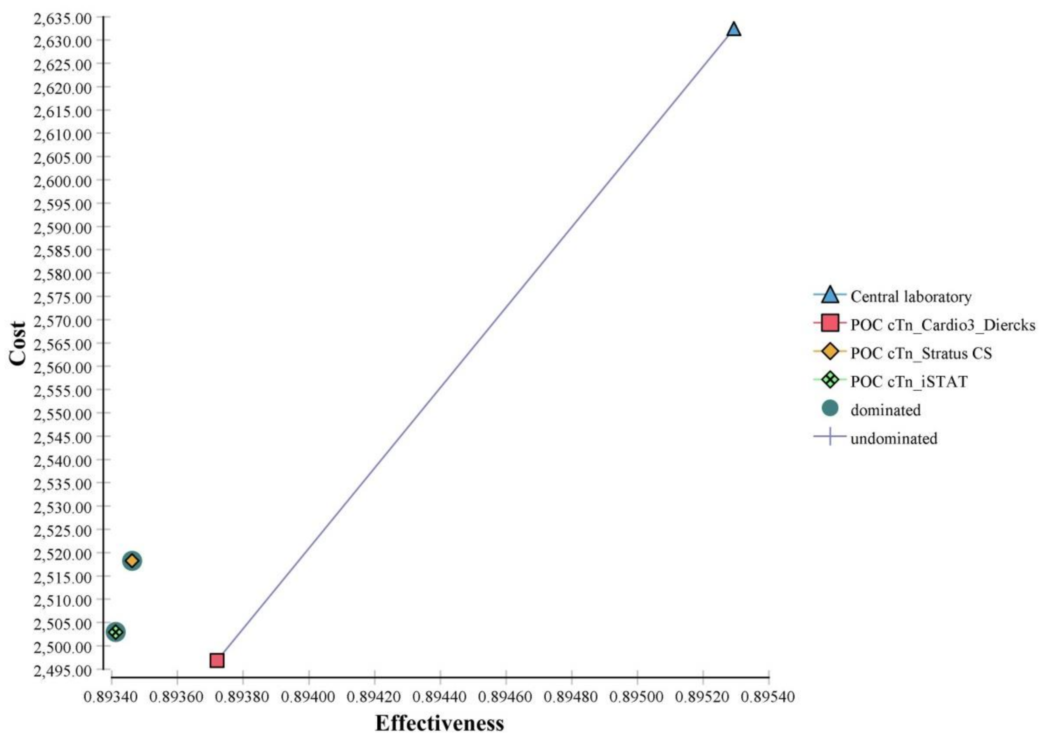
The base-case results of the cost-utility analysis for context 1 are summarized in Table 7 and the total costs and QALYs of each strategy are plotted in Figure 3. The base-case analysis compared central laboratory cTn testing to each of the i-STAT, Stratus CS, and Cardio3 Panel POC cTn testing strategies. Central laboratory cTn testing was associated with an average total cost of $2,632 and 0.8953 QALYs per patient. The Stratus CS, Cardio3 Panel and i-STAT POC cTn testing strategies were found to cost less and result in fewer QALYs per patient compared with a central laboratory, resulting in an incremental cost-utility ratio of $62,322, $86,123, and $68,782 saved per QALY lost, respectively.

Table 7: Results of Base-Case Analysis for Context 1

Strategy	Cost ($)	Incremental Cost Compared With a Central Laboratory ($)	Effectiveness (QALY)	Incremental Effectiveness Compared with a Central Laboratory (QALY)	Cost per QALY ($/QALY)
Central laboratory	2,632		0.8953		
Status CS	2,518	–114	0.8935	–0.0018	62,322 for central laboratory
Cardio3 Panel	2,497	–135	0.8937	–0.0016	86,123 for central laboratory
i-STAT	2,503	–129	0.8934	–0.0019	68,782 for central laboratory

QALY = quality-adjusted life-year.

Figure 3: Base Case Cost-Effectiveness Analysis for Context 1



cTn= cardiac troponin; POC = point of care.

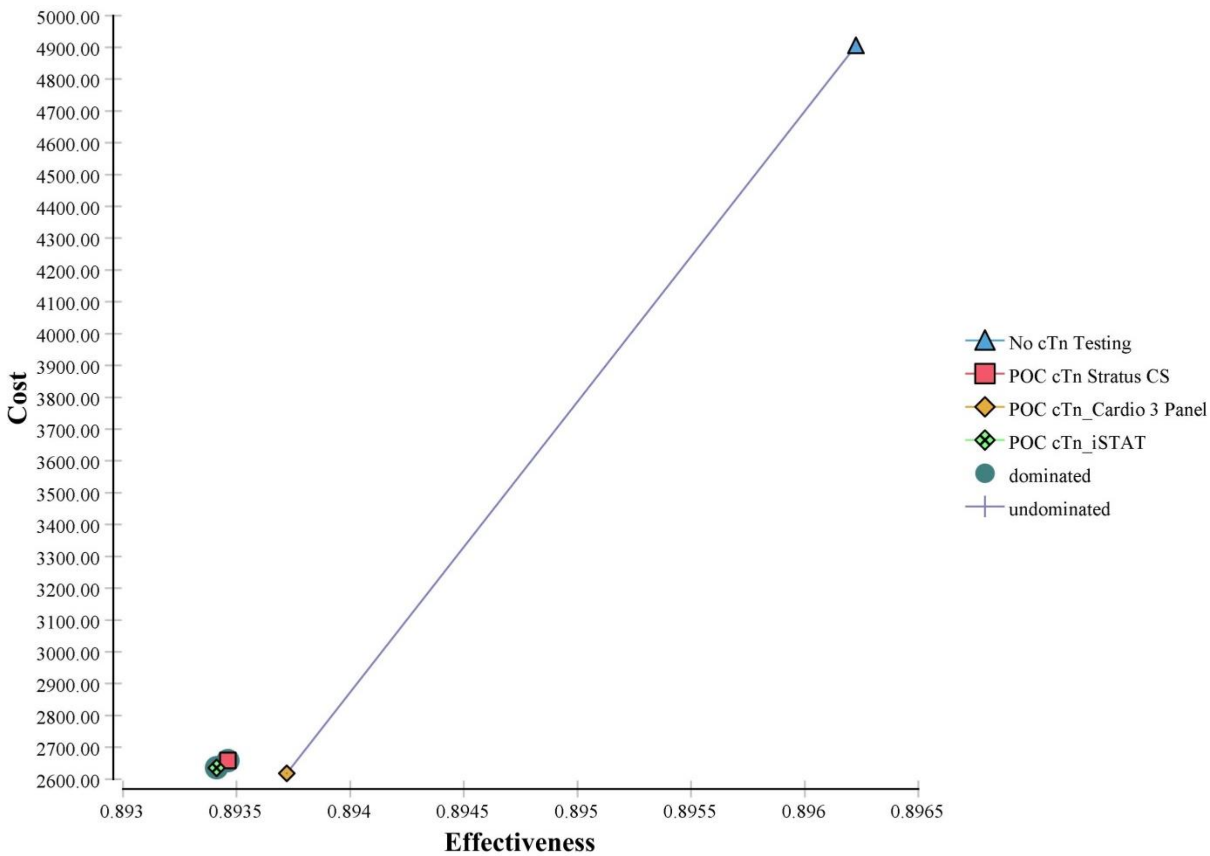
The base-case results of the cost-utility analysis for context 2 are presented in Table 8 and the total costs and QALYs of each strategy are plotted in Figure 4. Standard practice or no cTn testing was associated with an estimated total cost of $4,905 and 0.896 QALYs per patient. All three cTn POC devices were found to be less costly and less effective than no cTn testing.

Table 8: Results of Base-Case Analysis for Context 2

Strategy	Cost ($)	Incremental Cost Compared With No cTn Testing ($)	Effectiveness (QALY)	Incremental Effectiveness Compared with No cTn Testing (QALY)	Cost per QALY ($/QALY)
No cTn testing	4,905		0.8962		
Status CS	2,658	–2,247	0.8935	–0.00276	812,945 for no cTn testing
Cardio3 Panel	2,618	–2,287	0.8937	–0.00251	912,802 for no cTn testing
i-STAT	2,636	–2,269	0.8934	–0.00282	806,414 for no cTn testing

cTn = cardiac troponin; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Figure 4: Base Case Cost-Effectiveness Analysis, Context 2



cTn = cardiac troponin; POC = point of care.

7.2 Variability and Uncertainty

7.2.1 One-way sensitivity and scenario analyses

Overall, the model results were robust to variations in all parameters varied, with the exception of the utility value for those with NSTEMI assumed to receive treatment (i.e., admitted) in context 1. The results of this and other select one-way sensitivity and scenario analyses for context 1 and 2 are presented in Table 9 and Table 10, respectively.

Table 9: Results of Select One-Way Sensitivity and Scenario Analyses for Context 1

		Stratus CS	Cardio3 Panel	i-STAT
Parameter	**Value ($)**	**ICUR ($/QALY)**		
Base-case results		62,322 for CL	86,123 for CL	68,782 for CL
One-Way Sensitivity Analysis				
Annual number of POC cTn tests	500	62,299 for CL	78,932 for CL	62,299 for CL
	50,000	75,136 for CL	93,169 for CL	75,135 for CL
One-year utility NSTEMI, admitted	0.70	Dominates CL	Dominates CL	Dominates CL
	0.75	219,425 for CL	303,224 for CL	242,170 for CL
POC quality-control cost	600	62,322 for CL	86,123 for CL	68,782 for CL
	5,000	59,920 for CL	83,327 for CL	66,444 for CL
POC staff cost	10,000	62,322 for CL	86,123 for CL	68,782 for CL
	75,000	26,837 for CL	44,815 for CL	34,240 for CL
No capital cost of the POC device		64,570 for CL	86,577 for CL	69,633 for CL
No capital cost for CL		56,863 for CL	79,768 for CL	63,468 for CL
No cost for cTn testing in POC or CL		62,986 for CL	92,042 for CL	71,014 for CL
Cost of false negatives (readmission for missed diagnosis of NSTEMI)	50% decrease ($5,947)	62,476 for CL	86,286 for CL	68,935 for CL
	50% increase ($17,841)	62,168 for CL	85,960 for CL	68,629 for CL
hs cTn CL as comparator	Diagnostic accuracy values and cost per test for hs cTn (section 1.3)	215,010 for CL	248,509 for CL	216,749 for CL

CL = central laboratory; cTn = cardiac troponin; hs cTn = high-sensitivity cardiac troponin; ICUR = incremental cost-utility ratio; NSTEMI = non-ST elevation myocardial infarction; POC = point of care; QALY = quality-adjusted life-year.

Table 10: Results of Select One-Way Sensitivity and Scenario Analyses for Context 2

		Stratus CS	Cardio3 Panel	i-STAT
Parameter	**Value ($)**		**ICUR ($/QALY)**	
Base-case results		812,945 for no cTn testing	912,802 for no cTn testing	806,414 for no cTn testing
One-Way Sensitivity Analysis				
Annual number of POC cTn tests	500	807,620 for no cTn testing	908,286 for no cTn testing	802,078 for no cTn testing
	50,000	818,164 for no cTn testing	917,227 for no cTn testing	810,663 for no cTn testing
1-year utility NSTEMI, admitted	0.70	Dominates central laboratory	Dominates central laboratory	Dominates central laboratory
	0.75	2,862,238 for no cTn testing	3,213,816 for no cTn testing	2,839,244 for no cTn testing
POC quality-control cost	600	812,945 for no cTn testing	912,802 for no cTn testing	806,414 for no cTn testing
	5,000	811,353 for no cTn testing	911,045 for no cTn testing	804,850 for no cTn testing

		Stratus CS	Cardio3 Panel	i-STAT
POC staff cost	10,000	812,945 for no cTn testing	912,802 for no cTn testing	806,414 for no cTn testing
	75,000	789,426 for no cTn testing	886,858 for no cTn testing	783,312 for no cTn testing
No capital cost of the POC device		814,435 for no cTn testing	913,087 for no cTn testing	806,983 for no cTn testing
No cost for POC testing		821,346 for no cTn testing	925,300 for no cTn testing	815,726 for no cTn testing
Cost of transport	50% decrease ($464)	695,594 for no cTn testing	779,572 for no cTn testing	689,908 for no cTn testing
	50% increase ($1,392)	930,296 for no cTn testing	1,046,032 for no cTn testing	922,919 for no cTn testing
Indirect costs included	Including costs of lost productivity	894,164 for no cTn testing	1,004,033 for no cTn testing	887,100 for no cTn testing

cTn = cardiac troponin; ICUR = incremental cost-utility ratio; NSTEMI = Non-ST elevation myocardial infarction; POC = point of care; QALY = quality-adjusted life-year.

The per-patient cost of the POC cTn testing strategies varied by make and portability of the device (i.e., desktop or hand-held) and were based on the annual number of POC cTn tests. In the base case, the annual number of POC cTn tests was assumed to be 1,000. Anticipating potential variability in annual POC cTn tests among clinical settings of different sizes, the annual number of POC cTn tests was varied within expert-reported ranges plausible for each context (between 500 and 50,000). Within these range, the model results were robust: the Stratus CS, i-STAT, and Cardio3 Panel POC cTn testing strategies remained less expensive but also effective compared with a central laboratory. Similarly, in context 2, all cTn testing strategies remained less expensive and less effective compared with the no-cTn testing strategy within the range of annual POC cTn tests.

There was considerable uncertainty surrounding the estimated one-year utility value for patients who had NSTEMI and were assumed to receive treatment; therefore, a threshold analysis was conducted for this parameter. The range used in the threshold analysis was within ± 50% of the base-case estimate (based on applying a utility decrement of 0.0627 to the general population utility value of 0.933 (Mittmann 1999; Nikolic 2013).[74,75] In contexts 1 and 2, at a utility value of 0.75 or above, POC remains less expensive and less effective than central laboratory or no cTn testing. However, at a utility value below approximately 0.70, POC is less expensive and more effective than central laboratory or no cTn testing (POC becomes the dominant strategy). It is unknown if these are within a plausible range for the NSTEMI utility estimates.

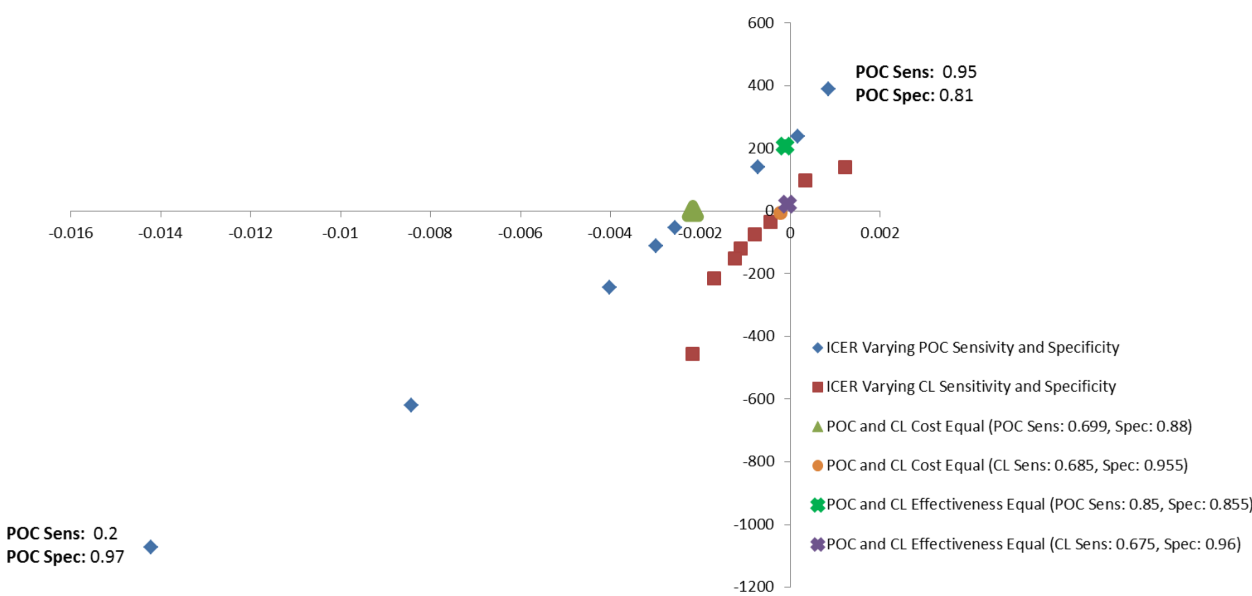
Lastly, for the base-case analysis it was assumed that the capital costs of the testing equipment (i.e., immunoanalyzer for the central laboratory and desktop or hand-held device for the POC strategy) would need to be accounted for in the cost per patient. However, given potential variability in the clinical settings' existing resources and capacity, purchasing decisions may be made with or without consideration of the capital cost of the device. For example, within context 1, the incremental investment into a given testing strategy would vary for a central laboratory already equipped with the appropriate immunoanalyzer equipment for cTn testing compared with a central laboratory with neither an immunoanalyzer nor POC cTn testing device. Therefore, to inform purchasing decisions made independent of capital costs, a scenario analysis that excluded POC cTn device costs was performed. In both context 1 and 2, the results of the model from the base case remained unchanged. This is due to the cost of the POC devices being relatively small. The major cost driver is the diagnostic accuracy and the costs of hospitalizations due to either true-positives, false-positives, or false-negatives (which are subsequently admitted to hospital).

7.3 Scenario Analysis for Diagnostic Accuracy

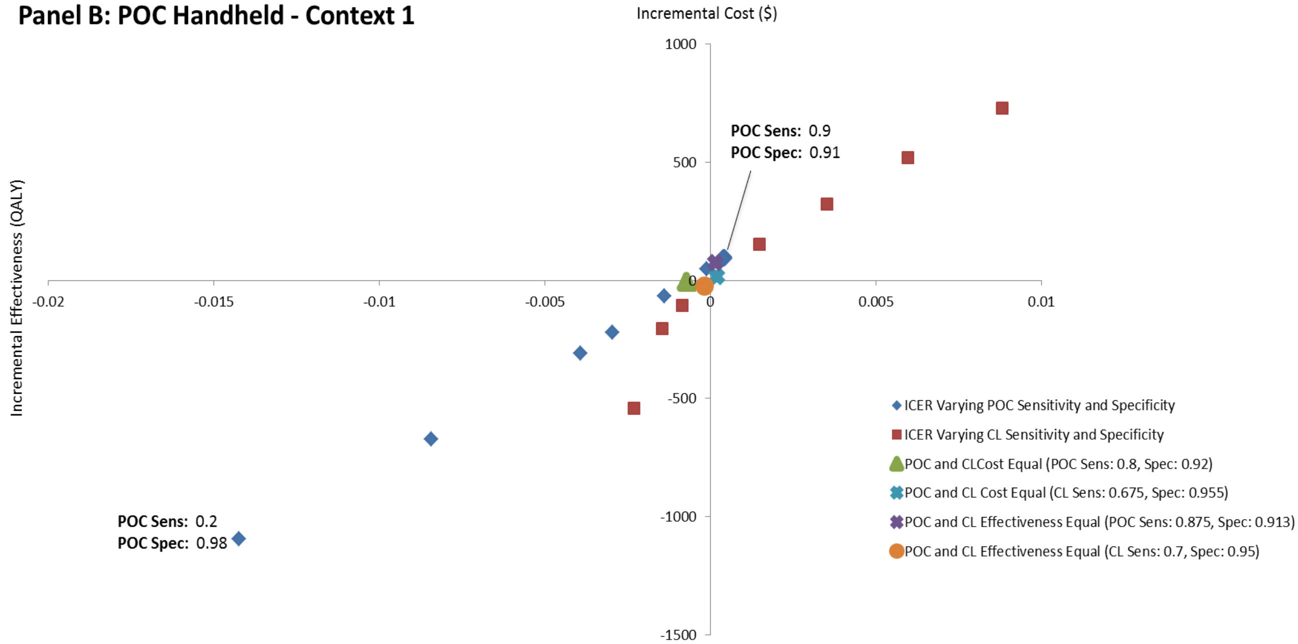
To assess the uncertainty due to the diagnostic accuracy of POC, central laboratory, and no cTn testing, Figure 5 presents the results of a range of sensitivity and specificity variations. A pooled ROC was calculated using all available studies identified by the clinical review. There was significant heterogeneity across studies; however, a pooled ROC was required, despite the heterogeneity to relate sensitivity and specificity. The results are presented on a cost-effectiveness plane with the y-axis presenting incremental cost compared with a central laboratory, and the x-axis representing incremental effectiveness compared with a central laboratory. There are large variations in the incremental cost and effectiveness within plausible ranges of the diagnostic accuracy. For example, at a sensitivity of 0.2 and a specificity of 0.97, a desktop POC device is associated with a cost savings of approximately $1,100 and a lower effectiveness of 0.015 QALYs compared with a central laboratory (Figure 5, Panel A). However, at a sensitivity of 0.95 and a specificity of 0.81, a desktop POC device is more expensive (an increase of roughly $400) and more effective (0.001 QALYs) than central laboratory testing. POC and central laboratory testing are equal in cost at a sensitivity of 0.699 and specificity of 0.88 for a POC desktop device or a sensitivity of 0.685 and specificity of 0.955 for central laboratory testing (Figure 5, Panel A). POC and central laboratory testing are equally effective at a POC sensitivity of 0.85, specificity of 0.855, or a central laboratory sensitivity of 0.675 and specificity of 0.96. Panel B demonstrates similar findings for hand-held POC devices. Figure 6 (panels A and B) presents similar analyses for context 2.

Figure 5: Scenario Analyses for Diagnostic Accuracy of POC Desktop (Panel A) and Hand-held (Panel B) Devices Compared with a Central Laboratory (Context 1)

Panel A: Desktop POC - Context 1



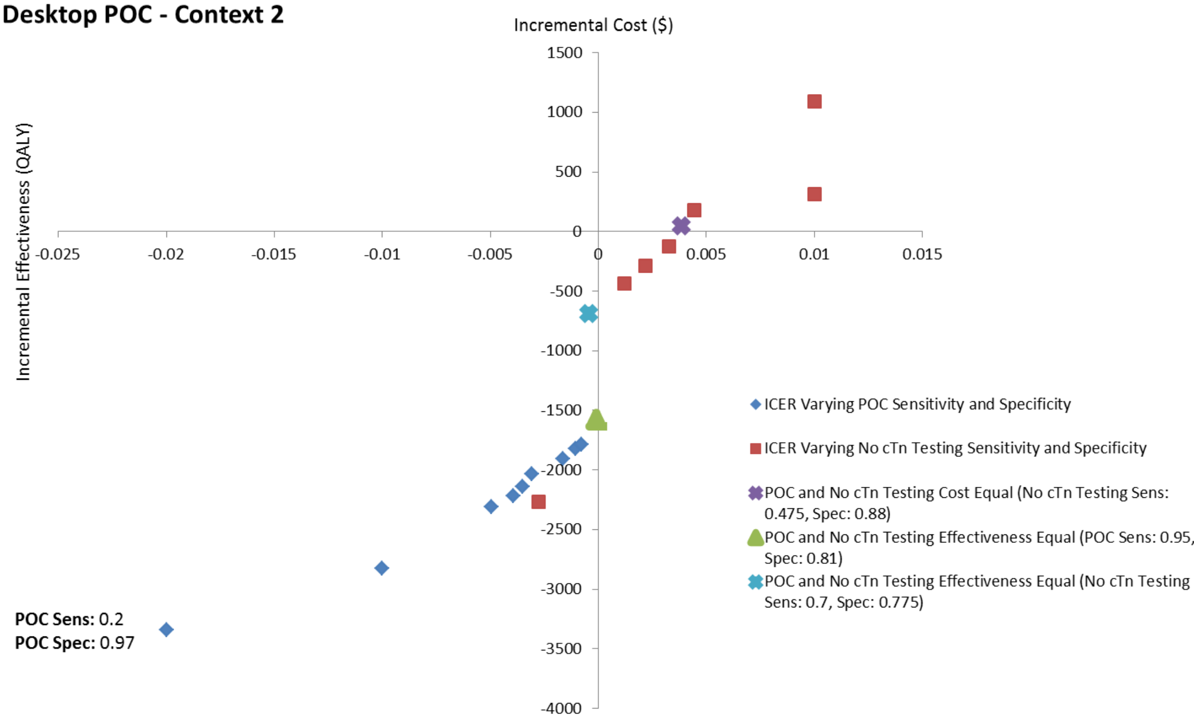
Panel B: POC Handheld - Context 1



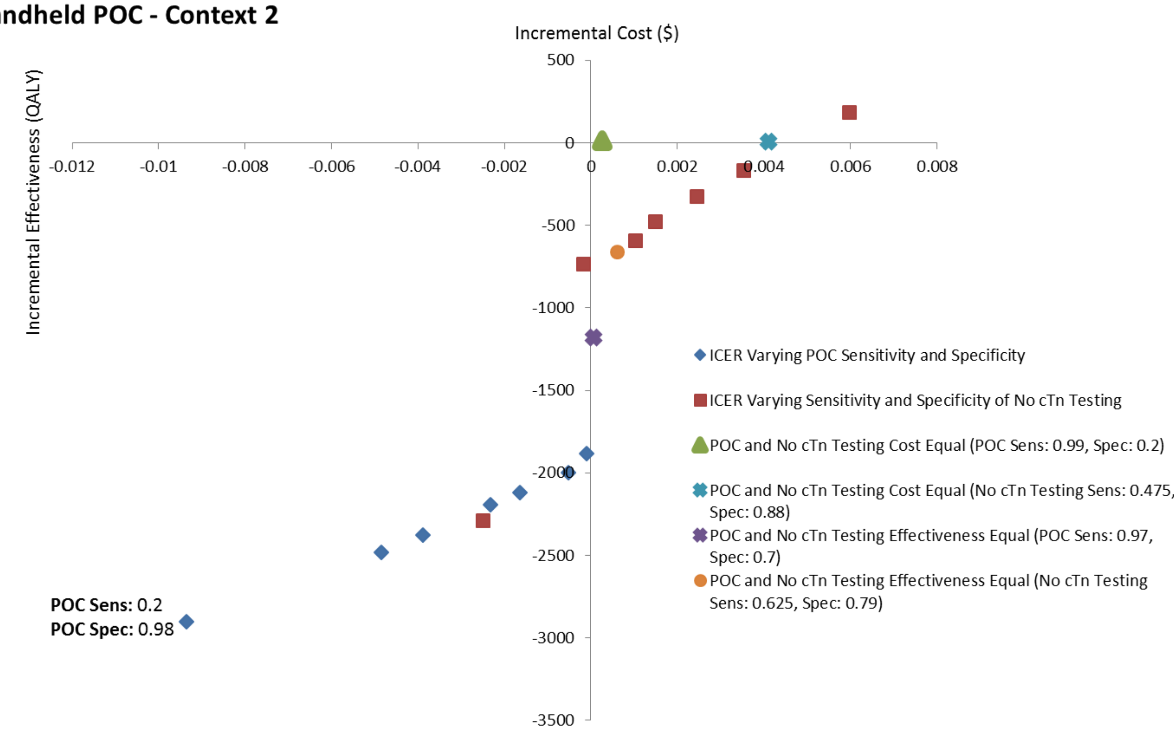
CL = central laboratory; ICER = incremental cost-effectiveness ratio; POC = point of care; QALY = quality-adjusted life-year; sens = sensitivity; spec = specificity.

Figure 6: Scenario Analyses for Diagnostic Accuracy of POC Desktop (Panel A) and Hand-held (Panel B) Devices Compared With No cTn Testing (Context 2)

Panel A: Desktop POC - Context 2



Panel B: Handheld POC - Context 2



cTn = cardiac troponin; ICER = incremental cost-effectiveness ratio; POC = point of care; QALY = quality-adjusted life-year; sens = sensitivity; spec = specificity.

7.4 Cost and Consequence Tables

Given the multiple health-system outcomes likely to be affected by the POC cTn testing strategies, a cost-consequence analysis was performed for both context 1 (Table 11) and context 2 (Table 12). The cost-consequence analysis draws directly from the decision analysis model. The clinical and cost inputs are the same as outlined earlier. The number of first tests (excluding serial tests) was assumed based on the estimated utilization within a typical urban ED (context 1) and a typical primary care practice (context 2).

In context 1, all three POC strategies (Stratus CS, i-STAT and Cardio3 Panel) resulted in cost savings compared with a central laboratory. Of note, there are trade-offs with each POC device resulting in more false-positives and false-negatives than central laboratory testing. In context 2, all POC strategies resulted in cost savings compared with no cTn testing. However, each POC strategy results in more missed NSTEMI compared with no cTn testing.

Table 11: Cost and Consequence Analysis of POC cTn Testing Strategies Compared With a Central Laboratory in Context 1

# Events	Central Laboratory		Stratus CS		Cardio3 Panel		i-STAT	
	Consequence	Cost	Consequence	Cost	Consequence	Cost	Consequence	Cost
Annual number of first tests	50,000	$1,100,000	50,000	$1,160,500	50,000	$1,565,500	50,000	$1,310,000
True-positives (NSTEMI cases)[a]	5,992	$70,356,147	5,088	$59,741,668	5,336	$62,653,604	5,040	$59,178,067
True-negatives (not NSTEMI cases)[a]	39,396	–	3,9102	–	40,278	–	39,480	–
False-negatives (missed NSTEMI cases)[a]	2,008	$21,362[b]	2,912	$123,148[c]	2,664	$112,659[c]	2,960	$125,177[c]
False-positives (misdiagnosed as NSTEMI)[a]	2,604	$5,735,388	2898	$14,801,001	1,722	$3,792,756	2,520	$5,550,375
TOTAL cost ($)		**77,212,897**		**$67,408,248**		**$68,124,521**		**$66,163,620**
Difference compared with a central laboratory ($)				**–$9,804,649**		**–$9,088,375**		**–$11,049,276**

cTn = cardiac troponin; NSTEMI = non-ST elevated myocardial infarction; POC = point of care; RCT = randomized controlled trial.
[a] After presentation cTn test.
[b] Based on RCT data, only 0.08% of those patients with a false-negative re-present at the hospital with an associated total hospitalization cost of $11,894.
[c] Based on RCT data, only 0.3% of those patients with a false-negative re-present at the hospital with an associated total hospitalization cost of $11,894.

Table 12: Cost and Consequence Analysis of POC cTn Testing Strategies Compared With No cTn Testing in Context 2

# Events	No cTn Testing		Stratus CS		Cardio3 Panel		i-STAT	
	Consequence	Cost	Consequence	Cost	Consequence	Cost	Consequence	Cost
Annual number of first tests	2,500	0	2,500	$58,025	2,500	$78,275	2,500	$65,500
True-positives (NSTEMI cases) [a]	373	$4,729,844	254	$3,223,167	267	$3,380,270	252	$3,192,759
True-negatives (not NSTEMI cases) [a]	477	--	1,955	--	2014	--	1,974	
False-negatives (missed NSTEMI cases)[a]	27	--	146	--	133	--	148	--
True-positives identified with serial test within 4 to 6 hours (NSTEMI cases)	25	$292,373	93	$1,090,678	57	$678,479	80	$935,932
False-positives (misdiagnosed as NSTEMI)[a]	1623	$5,080,474	145	$453,614	86	$269,538	126	$394,446
TOTAL Cost ($)		**$10,102,692**		**$4,825,483**		**$4,406,564**		**$4,588,638**
Difference compared with no cTn testing ($)				**–$5,277,209**		**–$5,669,128**		**–$5,514,054**

cTn = cardiac troponin; NSTEMI = non-ST elevated myocardial infarction; POC = point of care.
[a] After presentation cTn test.

8. Economic Discussion

All three of the POC cTn testing strategies examined were less effective than central laboratory cTn testing for patients presenting to the ED with symptoms suggestive of ACS. The Stratus CS, Cardio3 Panel and i-STAT POC cTn testing strategies cost less per patient compared with a central laboratory. When POC cTn testing was compared with no cTn testing, the POC cTn testing strategy was less effective and cost less per test.

In both contexts, the model was sensitive to the variability in the utility value for those with NSTEMI who were admitted and assumed to receive treatment. When this parameter was lowered below the identified threshold values, all of the POC cTn testing strategies became the dominant strategy. However, it is unknown if the threshold values evaluated were within the plausible range for the NSTEMI utility estimates. The cost for each cTn testing strategy was based on information provided by the manufacturers, with the exception of the i-STAT POC cTn test and central laboratory costs, which were provided by experts in Alberta and Ontario. It was unclear whether these provided costs were the manufacturers' wholesale or list prices. Despite the uncertainty in the cTn testing costs, sensitivity analyses varying the cost per assay and removing the POC device costs found the model findings were not sensitive to variability in these costs.

The model results varied significantly with the estimates of diagnostic accuracy for both central laboratory and POC devices. Within plausible ranges of sensitivity and specificity, POC devices (both hand-held and desktop) varied from less costly to more costly and less effective to more effective. There is significant uncertainty associated with the point estimates of cost-effectiveness due to the uncertainty in the diagnostic accuracy.

9. Clinical And Economic Review Limitations

The results from our clinical review must be interpreted with caution, given the heterogeneity of the included studies and the small number of RCTs. The analysis of clinical utility is based on mostly observational studies, which have a level of evidence that is not as robust as RCT data. In many of the diagnostic-accuracy studies, it was unclear whether the POC cTn test results were interpreted without knowledge of the central laboratory test results, and vice versa. Furthermore, if final clinical adjudication was done with knowledge of the troponin results, this could introduce additional potential bias. The diagnostic-accuracy results may have been affected by the prior MI rate among included participants, the use of the manufacturer's 99th percentile (as opposed to the 99th percentile at a 10% coefficient of variation), the exclusion of patients with STEMI, and time to presentation to the ED. In addition, there were some inconsistencies between studies and the reported 99th percentile for the same device.

Many studies on clinical utility did not have sufficient power to detect a clinically important effect for the primary outcomes. The mortality and adverse events outcomes analyzed are reflective of the short-term follow-up times that have been reported to date. The included studies were conducted in different settings, using different POC tests and different reference-standard tests, leading to a large variability in findings. Further, the majority of included studies include data collected in EDs or other settings with access to central laboratory testing, but include limited available data from settings without access to a central laboratory. More data on the utility of POC cTn testing in rural health care centres or remote settings would have been informative. For this HTA, the data analyzed on the clinical utility of POC testing is not from Canadian centres and, as such, might limit generalizability to the Canadian setting. A pooled estimate of the clinical outcomes is not provided, since a meta-analysis was not possible due to clinical heterogeneity among trials, such as differences in definitions of outcomes and inconsistencies in reporting.

There are significant limitations to the economic evaluation. The limited availability of accurate cost data influenced the costs that were included in the model. The exact cost per POC test, the cost of central laboratory testing and the cost of missed diagnoses were imprecise. However, the model was robust to multiple variations in these estimates. The time horizon was limited to one year. However, given that the testing with POC or a central laboratory is unlikely to affect the long-term survival of patients, this is a realistic assumption. The largest limitations are with the observed changes in cost-effectiveness, with plausible changes in the utility estimate for the NSTEMI patients, and the diagnostic accuracy of the both POC and central laboratory testing. More robust estimates for these variables would allow for more certainty in the cost-effectiveness of all strategies.

The indirect costs (patient-borne costs) that were included were limited. In the literature, we were able to identify only the costs of lost productivity. The lack of published estimates limited the findings, particularly in context 2 where the costs of travel and accommodation for the family may be significant.

10. Conclusions

cTn testing has an important role in the diagnostic workup of patients presenting to EDs with acute chest pain and non-diagnostic ECG. Our findings concur with observations from other systematic reviews that a preferred POC assay for the diagnosis of AMI does not yet exist and, despite improvement in TAT and LOS, there is no strong evidence of improvement in clinical outcomes compared with cTn testing by a central laboratory. In the absence of a central laboratory, POC cTn testing may be of benefit.

In rural health care centres or remote settings where a central laboratory is not available, POC cTn testing increased staff satisfaction and may reduce the transfer rate of patients to emergency rooms. In rural centres or remote settings, the use of POC troponin testing may lead to improved patient care, as the assessment of the patient along with cTn results may prevent unnecessary transfer to hospital, thereby allowing patients to remain in their community for follow-up and care. This may result in other benefits, such as reduced out-of-pocket costs and familial disruption and ensuring the transfer of only those patients who require it.

The results from our clinical review must be interpreted with caution, given the limited quality of the included studies, and because the outcomes analyzed are reflective of short-term follow-up times.

Generally, POC cTn testing strategies were found to be less effective and less expensive than standard of care, regardless of context. However, there are plausible variations in diagnostic accuracy that change the cost-effectiveness from cost-saving to cost-incurring. Generally, the weak evidence base for effectiveness and costs limited the scope of this economic evaluation.

Overall, given the limitations with the data and the inconsistency in diagnostic test accuracy, the usefulness of POC in settings with access to central laboratories may be limited. However, in settings with no access to a central laboratory, such as in rural health care centres or remote settings, POC troponin testing may be useful, as it could help reduce unnecessary transfers to larger centres.

References

1. Andersson PO, Karlsson JE, Landberg E, Festin K, Nilsson S. Consequences of high-sensitivity troponin T testing applied in a primary care population with chest pain compared with a commercially available point-of-care troponin T analysis: an observational prospective study. BMC Res Notes [Internet]. 2015 [cited 2015 Jul 23];8:210. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4467613/pdf/13104_2015_Article_1174.pdf
2. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Third universal definition of myocardial infarction. Eur Heart J [Internet]. 2012 Aug 24 [cited 2015 Jan 29];33:2551-67. Available from: http://eurheartj.oxfordjournals.org/content/33/20/2551.full.pdf+html
3. Cost-effectiveness of diagnostic strategies for suspected acute coronary syndrome (ACS). London (UK): National Institute for Health Research (NIHR); 2009. (NIHR Health Technology Assessment programme).
4. Bingisser R, Cairns C, Christ M, Hausfater P, Lindahl B, Mair J, et al. Cardiac troponin: a critical review of the case for point-of-care testing in the ED. Am J Emerg Med. 2012 May 23.
5. High-sensitivity cardiac troponin for the rapid diagnosis of acute coronary syndrome in the emergency department: a clinical and cost-effectiveness evaluation [Internet]. Ottawa: CADTH; 2013 Mar. [cited 2015 Jan 29]. (CADTH optimal use report; vol.2, no.1a). Available from: http://www.cadth.ca/media/pdf/OP0511_Troponin_ScienceReport_e.pdf
6. Kanichay R, Wilsdon T, Connolly S, Sauri L. The economic and societal burden of acute coronary syndrome in Canada. London (ON): Charles River Associates; 2010 Nov.
7. The cost of acute care hospital stays by medical condition in Canada, 2004-2005 [Internet]. Ottawa: Canadian Institute for Health Information; 2008. [cited 2015 Jan 29]. Available from: https://secure.cihi.ca/free_products/nhex_acutecare07_e.pdf
8. Bhuyia FA, Pitts SR, McCaig LF, Division of Healthcare Statistics. Emergency Department Visits for Chest Pain and Abdominal Pain: United States, 1999–2008 [Internet]. Hyattsville (MD): National Center for Health Statistics; 2010 Sep. (NCHS data brief no. 43). [cited 2015 May 4]. Available from: http://www.cdc.gov/nchs/data/databriefs/db43.pdf
9. Geary M, Abangma G, Pl d, Heneghan C, Thompson M, Price CP. Point-of-care test for cardiac troponin. Oxford (UK): The Oxford Centre for Monitoring and Diagnosis in Primary Care (MaDOx); 2011. (Horizon Scan Report; No. 0013).
10. The American Association for Clinical Chemistry. Laboratory medicine practice guidelines: biomarkers of acute coronary syndromes and heart failure [Internet]. Washington (DC): The Association; 2007. [cited 2015 Jun 5]. Available from: https://www.aacc.org/~/media/practice-guidelines/acs-and-heart-failure/acs_pdf_online.pdf?la = en
11. Mahajan VS, Jarolim P. How to interpret elevated cardiac troponin levels. Circulation [Internet]. 2011 Nov 22 [cited 2015 Jan 29];124(21):2350-4. Available from: http://circ.ahajournals.org/content/124/21/2350.full.pdf+html
12. Kelley WE, Januzzi JL, Christenson RH. Increases of cardiac troponin in conditions other than acute coronary syndrome and heart failure. Clin Chem [Internet]. 2009 Dec [cited 2015 Jan 30];55(12):2098-112. Available from: http://www.clinchem.org/content/55/12/2098.full.pdf+html
13. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011 Oct 18;155(8):529-36.
14. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health [Internet]. 1998 Jun [cited 2015 Jan 29];52(6):377-84. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf

15. Brouwers M, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in healthcare. CMAJ [Internet]. 2010 Dec [cited 2015 Jan 29];182(18):E839-E842. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3001530/pdf/182e839.pdf

16. Aldous S, Mark RA, George PM, Cullen L, Parsonage WA, Flaws D, et al. Comparison of new point-of-care troponin assay with high sensitivity troponin in diagnosing myocardial infarction. Int J Cardiol. 2014 Nov 15;177(1):182-6.

17. Ivandic BT, Spanuth E, Giannitsis E. Performance of the AQT90 FLEX cTnI point-of-care assay for the rapid diagnosis of acute myocardial infarction in the emergency room. Clin Lab. 2014;60(6):903-8.

18. Palamalai V, Murakami MM, Apple FS. Diagnostic performance of four point of care cardiac troponin I assays to rule in and rule out acute myocardial infarction. Clin Biochem. 2013 Nov;46(16-17):1631-5.

19. Diercks DB, Peacock WF, Hollander JE, Singer AJ, Birkhahn R, Shapiro N, et al. Diagnostic accuracy of a point-of-care troponin I assay for acute myocardial infarction within 3 hours after presentation in early presenters to the emergency department with chest pain. Am Heart J. 2012 Jan;163(1):74-80.

20. Lee-Lewandrowski E, Januzzi JL, Jr., Grisson R, Mohammed AA, Lewandrowski G, Lewandrowski K. Evaluation of first-draw whole blood, point-of-care cardiac markers in the context of the universal definition of myocardial infarction: a comparison of a multimarker panel to troponin alone and to testing in the central laboratory. Arch Pathol Lab Med. 2011 Apr;135(4):459-63.

21. Hjortshoj S, Venge P, Ravkilde J. Clinical performance of a new point-of-care cardiac troponin I assay compared to three laboratory troponin assays. Clin Chim Acta. 2011 Jan 30;412(3-4):370-5.

22. ter Avest E, Visser A, Reitsma B, Breedveld R, Wolthuis A. Point-of-care troponinT is inferior to high-sensitivity troponinT for ruling out acute myocardial infarction in the emergency department. Eur J Emerg Med. 2014 Dec 22.

23. Di Serio F, Amodio G, Varraso L, Campaniello M, Coluccia P, Trerotoli P, et al. Integration between point-of-care cardiac markers in an emergency/cardiology department and the central laboratory: methodological and preliminary clinical evaluation. Clin Chem Lab Med. 2005;43(2):202-9.

24. Di Serio F, Amodio G, Varraso L, Ruggieri V, Antonelli G, Pansini N. Point-of-care cardiac markers: clinical impact of the troponin 99th percentile cutoff and clinical utility of the myoglobin measurement in the early management of chest pain patients in a low to intermediate acute coronary syndrome risk population admitted to emergency cardiology department. Point Care. 2007 Sep;6(3):183-6.

25. Amodio G, Antonelli G, Varraso L, Ruggieri V, Di SF. Clinical impact of the troponin 99th percentile cut-off and clinical utility of myoglobin measurement in the early management of chest pain patients admitted to the Emergency Cardiology Department. Coron Artery Dis. 2007 May;18(3):181-6.

26. Ryan RJ, Lindsell CJ, Hollander JE, O'Neil B, Jackson R, Schreiber D, et al. A multicenter randomized controlled trial comparing central laboratory and point-of-care cardiac marker testing strategies: the Disposition Impacted by Serial Point of Care Markers in Acute Coronary Syndromes (DISPO-ACS) trial. Ann Emerg Med. 2009 Mar;53(3):321-8.

27. Koehler J, Flarity K, Hertner G, Aker J, Stout JP, Gifford M, et al. Effect of troponin I point-of-care testing on emergency department throughput measures and staff satisfaction. Adv Emerg Nurs J. 2013 Jul;35(3):270-7.

28. Meek R, Braitberg G, Nicolas C, Kwok G. Effect on emergency department efficiency of an accelerated diagnostic pathway for the evaluation of chest pain. Emerg Med Australas. 2012 Jun;24(3):285-93.
29. Renaud B, Maison P, Ngako A, Cunin P, Santin A, Hervé J, et al. Impact of point-of-care testing in the emergency department evaluation and treatment of patients with suspected acute coronary syndromes. Acad Emerg Med. 2008 Mar;15(3):216-24.
30. Singer AJ, Ardise J, Gulla J, Cangro J. Point-of-care testing reduces length of stay in emergency department chest pain patients. Ann Emerg Med. 2005 Jun;45(6):587-91.
31. Di Serio F, Antonelli G, Trerotoli P, Tampoia M, Matarrese A, Pansini N. Appropriateness of point-of-care testing (POCT) in an emergency department. Clin Chim Acta. 2003 Jul 15;333(2):185-9.
32. Caragher TE, Fernandez BB, Jacobs FL, Barr LA. Evaluation of quantitative cardiac biomarker point-of-care testing in the emergency department. J Emerg Med. 2002 Jan;22(1):1-7.
33. Altinier S, Zaninotto M, Mion M, Carraro P, Rocco S, Tosato F, et al. Point-of-care testing of cardiac markers: results from an experience in an Emergency Department. Clin Chim Acta. 2001 Sep 15;311(1):67-72.
34. Cramer GE, Kievit PC, Brouwer MA, de Keijzer MH, Luijten HE, Verheugt FW. Lack of concordance between a rapid bedside and conventional laboratory method of cardiac troponin testing: impact on risk stratification of patients suspected of acute coronary syndrome. Clin Chim Acta. 2007 Jun;381(2):164-6.
35. Mozina H, Vukan V, Lenart K, Skitek M, Osredkar J. Quantitative point-of-care troponin I in emergency department in comparison with troponin I in central laboratory. Point Care. 2010 Mar;9(1):8-11.
36. Storrow AB, Lindsell CJ, Collins SP, Fermann GJ, Blomkalns AL, Williams JM, et al. Emergency department multimarker point-of-care testing reduces time to cardiac marker results without loss of diagnostic accuracy. Point Care. 2006 Sep;5(3):132-6.
37. Lee-Lewandrowski E, Benzer T, Corboy D, Lewandrowski K. Cardiac marker testing as part of an emergency department point-of-care satellite laboratory in a large academic medical center: practical issues concerning implementation. Point Care. 2002 Sep;1(3):145-54.
38. Singer AJ, Williams J, Taylor M, Le Blanc D, Thode HC, Jr. Comprehensive bedside point of care testing in critical ED patients: a before and after study. Am J Emerg Med. 2015 Mar 18.
39. Goodacre S, Bradburn M, Fitzgerald P, Cross E, Collinson P, Gray A, et al. The RATPAC (Randomised Assessment of Treatment using Panel Assay of Cardiac markers) trial: a randomised controlled trial of point-of-care cardiac markers in the emergency department. Health Technol Assess [Internet]. 2011 May [cited 2015 Jan 30];15(23):iii-ixi. Available from: http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0004/64714/FullReport-hta15230.pdf
40. Loten C, Attia J, Hullick C, Marley J, McElduff P. Point of care troponin decreases time in the emergency department for patients with possible acute coronary syndrome: a randomised controlled trial. Emerg Med J. 2010 Mar;27(3):194-8.
41. Asha SE, Cooke A, Walter E, Weaver J. Three-month outcome of patients with suspected acute coronary syndrome using point-of-care cardiac troponin-T testing compared with laboratory-based cardiac troponin-T testing: a randomised trial. Emerg Med J. 2014 Sep 26.
42. Deledda JM, Fermann GJ, Lindsell CJ, Rohlfing RA, Gibler BW. Cardiac point-of-care testing: impact on emergency department door to disposition time is modified by patient acuity and hospital setting. Point Care. 2011 Mar;10(1):1-6.
43. Venge P, Lindahl B. Cardiac troponin assay classification by both clinical and analytical performance characteristics: a study on outcome prediction. Clin Chem [Internet]. 2013 Jun [cited 2015 Jan 29];59(6):976-81. Available from: http://www.clinchem.org/content/59/6/976.full.pdf+html

44. Cullen L, Parsonage WA, Greenslade J, Lamanna A, Hammett CJ, Than M, et al. Comparison of early biomarker strategies with the Heart Foundation of Australia/Cardiac Society of Australia and New Zealand guidelines for risk stratification of emergency department patients with chest pain. Emerg Med Australas. 2012 Dec;24(6):595-603.

45. Eggers KM, Jaffe AS, Venge P, Lindahl B. Clinical implications of the change of cardiac troponin I levels in patients with acute chest pain - an evaluation with respect to the Universal Definition of Myocardial Infarction. Clin Chim Acta. 2011 Jan 14;412(1-2):91-7.

46. Venge P, Öhberg C, Flodin M, Lindahl B. Early and late outcome prediction of death in the emergency room setting by point-of-care and laboratory assays of cardiac troponin I. Am Heart J. 2010 Nov;160(5):835-41.

47. Ordóñez-Llanos J, Santaló-Bel M, Merce-Muntanola J, Collinson PO, Gaze D, Haass M, et al. Risk stratification of chest pain patients by point-of-care cardiac troponin T and myoglobin measured in the emergency department. Clin Chim Acta. 2006 Mar;365(1-2):93-7.

48. Sorensen JT, Terkelsen CJ, Steengaard C, Lassen JF, Trautner S, Christensen EF, et al. Prehospital troponin T testing in the diagnosis and triage of patients with suspected acute myocardial infarction. Am J Cardiol. 2011 May 15;107(10):1436-40.

49. Apple FS, Chung AY, Kogut ME, Bubany S, Murakami MM. Decreased patient charges following implementation of point-of-care cardiac troponin monitoring in acute coronary syndrome patients in a community hospital cardiology unit. Clin Chim Acta. 2006 Aug;370(1-2):191-5.

50. Collinson PO, John C, Lynch S, Rao A, Canepa-Anson R, Carson E, et al. A prospective randomized controlled trial of point-of-care testing on the coronary care unit. Ann Clin Biochem. 2004 Sep;41(Pt 5):397-404.

51. Guo X, Feng J, Guo H. The predictive value of the bedside troponin T test for patients with acute chest pain. Exp Clin Cardiol [Internet]. 2006 [cited 2015 Jan 29];11(4):298-301. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2274843/pdf/ecc11298.pdf

52. Shephard MD, Spaeth BA, Mazzachi BC, Auld M, Schatz S, Lingwood A, et al. Toward sustainable point-of-care testing in remote Australia-the Northern Territory i-STAT point-of-care testing program. Point Care. 2014 Mar;13(1):6-11.

53. FitzGibbon F, Huckle D, Meenan BJ. Barriers affecting the adoption of point-of-care technologies used in chest pain diagnosis within the UK National Health Service: part 1-user issues. Point Care. 2010 Jun;9(2):70-9.

54. Liikanen E, Penttila I, Laitinen M, Vehvilainen-Julkunen K. Point-of-care testing for heart and cardiovascular diseases in Finnish health care units. Point Care. 2005 Jun;4(2):101-4.

55. Ezekowitz JA, Welsh RC, Weiss D, Chan M, Keeble W, Khadour F, et al. Providing rapid out of hospital acute cardiovascular treatment 4 (PROACT-4). J Am Heart Assoc. 2015;4(12).

56. Shephard MD, Spaeth B, Mazzachi BC, Auld M, Schatz S, Loudon J, et al. Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program. Aust J Rural Health. 2012 Feb;20(1):16-21.

57. Asha SE, Chan AC, Walter E, Kelly PJ, Morton RL, Ajami A, et al. Impact from point-of-care devices on emergency department patient processing times compared with central laboratory testing of blood samples: a randomised controlled trial and cost-effectiveness analysis. Emerg Med J. 2014 Sep;31(9):714-9.

58. FitzGibbon F, Brown A, Meenan BJ. Assessment of user perspectives of cardiac point of care technologies in chest pain diagnosis. Conf Proc IEEE Eng Med Biol Soc. 2007;2007:1762-5.

59. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J [Internet]. 2011 [cited 2014 Jan 29];32(23):2999-3054. Available from: http://eurheartj.oxfordjournals.org/content/ehj/32/23/2999.full.pdf

60. Nichols JH, Christenson RH, Clarke W, Gronowski A, Hammett-Stabler CA, Jacobs E, et al. Executive summary. The National Academy of Clinical Biochemistry Laboratory Medicine Practice Guideline: evidence-based practice for point-of-care testing. Clin Chim Acta. 2007;379(1-2):14-28.

61. Nilsson S, Andersson PO, Borgquist L, Grodzinsky E, Janzon M, Kvick M, et al. Point-of-care troponin T testing in the management of patients with chest pain in the Swedish primary care. Int J Family Med [Internet]. 2013 [cited 2015 Jan 29];2013. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3556440/pdf/IJFM2013-532093.pdf

62. Stengaard C, Sorensen JT, Ladefoged SA, Christensen EF, Lassen JF, Botker HE, et al. Quantitative point-of-care troponin T measurement for diagnosis and prognosis in patients with a suspected acute myocardial infarction. Am J Cardiol. 2013 Nov 1;112(9):1361-6.

63. Jalal S, Habib K, Rauoof MA. Prognostic significance of rapid bedside cardiac troponin T testing in unstable angina. Indian Heart J. 2002 Mar;54(2):220, 2002-220, 2Apr.

64. Bradburn M, Goodacre SW, Fitzgerald P, Coats T, Gray A, Hassan T, et al. Interhospital variation in the RATPAC trial (Randomised Assessment of Treatment using Panel Assay of Cardiac markers). Emerg Med J. 2012 Mar;29(3):233-8.

65. Bruins Slot MH, van der Heijden GJ, Stelpstra SD, Hoes AW, Rutten FH. Point-of-care tests in suspected acute myocardial infarction: a systematic review. Int J Cardiol. 2013 Oct 15;168(6):5355-62.

66. Storrow AB, Lyon JA, Porter MW, Zhou C, Han JH, Lindsell CJ. A systematic review of emergency department point-of-care cardiac markers and efficiency measures. Point Care. 2009 Sep;8(3):121-5.

67. Layfield C, Rose J, Alford A, Snyder SR, Apple FS, Chowdhury FM, et al. Effectiveness of practices for improving the diagnostic accuracy of Non ST Elevation Myocardial Infarction in the Emergency Department: A Laboratory Medicine Best Practices systematic review. Clin Biochem. 2015 Feb 7.

68. Halim S, Poyer J. Removal of hospital outpatient quality reporting measure (OQR) OP-16: troponin results for Emergency Department acute myocardial infarction (AMI) patients or chest pain patients (with Probable Cardiac Chest Pain) received within 60 minutes of arrival [Internet]. Centers for Medicare & Medicaid Services. Woodlawn (MD): 2012 Aug 13. [cited 2016 Feb 1]. Available from: http://www.aha.org/content/12/op-16.pdf

69. Kost GJ, Kost LE, Suwanyangyuen A, Cheema SK, Curtis C, Sumner S, et al. Emergency cardiac biomarkers and point-of-care testing: optimizing acute coronary syndrome care using small-world networks in rural settings. Point Care [Internet]. 2010 Jun [cited 2015 Feb 25];9(2):53-64. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2888163/pdf/nihms190092.pdf

70. Tideman P, Simpson P, Tirimacco R. Integrating PoCT into clinical care. Clin Biochem Rev [Internet]. 2010 Aug [cited 2015 Jan 29];31(3):99-104. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2924130/pdf/cbr31_3_pg99.pdf

71. Lipinski MJ, Baker NC, Escarcega RO, Torguson R, Chen F, Aldous SJ, et al. Comparison of conventional and high-sensitivity troponin in patients with chest pain: a collaborative meta-analysis. Am Heart J. 2015 Jan;169(1):6-16.

72. Bruins Slot MH, Rutten FH, van der Heijden GJ, Geersing GJ, Glatz JF, Hoes AW. Diagnosing acute coronary syndrome in primary care: comparison of the physicians' risk estimation and a clinical decision rule. Fam Pract. 2011 Jun;28(3):323-8.

73. Statistics Canada. Life tables, Canada, Provinces and Territories, 2012-2014. Ottawa: Statistics Canada; 2014.

74. Mittmann N, Trakas K, Risebrough N, Liu BA. Utility scores for chronic conditions in a community-dwelling population. Pharmacoeconomics. 1999 Apr;15(4):369-76.

75. Nikolic E, Janzon M, Hauch O, Wallentin L, Henriksson M, PLATO Health Economic Substudy Group. Cost-effectiveness of treating acute coronary syndrome patients with ticagrelor for 12 months: results from the PLATO study. Eur Heart J. 2013 Jan;34(3):220-8.
76. Ward S, Lloyd JM, Pandor A, Holmes M, Ara R, Ryan A, et al. A systematic review and economic evaluation of statins for the prevention of coronary events. Health Technol Assess. 2007 Apr;11(14):1-iv.
77. Thokala P, Goodacre SW, Collinson PO, Stevens JW, Mills NL, Newby DE, et al. Cost-effectiveness of presentation versus delayed troponin testing for acute myocardial infarction. Heart. 2012 Oct;98(20):1498-503.
78. Bank of Canada. Inflation calculator [Internet]. Ottawa: Bank of Canada; 2015. [cited 2015 Sep 15]. Available from: http://www.bankofcanada.ca/rates/related/inflation-calculator/
79. OCCI costing analysis tool. Toronto: Ontario Case Costing Initiative; 2012.
80. Ontario Ministry of Health and Long-term Care. Schedule of benefits for physician services under the Health Insurance Act [Internet]. Toronto: The Ministry; 2015. [cited 2015 Sep 15]. Available from: http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html
81. Goldberg RJ, Currie K, White K, Brieger D, Steg PG, Goodman SG, et al. Six-month outcomes in a multinational registry of patients hospitalized with an acute coronary syndrome (the Global Registry of Acute Coronary Events [GRACE]). Am J Cardiol. 2004 Feb 1;93(3):288-93.
82. Thygesen K, Mair J, Giannitsis E, Mueller C, Lindahl B, Blankenberg S, et al. How to use high-sensitivity cardiac troponins in acute cardiac care. Eur Heart J. 2012 Sep;33(18):2252-7.
83. Bennett M, Ignaszewski A. Acute coronary syndrome part 1: interpreting chest pain to pinpoint an accurate diagnosis. Parkhurst Exchange. 2006;14(5).
84. Shrive FM, Manns BJ, Galbraith PD, Knudtson ML, Ghali WA, APPROACH Investigators. Economic evaluation of sirolimus-eluting stents. CMAJ. 2005 Feb 1;172(3):345-51.
85. Mourad G, Alwin J, Stromberg A, Jaarsma T. Societal costs of non-cardiac chest pain compared with ischemic heart disease--a longitudinal study. BMC Health Serv Res. 2013;13:403.
86. Moesker M. Assessing the cost-effectiveness of point-of-care testing for primary care patients with symptoms suggestive of acute coronary syndrome: a threshold analysis [thesis on the Internet]. Enschede, Netherlands: University of Twente; 2014. [cited 2015 Dec 21]. Available from: http://essay.utwente.nl/66324/1/MOESKER_MA_MB.pdf
87. International Federation of Clinical Chemistry and Laboratory Medicine. Table. Analytical characteristics of commercial cardiac troponin I and T assays declared by the manufacturer. [Internet]. Milano (IT): The Federation; 2014 Nov. [cited 2015 Dec 16]. Available from: http://www.ifcc.org/media/276661/IFCC%20Troponin%20Tables%20ng_L%20DRAFT%20Update%20NOVEMBER%202014.pdf

Appendix 1: Point-of-Care Troponin Devices

Table 13: POC Troponin Devices

Manufacturer	Device Name	99th Percentile, mcg/L (% CV)
Abbott	i-STAT (cTnI)	80 (16.5)
Alere	• Cardio3 (cTnI) • Cardio2 • Triage Troponin I To be used with Triage MeterPro testing platform	Cardio3: 0.022 (17)
LifeSign/ Princeton BioMeditech Corp.	• LifeSign MI Troponin I • LifeSign MI Myoglobin/Troponin I • LifeSign MI CK-MB/Myoglobin/Troponin I	NR
Radiometer	AQT90 Flex	cTnI: 0.023 (12.3) cTnT: 0.017 (15.2)
Response Biomedical	RAMP	0.0100 (20)
Roche/Cobas	• Cobas h 232 (cTnT) • CARDIAC Trop T Sensitive • Cardiac Reader	NR
Siemens	Stratus CS (cTnI)	0.070 (10)
ZBx Corporation/Innova	• ZAP Troponin I • ZAP Troponin I/Myoglobin	NR

cTnI = cardiac troponin I; CTnT = cardiac troponin T; CV = coefficient of variation; NR = not reported; POC = point-of-care.

Appendix 2: Literature Search Strategy

Overview	
Interface:	Ovid
Databases:	Embase 1974 to 2015 (with daily update) MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present **Note:** Subject headings have been customized for each database. Duplicates between databases were removed in Ovid.
Date of search:	January 14, 2015
Alerts:	Monthly search updates began January 14, 2015 and ran until the final draft was completed (February 12, 2016)
Study types:	No filters were applied to limit the retrieval by study type Conference abstracts were removed
Limits:	Humans No date limits were applied
Syntax Guide	
/	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
adj	Requires words are adjacent to each other (in any order)
adj#	Adjacency within # number of words (in any order)
.ti	Title
.ab	Abstract
.pt	Publication type
.po	Population group [PsycInfo only]
.dm	Device manufacturer (in Embase)
.dv	Device trade name (in Embase)
use pmez	Limit search line to MEDLINE database only
use oemezd	Limit search line to Embase database only

Multi-database Strategy

#	Strategy
1	exp Troponin/
2	(troponin* or cTn* or TnI* or TnT*).ti,ab.
3	or/1-2
4	Point-of-Care Systems/
5	("point of care" or POC or POCT or near patient or bedside* or bed-side* or portable or hand-held or handheld or ambulatory or rapid screen* OR rapid diagnos* or test kit* or transportable).ti,ab.
6	((test* or assay) adj10 (rapid* or quick or remot* or immediate* or mobile)).ti,ab.
7	or/4-6
8	3 and 7
9	("i-STAT" or iSTAT or triage cardiac or cardio2 or cardio3 or Alfa Scientific or Instant View or (Vidas adj5 ultra) or miniVidas or LifeSign or Meritas or PathFast or Cardiac STATus or AQT90 or AQT90flex or (Response and RAMP) or Cobas h232 or "Cobas h 232" or Cardiac Reader or "Stratus CS" or (ZAP and troponin) or GEM Immuno).ti,ab.
10	(triage and Alere).ti,ab.
11	(bioMerieux and Vidas).ti,ab.
12	(Roche and ("Trop T" or "Troponin T" or TropT) and cardiac).ti,ab.
13	or/9-12

Multi-database Strategy	
#	**Strategy**
14	(3 or 7) and 13
15	8 or 14
16	15 use pmez
17	exp Troponin/
18	(troponin* or cTn* or TnI* or TnT*).ti,ab,dv,dm.
19	or/17-18
20	Point of care testing/
21	("point of care" or POC or POCT or near patient or bedside* or bed-side* or portable or hand-held or handheld or ambulatory or rapid screen* OR rapid diagnos* or test kit* or transportable).ti,ab.
22	((test* or assay) adj10 (rapid* or quick or remot* or immediate* or mobile)).ti,ab.
23	or/20-22
24	19 and 23
25	("i-STAT" or iSTAT or triage cardiac or cardio2 or cardio3 or Alfa Scientific or Instant View or (Vidas adj5 ultra) or miniVidas or LifeSign or Meritas or PathFast or Cardiac STATus or AQT90 or AQT90flex or (Response and RAMP) or Cobas h232 or "Cobas h 232" or Cardiac Reader or "Stratus CS" or (ZAP and troponin) or GEM Immuno).ti,ab,dv,dm.
26	(triage and Alere).ti,ab,dv,dm.
27	(bioMerieux and Vidas).ti,ab,dv,dm.
28	(Roche and ("Trop T" or "Troponin T" or TropT) and cardiac).ti,ab,dv,dm.
29	or/25-28
30	(19 or 23) and 29
31	24 or 30
32	31 use oemezd
33	16 or 32
34	exp animals/
35	exp animal experimentation/ or exp animal experiment/
36	exp models animal/
37	nonhuman/
38	exp vertebrate/ or exp vertebrates/
39	animal.po.
40	or/34-39
41	exp humans/
42	exp human experimentation/ or exp human experiment/
43	human.po.
44	or/41-43
45	40 not 44
46	33 not 45
47	conference abstract.pt.
48	46 not 47
49	remove duplicates from 48

Other Databases	
PubMed	Same MeSH, keywords, limits, and study types used as per MEDLINE search, with appropriate syntax used.
Cochrane Library Via Wiley	Same MeSH, keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Cochrane Library databases.

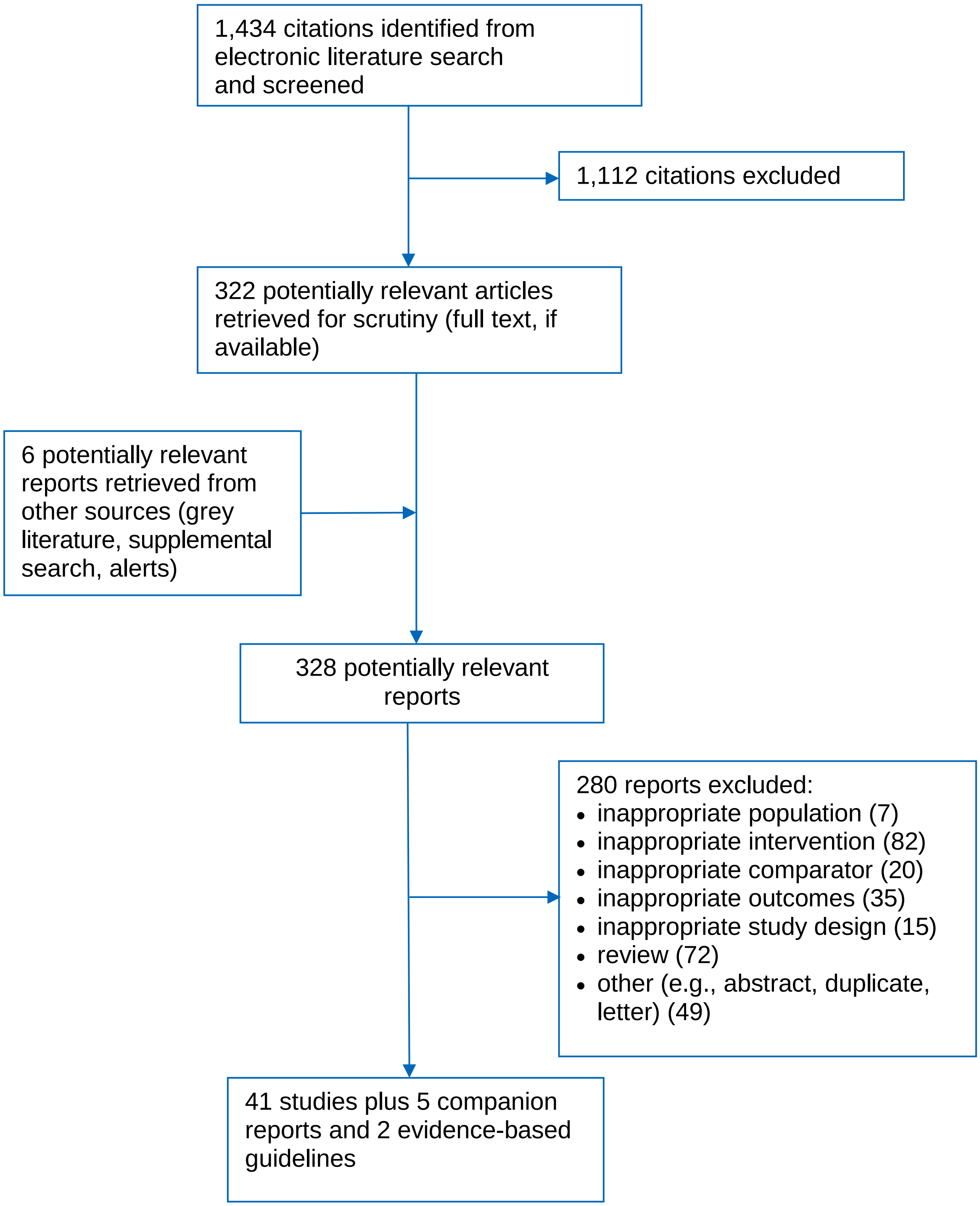
Grey Literature

Dates for Search:	January 2015
Keywords:	Included terms for point of care (POC) and troponin
Limits:	No date limits

Relevant websites from the following sections of the CADTH grey literature checklist, “Grey matters: a practical tool for searching health-related grey literature” (http://www.cadth.ca/resources/grey-matters), were searched:

- Health Technology Assessment Agencies
- Clinical Practice Guidelines
- Health Economics
- Advisories & Warnings
- Drug and Device Regulatory Approvals
- Databases (free) Internet Search.

Appendix 3: Flow Chart of Included Studies



Appendix 4: List of Included Diagnostic Accuracy and Clinical-Utility Studies

Aldous S, Mark RA, George PM, Cullen L, Parsonage WA, Flaws D, et al. Comparison of new point-of-care troponin assay with high-sensitivity troponin in diagnosing myocardial infarction. Int J Cardiol.2014 Nov 15;177(1):182-6.

Altinier S, Zaninotto M, Mion M, Carraro P, Rocco S, Tosato F, et al. Point-of-care testing of cardiac markers: results from an experience in an Emergency Department. Clin Chim Acta.2001 Sep 15;311(1):67-72.

Amodio G, Antonelli G, Varraso L, Ruggieri V, Di SF. Clinical impact of the troponin 99th percentile cut-off and clinical utility of myoglobin measurement in the early management of chest pain patients admitted to the Emergency Cardiology Department. Coron Artery Dis.2007 May;18(3):181-6.

Andersson PO, Karlsson JE, Landberg E, Festin K, Nilsson S. Consequences of high-sensitivity troponin T testing applied in a primary care population with chest pain compared with a commercially available point-of-care troponin T analysis: an observational prospective study. BMC Res Notes [Internet].2015 [cited 2015 Jul 23];8:210. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4467613/pdf/13104_2015_Article_1174.pdf

Apple FS, Chung AY, Kogut ME, Bubany S, Murakami MM. Decreased patient charges following implementation of point-of-care cardiac troponin monitoring in acute coronary syndrome patients in a community hospital cardiology unit. Clin Chim Acta.2006 Aug;370(1-2):191-5.

Asha SE, Chan AC, Walter E, Kelly PJ, Morton RL, Ajami A, et al. Impact from point-of-care devices on emergency department patient processing times compared with central laboratory testing of blood samples: a randomised controlled trial and cost-effectiveness analysis. Emerg Med J.2014 Sep;31(9):714-9.

Asha SE, Cooke A, Walter E, Weaver J. Three-month outcome of patients with suspected acute coronary syndrome using point-of-care cardiac troponin-T testing compared with laboratory-based cardiac troponin-T testing: a randomised trial. Emerg Med J.2014 Sep 26.

Caragher TE, Fernandez BB, Jacobs FL, Barr LA. Evaluation of quantitative cardiac biomarker point-of-care testing in the emergency department. J Emerg Med.2002 Jan;22(1):1-7.

Collinson PO, John C, Lynch S, Rao A, Canepa-Anson R, Carson E, et al. A prospective randomized controlled trial of point-of-care testing on the coronary care unit. Ann Clin Biochem.2004 Sep;41(Pt 5):397-404.

Cramer GE, Kievit PC, Brouwer MA, de Keijzer MH, Luijten HE, Verheugt FW. Lack of concordance between a rapid bedside and conventional laboratory method of cardiac troponin testing: impact on risk stratification of patients suspected of acute coronary syndrome. Clin Chim Acta.2007 Jun;381(2):164-6.

Cullen L, Parsonage WA, Greenslade J, Lamanna A, Hammett CJ, Than M, et al. Comparison of early biomarker strategies with the Heart Foundation of Australia/Cardiac Society of Australia and New Zealand guidelines for risk stratification of emergency department patients with chest pain. Emerg Med Australas.2012 Dec;24(6):595-603.

Deledda JM, Fermann GJ, Lindsell CJ, Rohlfing RA, Gibler BW. Cardiac point-of-care testing: impact on emergency department door to disposition time is modified by patient acuity and hospital setting. Point Care.2011 Mar;10(1):1-6.

Di Serio F, Amodio G, Varraso L, Campaniello M, Coluccia P, Trerotoli P, et al. Integration between point-of-care cardiac markers in an emergency/cardiology department and the central laboratory: methodological and preliminary clinical evaluation. Clin Chem Lab Med.2005;43(2):202-9.

Di Serio F, Amodio G, Varraso L, Ruggieri V, Antonelli G, Pansini N. Point-of-care cardiac markers: clinical impact of the troponin 99th percentile cutoff and clinical utility of the myoglobin measurement in the early management of chest pain patients in a low to intermediate acute coronary syndrome risk population admitted to emergency cardiology department. Point Care.2007 Sep;6(3):183-6.

Di Serio F, Antonelli G, Trerotoli P, Tampoia M, Matarrese A, Pansini N. Appropriateness of point-of-care testing (POCT) in an emergency department. Clin Chim Acta.2003 Jul 15;333(2):185-9.

Diercks DB, Peacock WF, Hollander JE, Singer AJ, Birkhahn R, Shapiro N, et al. Diagnostic accuracy of a point-of-care troponin I assay for acute myocardial infarction within 3 hours after presentation in early presenters to the emergency department with chest pain. Am Heart J.2012 Jan;163(1):74-80.

Eggers KM, Jaffe AS, Venge P, Lindahl B. Clinical implications of the change of cardiac troponin I levels in patients with acute chest pain - an evaluation with respect to the Universal Definition of Myocardial Infarction. Clin Chim Acta.2011 Jan 14;412(1-2):91-7.

Ezekowitz JA, Welsh RC, Weiss D, Chan M, Keeble W, Khadour F, et al. Providing rapid out of hospital acute cardiovascular treatment 4 (PROACT-4). J Am Heart Assoc. 2015;4(12).

FitzGibbon F, Brown A, Meenan BJ. Assessment of user perspectives of cardiac point of care technologies in chest pain diagnosis. Conf Proc IEEE Eng Med Biol Soc.2007;2007:1762-5, 2007.:-5.

FitzGibbon F, Huckle D, Meenan BJ. Barriers affecting the adoption of point-of-care technologies used in chest pain diagnosis within the UK National Health Service: part 1-user issues. Point Care.2010 Jun;9(2):70-9.

Goodacre S, Bradburn M, Fitzgerald P, Cross E, Collinson P, Gray A, et al. The RATPAC (Randomised Assessment of Treatment using Panel Assay of Cardiac markers) trial: a randomised controlled trial of point-of-care cardiac markers in the emergency department. Health Technol Assess [Internet].2011 May [cited 2015 Jan 30];15(23):iii-ixi. Available from: http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0004/64714/FullReport-hta15230.pdf

Guo X, Feng J, Guo H. The predictive value of the bedside troponin T test for patients with acute chest pain.Exp Clin Cardiol [Internet].2006 [cited 2015 Jan 29];11(4):298-301. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2274843/pdf/ecc11298.pdf

Hjortshoj S, Venge P, Ravkilde J. Clinical performance of a new point-of-care cardiac troponin I assay compared with three laboratory troponin assays. Clin Chim Acta.2011 Jan 30;412(3-4):370-5.

Ivandic BT, Spanuth E, Giannitsis E. Performance of the AQT90 FLEX cTnI point-of-care assay for the rapid diagnosis of acute myocardial infarction in the emergency room. Clin Lab.2014;60(6):903-8.

Koehler J, Flarity K, Hertner G, Aker J, Stout JP, Gifford M, et al. Effect of troponin I point-of-care testing on emergency department throughput measures and staff satisfaction. Adv Emerg Nurs J.2013 Jul;35(3):270-7.

Lee-Lewandrowski E, Benzer T, Corboy D, Lewandrowski K. Cardiac marker testing as part of an emergency department point-of-care satellite laboratory in a large academic medical center: practical issues concerning implementation. Point Care.2002 Sep;1(3):145-54.

Lee-Lewandrowski E, Januzzi JL, Jr., Grisson R, Mohammed AA, Lewandrowski G, Lewandrowski K. Evaluation of first-draw whole blood, point-of-care cardiac markers in the context of the universal definition of myocardial infarction: a comparison of a multimarker panel to troponin alone and to testing in the central laboratory. Arch Pathol Lab Med.2011 Apr;135(4):459-63.

Liikanen E, Penttila I, Laitinen M, Vehvilainen-Julkunen K. Point-of-care testing for heart and cardiovascular diseases in Finnish health care units.Point Care.2005 Jun;4(2):101-4.

Loten C, Attia J, Hullick C, Marley J, McElduff P. Point of care troponin decreases time in the emergency department for patients with possible acute coronary syndrome: a randomised controlled trial. Emerg Med J.2010 Mar;27(3):194-8.

Meek R, Braitberg G, Nicolas C, Kwok G. Effect on emergency department efficiency of an accelerated diagnostic pathway for the evaluation of chest pain. Emerg Med Australas.2012 Jun;24(3):285-93.

Mozina H, Vukan V, Lenart K, Skitek M, Osredkar J. Quantitative point-of-care troponin I in emergency department in comparison with troponin I in central laboratory. Point Care.2010 Mar;9(1):8-11.

Nilsson S, Andersson PO, Borgquist L, Grodzinsky E, Janzon M, Kvick M, et al. Point-of-Care Troponin T Testing in the Management of Patients with Chest Pain in the Swedish Primary Care. Int J Family Med [Internet].2013 [cited 2015 Jan 29];2013. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3556440/pdf/IJFM2013-532093.pdf

Ordóñez-Llanos J, Santaló-Bel M, Merce-Muntanola J, Collinson PO, Gaze D, Haass M, et al. Risk stratification of chest pain patients by point-of-care cardiac troponin T and myoglobin measured in the emergency department. Clin Chim Acta.2006 Mar;365(1-2):93-7.

Palamalai V, Murakami MM, Apple FS. Diagnostic performance of four point of care cardiac troponin I assays to rule in and rule out acute myocardial infarction. Clin Biochem.2013 Nov;46(16-17):1631-5.

Renaud B, Maison P, Ngako A, Cunin P, Santin A, Hervé J, et al. Impact of point-of-care testing in the emergency department evaluation and treatment of patients with suspected acute coronary syndromes. Acad Emerg Med.2008 Mar;15(3):216-24.

Ryan RJ, Lindsell CJ, Hollander JE, O'Neil B, Jackson R, Schreiber D, et al. A multicenter randomized controlled trial comparing central laboratory and point-of-care cardiac marker testing strategies: the Disposition Impacted by Serial Point of Care Markers in Acute Coronary Syndromes (DISPO-ACS) trial. Ann Emerg Med.2009 Mar;53(3):321-8.

Shephard MD, Spaeth B, Mazzachi BC, Auld M, Schatz S, Loudon J, et al. Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program. Aust J Rural Health.2012 Feb;20(1):16-21.

Shephard MD, Spaeth BA, Mazzachi BC, Auld M, Schatz S, Lingwood A, et al. Toward sustainable point-of-care testing in remote Australia-the Northern Territory i-STAT point-of-care testing program. Point Care.2014 Mar;13(1):6-11.

Singer AJ, Ardise J, Gulla J, Cangro J. Point-of-care testing reduces length of stay in emergency department chest pain patients. Ann Emerg Med.2005 Jun;45(6):587-91.

Singer AJ, Williams J, Taylor M, Le Blanc D, Thode HC, Jr. Comprehensive bedside point of care testing in critical ED patients: a before and after study. Am J Emerg Med.2015 Mar 18.

Sorensen JT, Terkelsen CJ, Steengaard C, Lassen JF, Trautner S, Christensen EF, et al. Prehospital troponin T testing in the diagnosis and triage of patients with suspected acute myocardial infarction. Am J Cardiol.2011 May 15;107(10):1436-40.

Stengaard C, Sorensen JT, Ladefoged SA, Christensen EF, Lassen JF, Botker HE, et al. Quantitative point-of-care troponin T measurement for diagnosis and prognosis in patients with a suspected acute myocardial infarction. Am J Cardiol.2013 Nov 1;112(9):1361-6.

Storrow AB, Lindsell CJ, Collins SP, Fermann GJ, Blomkalns AL, Williams JM, et al. Emergency department multimarker point-of-care testing reduces time to cardiac marker results without loss of diagnostic accuracy. Point Care.2006 Sep;5(3):132-6.

ter Avest E, Visser A, Reitsma B, Breedveld R, Wolthuis A. Point-of-care troponinT is inferior to high-sensitivity troponinT for ruling out acute myocardial infarction in the emergency department. Eur J Emerg Med.2014 Dec 22.

Venge P, Lindahl B. Cardiac troponin assay classification by both clinical and analytical performance characteristics: a study on outcome prediction. Clin Chem [Internet].2013 Jun [cited 2015 Jan 29];59(6):976-81. Available from: http://www.clinchem.org/content/59/6/976.full.pdf+html

Venge P, Öhberg C, Flodin M, Lindahl B. Early and late outcome prediction of death in the emergency room setting by point-of-care and laboratory assays of cardiac troponin I. Am Heart J.2010 Nov;160(5):835-41.

Included Guidelines

Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST segment elevation. Eur Heart J [Internet]. 2011 [cited 2015 Jan 29];32(23):2999-3054. Available from: http://eurheartj.oxfordjournals.org/content/ehj/32/23/2999.full.pdf

Nichols JH, Christenson RH, Clarke W, Gronowski A, Hammett-Stabler CA, Jacobs E, et al. Executive summary. The National Academy of Clinical Biochemistry Laboratory Medicine Practice Guideline: Evidence-based practice for point-of-care testing. Clin Chim Acta. 2007;379(1-2):14-28.

Appendix 5: List of Excluded Studies

Inappropriate Population

Apple FS, Ler R, Murakami MM. Determination of 19 cardiac troponin I and T assay 99th percentile values from a common presumably healthy population. Clin Chem [Internet].2012 Nov [cited 2015 Jan 29];58(11):1574-81. Available from: http://www.clinchem.org/content/58/11/1574.full.pdf+html

Calzavacca P, Licari E, Tee A, Bellomo R. Point-of-care testing during medical emergency team activations: a pilot study. Resuscitation.2012 Sep;83(9):1119-23.

Christenson RH, Fitzgerald RL, Ochs L, Rozenberg M, Frankel WL, Herold DA, et al. Characteristics of a 20-minute whole blood rapid assay for cardiac troponin T. Clin Biochem.1997 Feb;30(1):27-33.

De Antonio M, Lupon J, Galan A, Vila J, Zamora E, Urrutia A, et al. Head-to-head comparison of high-sensitivity troponin T and sensitive-contemporary troponin I regarding heart failure risk stratification. Clin Chim Acta.2013 Nov 15;426:18-24.

Lee W, Jung J, Hahn YK, Kim SK, Lee Y, Lee J, et al. A centrifugally actuated point-of-care testing system for the surface acoustic wave immunosensing of cardiac troponin I. Analyst.2013 May 7;138(9):2558-66.

Rittoo D, Jones A, Lecky B, Neithercut D. Elevation of cardiac troponin T, but not cardiac troponin I, in patients with neuromuscular diseases: implications for the diagnosis of myocardial infarction. J Am Coll Cardiol.2014 Jun 10;63(22):2411-20.

Steinfelder-Visscher J, Teerenstra S, Gunnewiek JM, Weerwind PW. Evaluation of the i-STAT point-of-care analyzer in critically ill adult patients. J Extra Corporeal Technol.2008 Mar;40(1):57-60.

Inappropriate Intervention

Agewall S. Evaluation of point-of-care test systems using the new definition of myocardial infarction. Clin Biochem.2003 Feb;36(1):27-30.

Aldous SJ, Richards MA, Cullen L, Troughton R, Than M. A new improved accelerated diagnostic protocol safely identifies low-risk patients with chest pain in the emergency department. Acad Emerg Med.2012 May;19(5):510-6.

Altinier S, Zaninotto M, Mion MM, Plebani M. Innotrac Aio!: a point-of-care or a routine analyzer? Analytical performance and plasma/whole blood comparison. Clin Chem Lab Med.2006;44(10):1278-82.

Antman EM, Grudzien C, Sacks DB. Evaluation of a rapid bedside assay for detection of serum cardiac troponin T. JAMA.1995 Apr 26;273(16):1279-82.

Apple FS, Anderson FP, Collinson P, Jesse RL, Kontos MC, Levitt MA, et al. Clinical evaluation of the first medical whole blood, point-of-care testing device for detection of myocardial infarction. Clin Chem [Internet].2000 Oct [cited 2015 Feb 18];46(10):1604-9. Available from: http://www.clinchem.org/content/46/10/1604.full.pdf+html

Apple FS, Christenson RH, Valdes R, Jr., Andriak AJ, Berg A, Duh SH, et al. Simultaneous rapid measurement of whole blood myoglobin, creatine kinase MB, and cardiac troponin I by the triage cardiac panel for detection of myocardial infarction. Clin Chem.1999 Feb;45(2):199-205.

Apple FS, Smith SW, Pearce LA, Ler R, Murakami MM, Benoit MO, et al. Use of the bioMerieux VIDAS troponin I ultra assay for the diagnosis of myocardial infarction and detection of adverse events in patients presenting with symptoms suggestive of acute coronary syndrome. Clin Chim Acta.2008 Apr;390(1-2):72-5.

Balmelli C, Meune C, Twerenbold R, Reichlin T, Rieder S, Drexler B, et al. Comparison of the performances of cardiac troponins, including sensitive assays, and copeptin in the diagnostic of acute myocardial infarction and long-term prognosis between women and men. Am Heart J.2013 Jul;166(1):30-7.

Birkhahn RH, Wen W, Datillo PA, Briggs WM, Parekh A, Arkun A, et al. Improving patient flow in acute coronary syndromes in the face of hospital crowding. J Emerg Med.2012 Aug;43(2):356-65.

Buffet-Bataillon S, Incaurgarat B, Tourneur C, Varret F, Coisne D, Mauco G, et al. Evaluation of troponin Ic assay using VIDAS bioMerieux. Immuno-Analyse et Biologie Specialisee.2002;17(5):326-9.

Bugugnani MJ. [Triage Cardiac Panel BioSite: evaluation of analytical performances]. Immuno-Analyse et Biologie Specialisee.2000;15(3):191-3. French.

Charpentier S, Maupas-Schwalm F, Cournot M, Elbaz M, Botella JM, Lauque D. Combination of copeptin and troponin assays to rapidly rule out non-ST elevation myocardial infarction in the emergency department. Acad Emerg Med.2012 May;19(5):517-24.

Collinson PO, Gaze D, Goodacre S. The clinical and diagnostic performance characteristics of the high sensitivity Abbott cardiac troponin I assay. Clin Biochem.2014 Dec 27.

Davarani H, Afzalimoghadam M, Hosseinnejad H, Hamidian R. Increasing serum troponin I and early prognosis in patients with chest pain or angina equivalent symptoms in the emergency department. Iran J Public Health [Internet].2012 [cited 2015 Jan 30];41(2):63-9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3481681

DeFilippi CR, Parmar RJ, Potter MA, Tocchi M. Diagnostic accuracy, angiographic correlates and long-term risk stratification with the troponin T ultra sensitive Rapid Assay in chest pain patients at low risk for acute myocardial infarction. Eur Heart J.1998 Nov;19 Suppl N:N42-7.

Derhaschnig U, Hirschl MM, Collinson PO, Gaze D, Haass M, Katus HA, et al. Diagnostic efficiency of a point-of-care system for quantitative determination of troponin T and myoglobin in the coronary care unit. Point Care.2004 Dec;3(4):162-4.

Dittmer WU, Evers TH, Hardeman WM, Huijnen W, Kamps R, de Kievit P, et al. Rapid, high sensitivity, point-of-care test for cardiac troponin based on optomagnetic biosensor. Clin Chim Acta.2010 Jun 3;411(11-12):868-73.

Eggers KM, Oldgren J, Berg A, Lindahl B. Analytic performance of a point-of-care instrument for measurement of cardiac markers: an evaluation under clinical conditions. Point Care.2003 Dec;2(4):235-42.

Ervasti M, Penttila K, Siltari S, Delezuch W, Punnonen K. Diagnostic, clinical and laboratory turnaround times in troponin T testing. Clin Chem Lab Med.2008;46(7):1030-2.

Ezekowitz JA, Welsh RC, Gubbels C, Brass N, Chan M, Keeble W, et al. Providing rapid out of hospital acute cardiovascular treatment 3 (PROACT-3). Can J Cardiol.2014 Oct;30(10):1208-15.

Farsi D, Pishbin E, Abbasi S, Hafezimoghadam P, Fathi M, Zare MA. Operating characteristics of a qualitative troponin assay for the diagnosis of acute coronary syndrome. Eur J Emerg Med.2013 Apr;20(2):120-2.

Flores-Solís LM, Hernández-Domínguez JL. Cardiac troponin I in patients with chronic kidney disease stage 3 to 5 in conditions other than acute coronary syndrome. Clin Lab.2014;60(2):281-90.

Gerhardt W, Ljungdahl L, Collinson PO, Lovis C, Mach F, Sylvén C, et al. An improved rapid troponin T test with a decreased detection limit: a multicentre study of the analytical and clinical performance in suspected myocardial damage. Scand J Clin Lab Invest.1997 Oct;57(6):549-57.

Goldmann BU, Langenbrink L, Matschuck G, Heeschen C, Kolbe-Busch S, Niederau C, et al. Quantitative bedside testing of troponin T: is it equal to laboratory testing? The Cardiac Reader Troponin T (CARE T) study. Clin Lab.2004;50(1-2):1-10.

Gruson D, Thys F, Ketelslegers JM, Pasquet A, Delvau N, Deneys V, et al. Multimarker panel in patients admitted to emergency department: a comparison with reference methods. Clin Biochem.2009 Feb;42(3):185-8.

Gupta S, Singh KN, Bapat V, Mishra V, Agarwal DK, Gupta P. Diagnosis of acute myocardial infarction: CK-MB versus cTn-T in Indian patients. Indian J Clin Biochem [Internet].2008 Jan [cited 2015 Jan 30];23(1):89-91. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3453645

Hafner G, Peetz D, Dati F, Post F, Blankenberg S, Peivandi AA, et al. Analytical and clinical evaluation of troponin I determination on dimension RXL-HM. Clin Chem Lab Med.2000;38(4):355-61.

Hallani H, Leung DY, Newland E, Juergens CP. Use of a quantitative point-of-care test for the detection of serum cardiac troponin T in patients with suspected acute coronary syndromes. Intern Med J.2005 Sep;35(9):560-2.

Hamilton AJ, Swales LA, Neill J, Murphy JC, Darragh KM, Rocke LG, et al. Risk stratification of chest pain patients in the emergency department by a nurse utilizing a point of care protocol. Eur J Emerg Med.2008 Feb;15(1):9-15.

Hamm CW, Goldmann BU, Heeschen C, Kreymann G, Berger J, Meinertz T. Emergency room triage of patients with acute chest pain by means of rapid testing for cardiac troponin T or troponin I. N Engl J Med.1997 Dec 4;337(23):1648-53.

Hammerer-Lercher A, Ploner T, Neururer S, Schratzberger P, Griesmacher A, Pachinger O, et al. High-sensitivity cardiac troponin T compared with standard troponin T testing on emergency department admission: How much does it add in everyday clinical practice? J Am Heart Assoc [Internet].2013[cited 2016 Mar 08];2(3). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3698787/pdf/jah3-2-e000204.pdf

Hayat U, Motwani J, Burrell CJ. Troponin-I positivity in patients referred to rapid access chest pain clinic. J Ayub Med Coll Abbottabad.2010 Oct;22(4):3-5.

Heeschen C, Goldmann BU, Moeller RH, Hamm CW. Analytical performance and clinical application of a new rapid bedside assay for the detection of serum cardiac troponin I. Clin Chem.1998 Sep;44(9):1925-30.

Hindle HR, Hindle SK. Qualitative troponin I estimation in the diagnosis of acute coronary syndromes in three rural hospitals. Can J Rural Med.2005;10(4):225-30.

Hirschl MM, Lechleitner P, Friedrich G, Sint G, Sterz F, Binder M, et al. Usefulness of a new rapid bedside troponin T assay in patients with chest pain. Resuscitation.1996 Oct;32(3):193-8.

Hisamuddin NN, Suhailan MA. Evaluation of the diagnostic indices and clinical utility of qualitative cardiodetect test kit in diagnosis of ami within 12 hours of onset of chest pain in the emergency department.Int J Emerg Med [Internet].2011 [cited 2015 Jan 30];4:67. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3219693

Ho CH, Cheng W, Chu G, Ho HF. Early diagnosis of acute myocardial infarction by bedside multimarker test at an emergency department in Hong Kong.Hong Kong Journal of Emergency Medicine [Internet].2010 [cited 2015 Jan 29];17(2):142-8. Available from: http://www.hkjem.com/sites/default/files/p142-148.pdf

Hong B, Kai J, Ren Y, Han J, Zou Z, Ahn CH, et al. Highly sensitive rapid, reliable, and automatic cardiovascular disease diagnosis with nanoparticle fluorescence enhancer and mems. Adv Exp Med Biol.2008;614:265-73.

Illahi MN, Lapworth R, Bates P. The effect of point of care testing on clinical decision making in an emergency department.Journal of the Liaquat University of Medical and Health Sciences.2012;11(3):153-7.

James SK, Lindahl B, Armstrong P, Califf R, Simoons ML, Venge P, et al. A rapid troponin I assay is not optimal for determination of troponin status and prediction of subsequent cardiac events at suspicion of unstable coronary syndromes. Int J Cardiol.2004 Feb;93(2-3):113-20.

Kar P, Pandey A, Greer JJ, Shankar K. Ultrahigh sensitivity assays for human cardiac troponin I using TiO2 nanotube arrays. Lab chip.2012 Feb 21;12(4):821-8.

Kim TK, Oh SW, Hong SC, Mok YJ, Choi EY.Point-of-care fluorescence immunoassay for cardiac panel biomarkers.J Clin Lab Anal.2014 Nov;28(6):419-27.

Kratz A, Januzzi JL, Lewandrowski KB, Lee-Lewandrowski E. Positive predictive value of a point-of-care testing strategy on first-draw specimens for the emergency department-based detection of acute coronary syndromes. Arch Pathol Lab Med.2002 Dec;126(12):1487-93.

Kratz A, Lewandrowski KB, McDermott S, Chun KY, Lee-Lewandrowski E. Performance of a point-of-care qualitative triple cardiac marker screen under controlled laboratory conditions and in an emergency department setting. Clin Chim Acta.2002 Nov;325(1-2):79-85.

Kurihara T, Yanagida A, Yokoi H, Koyata A, Matsuya T, Ogawa J, et al. Evaluation of cardiac assays on a benchtop chemiluminescent enzyme immunoassay analyzer, PATHFAST. Anal Biochem.2008 Apr 1;375(1):144-6.

Law K, Elley R, Tietjens J, Mann S. Troponin testing for chest pain in primary healthcare: a survey of its use by general practitioners in New Zealand. N Z Med J.2006;119(1238):U2082.

Lee CY, Whitman B, Chen J, Fung A, Lin X. Monoclonal antibody-based immunoassays for reliable clinical detection of human cardiac troponin I. J Clin Ligand Assay.2002;25(3):306-11.

Liang Y, Chan CP, Cheung KY, Cautherley GW, Glatz JF, Renneberg R, et al. CardioDetect rapid test for the diagnosis of early acute myocardial infarction. J Immunoassay Immunochem.2011;32(4):342-52.

Lüscher MS, Ravkilde J, Thygesen K. Clinical application of two novel rapid bedside tests for the detection of cardiac troponin T and creatine kinase-MB mass/myoglobin in whole blood in acute myocardial infarction. Cardiology.1998 Mar;89(3):222-8.

Macdonald SP, Nagree Y. Rapid risk stratification in suspected acute coronary syndrome using serial multiple cardiac biomarkers: a pilot study. Emerg Med Australas.2008 Oct;20(5):403-9.

Mach F, Lovis C, Chevrolet JC, Urban P, Unger PF, Bouillie M, et al. Rapid bedside whole blood cardiospecific troponin T immunoassay for the diagnosis of acute myocardial infarction. Am J Cardiol.1995 Apr 15;75(12):842-5.

McCord J, Nowak RM, McCullough PA, Foreback C, Borzak S, Tokarski G, et al. Ninety-minute exclusion of acute myocardial infarction by use of quantitative point-of-care testing of myoglobin and troponin I. Circulation [Internet].2001 Sep 25 [cited 2015 Feb 18];104(13):1483-8. Available from: http://circ.ahajournals.org/content/104/13/1483.full.pdf+html

McCullough PA, Nowak RM, Foreback C, Tokarski G, Tomlanovich MC, Khoury NE, et al. Performance of multiple cardiac biomarkers measured in the emergency department in patients with chronic kidney disease and chest pain. Acad Emerg Med.2002 Dec;9(12):1389-96.

McErlean ES, Deluca SA, van LF, Peacock F, Rao JS, Balog CA, et al. Comparison of troponin T versus creatine kinase-MB in suspected acute coronary syndromes. Am J Cardiol.2000 Feb 15;85(4):421-6.

Mogensen CB, Borch A, Brandslund I. Point of care technology or standard laboratory service in an emergency department: is there a difference in time to action? A randomised trial.Scand J Trauma Resusc Emerg Med [Internet].2011 [cited 2015 Mar 13];19:49. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3180400

Mueller M, Biener M, Vafaie M, Blankenberg S, White HD, Katus HA, et al. Prognostic performance of kinetic changes of high-sensitivity troponin T in acute coronary syndrome and in patients with increased troponin without acute coronary syndrome. Int J Cardiol.2014 Jul 1;174(3):524-9.

Muller-Bardorff M, Freitag H, Scheffold T, Remppis A, Kubler W, Katus HA. Development and characterization of a rapid assay for bedside determinations of cardiac troponin T. Circulation.1995 Nov 15;92(10):2869-75.

Muller-Bardorff M, Rauscher T, Kampmann M, Schoolmann S, Laufenberg F, Mangold D, et al. Quantitative bedside assay for cardiac troponin T: a complementary method to centralized laboratory testing. Clin Chem [Internet].1999 Jul [cited 2015 Jan 29];45(7):1002-8. Available from: http://www.clinchem.org/content/45/7/1002.full.pdf+html

Muller-Bardorff M, Sylven C, Rasmanis G, Jorgensen B, Collinson PO, Waldenhofer U, et al. Evaluation of a point-of-care system for quantitative determination of troponin T and myoglobin. Clin Chem Lab Med.2000 Jun;38(6):567-74.

Newman J, Aulick N, Cheng T, Faynor S, Curtis R, Mercer D, et al. Prehospital identification of acute coronary ischemia using a troponin T rapid assay. Prehosp Emerg Care.1999 Apr;3(2):97-101.

Oh SK, Foster K, Datta P, Orswell M, Tasaico K, Mai X, et al. Use of a dual monoclonal solid phase and a polyclonal detector to create an immunoassay for the detection of human cardiac troponin I. Clin Biochem.2000 Jun;33(4):255-62.

Ohman EM, Armstrong PW, White HD, Granger CB, Wilcox RG, Weaver WD, et al. Risk stratification with a point-of-care cardiac troponin T test in acute myocardial infarction.GUSTOIII Investigators. Global Use of Strategies To Open Occluded Coronary Arteries. Am J Cardiol.1999 Dec 1;84(11):1281-6.

Osredkar J, Mozina H, Lenart K, Skitek M. Quantitative point-of-care (POC) tropinin I in emergency department in comparison to troponin I in central laboratory. Point Care.2008 Sep;7(3):147.

Owen JJ, Worster A, Marie WB, Ward J, Kavsak P, Hill S. Root cause analysis of delays to discharge for patients held for serial cardiac troponin levels. CJEM [Internet].2014 [cited 2015 Jan 29];16(1):20-4. Available from: http://www.cjem-online.ca/sites/cjem-online.ca/files/CJEM_2013_131027.pdf

Panteghini M, Cuccia C, Pagani F, Turla C. Comparison of the diagnostic performance of two rapid bedside biochemical assays in the early detection of acute myocardial infarction. Clin Cardiol.1998 Jun;21(6):394-8.

Penttilä K, Koukkunen H, Halinen M, Punnonen K, Pyärälä K, Rantanen T, et al. Serum and plasma as alternative sample types in analysis of cardiac markers in the clinical routine. Scand J Clin Lab Invest.2002;62(7):553-60.

Planer D, Leibowitz D, Paltiel O, Boukhobza R, Lotan C, Weiss TA. The diagnostic value of troponin T testing in the community setting. Int J Cardiol.2006 Mar 8;107(3):369-75.

Rao MP, Panduranga P, Al-Mukhaini M, Sulaiman K, Al-Jufaili M. Predictive value of a 4-hour accelerated diagnostic protocol in patients with suspected ischemic chest pain presenting to an emergency department. Oman Medical Journal [Internet].2012 May [cited 2015 Jan 29];27(3):207-11. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3394349/pdf/OMJ-D-11-00162.pdf

Rathore S, Knowles P, Mann AP, Dodds PA. Is it safe to discharge patients from accident and emergency using a rapid point of care Triple Cardiac Marker test to rule out acute coronary syndrome in low to intermediate risk patients presenting with chest pain? Eur J Intern Med.2008 Nov;19(7):537-40.

Saadeddin S, Habbab M, Siddieg H, Fayomi M, Dafterdar R. Reliability of the rapid bedside whole-blood quantitative cardiac troponin T assay in the diagnosis of myocardial injury in patients with acute coronary syndrome. Med Sci Monit.2004 Mar;10(3):MT43-MT46.

Scharnhorst V, Krasznai K, van't Veer M, Michels R. Rapid detection of myocardial infarction with a sensitive troponin test. Am J Clin Pathol.2011 Mar;135(3):424-8.

Sireci AN. Hematology Testing in Urgent Care and Resource-Poor Settings.An Overview of Point of Care and Satellite Testing. Clin Lab Med.2015;35(1):197-207.

Straface AL, Myers JH, Kirchick HJ, Blick KE. A rapid point-of-care cardiac marker testing strategy facilitates the rapid diagnosis and management of chest pain patients in the emergency department. Am J Clin Pathol.2008 May;129(5):788-95.

Tanaka K, Seino Y, Ohbayashi K, Takano T. Cardiac emergency triage and therapeutic decisions using whole blood rapid troponin T test for patients with suspicious acute coronary syndrome. Jpn Circ J [Internet].2001 May [cited 2015 Jan 29];65(5):424-8. Available from: https://www.jstage.jst.go.jp/article/jcj/65/5/65_5_424/_pdf

Than M, Cullen L, Reid CM, Lim SH, Aldous S, Ardagh MW, et al. A 2-h diagnostic protocol to assess patients with chest pain symptoms in the Asia-Pacific region (ASPECT): a prospective observational validation study. Lancet.2011 Mar 26;377(9771):1077-84.

Tideman PA, Tirimacco R, Senior DP, Setchell JJ, Huynh LT, Tavella R, et al. Impact of a regionalised clinical cardiac support network on mortality among rural patients with myocardial infarction. Med J Aust.2014 Feb 17;200(3):157-60.

Tomonaga Y, Gutzwiller F, Luscher TF, Riesen WF, Hug M, Diemand A, et al. Diagnostic accuracy of point-of-care testing for acute coronary syndromes, heart failure and thromboembolic events in primary care: a cluster-randomised controlled trial. BMC Fam Pract [Internet].2011 [cited 2015 Jan 29];12:12. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3071323

Ungerer JP, Marquart L, O'Rourke PK, Wilgen U, Pretorius CJ. Concordance, variance, and outliers in 4 contemporary cardiac troponin assays: implications for harmonization. Clin Chem [Internet].2012 Jan [cited 2015 Jan 30];58(1):274-83. Available from: http://www.clinchem.org/content/58/1/274.full.pdf+html van Domburg RT, Cobbaert C, Kimman GJ, Zerback R, Simoons ML. Long-term prognostic value of serial troponin T bedside tests in patients with acute coronary syndromes. Am J Cardiol.2000 Sep 15;86(6):623-7.

van Domburg RT, Cobbaert C, Muller-Bardorff M, Kampmann M, Kimman GP, Rauscher T, et al. Time-dependent diagnostic performance of a rapid troponin T version 2 bedside test in patients with acute coronary syndromes. Scand J Clin Lab Invest.2000 Dec;60(8):665-75.

Viggiano M, Sicot J, Marx JS, Fievet ML, Laperche T, Cristofini P, et al. [Prehospital diagnosis and direction of patients suspected of acute coronary syndrome. Feasibility of the combined evaluation of a single blood sample value of cardiac troponin-I, myoglobin, and creatine phosphokinase MB].JEUR.2000;13(4):229-34. French.

Yamamoto M, Komiyama N, Koizumi T, Nameki M, Yamamoto Y, Toyoda T, et al. Usefulness of rapid quantitative measurement of myoglobin and troponin T in early diagnosis of acute myocardial infarction. Circ J.2004 Jul;68(7):639-44.

Inappropriate Comparator

Antman EM, Sacks DB, Rifai N, McCabe CH, Cannon CP, Braunwald E. Time to positivity of a rapid bedside assay for cardiac-specific troponin T predicts prognosis in acute coronary syndromes: a Thrombolysis in Myocardial Infarction (TIMI) 11A substudy. J Am Coll Cardiol [Internet].1998 Feb [cited 2015 Jan 29];31(2):326-30. Available from: http://ac.els-cdn.com/S0735109797004853/1-s2.0-S0735109797004853-main.pdf?_tid = 3e330c5e-a7dc-11e4-b4df-00000aab0f6b&acdnat = 1422552690_5ea33b4ae1107d09512b55dd6a0fb88b

Apple FS, Ler R, Chung AY, Berger MJ, Murakami MM. Point-of-care i-STAT cardiac troponin I for assessment of patients with symptoms suggestive of acute coronary syndrome. Clin Chem [Internet].2006 Feb [cited 2015 Jan 30];52(2):322-5. Available from: http://www.clinchem.org/content/52/2/322.full.pdf+html

Collinson PO, Gerhardt W, Katus HA, Muller-Bardorff M, Braun S, Schricke U, et al. Multicentre evaluation of an immunological rapid test for the detection of troponin T in whole blood samples. Eur J Clin Chem Clin Biochem.1996 Jul;34(7):591-8.

Eggers KM, Jaffe AS, Svennblad B, Lindahl B.A novel approach to cardiac troponins to improve the diagnostic work-up in chest pain patients. Crit Pathw Cardiol.2012 Dec;11(4):199-205.

Eggers KM, Oldgren J, Nordenskjold A, Lindahl B. Risk prediction in patients with chest pain: early assessment by the combination of troponin I results and electrocardiographic findings. Coron Artery Dis.2005 May;16(3):181-9.

Eisenman A, Rusetski V, Avital D, Stolero J, Snitkovsky T. Are all troponin assays equivalent in the emergency department? Singapore Med J [Internet].2005 Jul [cited 2015 Jan 30];46(7):325-7. Available from: http://www.sma.org.sg/smj/4607/4607a2.pdf

Gaze D, Collinson PO, Haass M, Derhaschnig U, Hirschl MM, Katus HA, et al. The use of a quantitative point-of-care system greatly reduces the turnaround time of cardiac marker determination. Point Care.2004 Dec;3(4):156-8.

Gerhardt W, Ljungdahl L. Detection of myocardial damage by serial measurements of cardiac troponin T, CK MBmass, and TROPT rapid test.Cardiovasc Drugs Ther.1997 May;11(Suppl 1):227-40.

Gust R, Gust A, Bottiger BW, Bohrer H, Martin E. Bedside troponin T testing is not useful for early out-of-hospital diagnosis of myocardial infarction. Acta Anaesthesiol Scand.1998 Apr;42(4):414-7.

Hirschl MM, Herkner H, Laggner AN, Sylven C, Rasmanis G, Collinson PO, et al. Analytical and clinical performance of an improved qualitative troponin T rapid test in laboratories and critical care units. Arch Pathol Lab Med.2000 Apr;124(4):583-7.

Hsu LF, Koh TH, Lim YL. Cardiac marker point-of-care testing: evaluation of rapid on-site biochemical marker analysis for diagnosis of acute myocardial infarction. Ann Acad Med Singapore.2000 Jul;29(4):421-7.

Loewenstein D, Stake C, Cichon M. Assessment of using fingerstick blood sample with i-STAT point-of-care device for cardiac troponin I assay. Am J Emerg Med.2013 Aug;31(8):1236-9.

Lu Y, Leong W, Wei B, Yu P, Wang C, Ying Y, et al. An Evaluation of Laboratory Efficiency in Shanghai Emergency by Turn Around Times Level. J Clin Lab Anal.2014 Aug 17.

Ooi SB, Lim YT, Lau TC, Chia BL, Pillai S, Liu T. Value of troponin-T rapid assay, cardiac enzymes, electrocardiogram and history of chest pain in the initial diagnosis of myocardial infarction in the emergency department. Eur J Emerg Med.2000 Jun;7(2):91-8.

Penttila K, Koukkunen H, Kemppainen A, Halinen M, Rantanen T, Pyorala K, et al. Myoglobin, creatine kinase MB, troponin T, and troponin I - rapid bedside assays in patients with acute chest pain. Int J Clin Lab Res.1999;29(2):93-101.

REACTT Investigators Study Group. Evaluation of a bedside whole-blood rapid troponin T assay in the emergency department.Rapid Evaluation by Assay of Cardiac Troponin T (REACTT) Investigators Study Group.Acad Emerg Med [Internet].1997 Nov [cited 2015 Jan 29];4(11):1018-24. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1553-2712.1997.tb03672.x/pdf

Schuchert A, Hamm C, Scholz J, Klimmeck S, Goldmann B, Meinertz T. Prehospital testing for troponin T in patients with suspected acute myocardial infarction. Am Heart J.1999 Jul;138(1 Pt 1):45-8.

Suzuki M, Hori S, Fujishima S, Takatsuki S, Nakamura I, Kimura H, et al. Diagnostic value of a bedside test for cardiac troponin T in the patient with chest pain presenting to the emergency room. Keio J Med [Internet].2000 Jun [cited 2015 Jan 29];49(2):74-9. Available from: https://www.jstage.jst.go.jp/article/kjm1952/49/2/49_2_74/_pdf

Sylvén C, Lindahl S, Hellkvist K, Nyquist O, Rasmanis G. Excellent reliability of nurse-based bedside diagnosis of acute myocardial infarction by rapid dry-strip creatine kinase MB, myoglobin, and troponin T. Am Heart J.1998 Apr;135(4):677-83.

Venturini JM, Stake CE, Cichon ME. Prehospital point-of-care testing for troponin: are the results reliable? Prehosp Emerg Care.2013 Jan;17(1):88-91.

Inappropriate Outcomes

Altinier S, Mion M, Cappelletti A, Zaninotto M, Plebani M. Rapid measurement of cardiac markers on Stratus CS. Clin Chem [Internet].2000 Jul [cited 2015 Jan 29];46(7):991-3. Available from: http://www.clinchem.org/content/46/7/991.full.pdf+html

Apple FS, Murakami MM, Christenson RH, Campbell JL, Miller CJ, Hock KG, et al. Analytical performance of the i-STAT cardiac troponin I assay. Clin Chim Acta.2004 Jul;345(1-2):123-7.

Bertsch T, Chapelle JP, Dempfle CE, Giannitsis E, Schwabs M, Zerback R. Multicentre analytical evaluation of a new point-of-care system for the determination of cardiac and thromboembolic markers. Clin Lab.2010;56(1-2):37-49.

Birkhahn RH, Haines E, Wen W, Reddy L, Briggs WM, Datillo PA. Estimating the clinical impact of bringing a multimarker cardiac panel to the bedside in the ED. Am J Emerg Med.2011 Mar;29(3):304-8.

Blick KE. The benefits of a rapid, point-of-care "TnI-Only" zero and 2-hour protocol for the evaluation of chest pain patients in the Emergency Department. Clin Lab Med.2014 Mar;34(1):75-85.

Bock JL, Singer AJ, Thode HC Jr. Comparison of emergency department patient classification by point-of-care and central laboratory methods for cardiac troponin I. Am J Clin Pathol.2008 Jul;130(1):132-5.

Cardinaels EP, Mingels AM, Van RT, Collinson PO, Prinzen FW, Van Dieijen-Visser MP. Time-dependent degradation pattern of cardiac troponin T following myocardial infarction. Clin Chem [Internet].2013 Jul [cited 2015 Jan 29];59(7):1083-90. Available from: http://www.clinchem.org/content/59/7/1083.full.pdf+html

Collinson P, Gaze D, Goodacre S. Comparison of contemporary troponin assays with the novel biomarkers, heart fatty acid binding protein and copeptin, for the early confirmation or exclusion of myocardial infarction in patients presenting to the emergency department with chest pain.Heart.2014 Jan;100(2):140-5.

Cuerq C, Rousson C, Berny C, Collin-Chavagnac D. Quantification of troponin I in an emergency context: A comparison of results obtained on Access 2 (Beckman Coulter) and AQT90FLEX (Radiometer). Immuno-Analyse et Biologie Specialisee.2010;25(3):153-8. In French.

Di Serio F, Lovero R, Leone M, De SR, Ruggieri V, Varraso L, et al. Integration between the tele-cardiology unit and the central laboratory: methodological and clinical evaluation of point-of-care testing cardiac marker in the ambulance. Clin Chem Lab Med.2006;44(6):768-73.

Dupuy AM, Sebbane M, Roubille F, Coste T, Bargnoux AS, Badiou S, et al. Analytical evaluation of point of care cTnT and clinical performances in an unselected population as compared with central laboratory highly sensitive cTnT. Clin Biochem.2014 Oct 12.

Esposito EC, Hollander JE, Ryan RJ, Schreiber D, O'Neil B, Jackson R, et al. Predictors of 30-day cardiovascular events in patients with prior percutaneous coronary intervention or coronary artery bypass grafting. Acad Emerg Med.2011 Jun;18(6):613-8.

Hart KW, Lindsell CJ, Ryan RJ. A time-and-motion study of the processes required to obtain cardiac biomarker assays using central laboratory, near-patient testing, and bedside point-of-care testing. Point Care.2012 Jun;11(2):61-8.

Howick J, Cals JW, Jones C, Price CP, Pluddemann A, Heneghan C, et al. Current and future use of point-of-care tests in primary care: an international survey in Australia, Belgium, The Netherlands, the UK and the USA. BMJ Open [Internet].2014 [cited 2015 Jan 30];4(8):e005611. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4127935

Jossi S, Gordon SL, Legge MA, Armstrong GP. All troponins are not created equal. Intern Med J.2006 May;36(5):325-7.

Kerguelen S, Salvignol C, Durand F, Stolidi P, Assadourian Y. [Troponin I assay in an emergency unit: comparison of results between AxSYM and Stratus CS]. Immuno-Analyse et Biologie Specialisee.2002;17(5):341-7. French.

Ko HF, Lee HY, Ho HF. A 2-hour accelerated chest pain protocol to assess patients with chest pain symptoms in an accident and emergency department in Hong Kong.Hong Kong Journal of Emergency Medicine [Internet].2013 [cited 2015 Jan 30];20(5):261-9. Available from: http://www.hkjem.com/sites/default/files/p261-269.pdf

Lee-Lewandrowski E, Corboy D, Lewandrowski K, Sinclair J, McDermot S, Benzer TI. Implementation of a point-of-care satellite laboratory in the emergency department of an academic medical center.Impact on test turnaround time and patient emergency department length of stay. Arch Pathol Lab Med.2003 Apr;127(4):456-60.

Lewandrowski EL, Lewandrowski K. Evaluation of the Roche troponin T cardiac reader in an emergency department STAT laboratory: comparison to the Elecsys troponin T method. Point Care.2002 Jun;1(2):78-83.

Loten C, Attia J, Hullick C, Marley J, McElduff P. Validation of a point of care troponin assay in real life emergency department conditions. Emerg Med Australas.2009 Aug;21(4):286-92.

Makam AN, Nguyen OK.Use of cardiac biomarker testing in the emergency department. JAMA Intern Med.2015 Jan 1;175(1):67-75.

Markota A, Bernhardt M, Palfy M. Comparison of point-of-care and laboratory troponin I assays. Zdravniski Vestnik.2011;80(12):905-8.

Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, et al. C-reactive protein is a potent predictor of mortality independently of and in combination with troponin T in acute coronary syndromes: a TIMI 11A substudy. J Am Coll Cardiol.1998 Jun;31(7):1460-5.

Munro AR, Jerram T, Morton T, Hamilton S. Use of an Accelerated Diagnostic Pathway allows rapid and safe discharge of 70% of chest pain patients from the Emergency Department. N Z Med J.2015;128(1408):62-71.

Newby LK, Storrow AB, Gibler WB, Garvey JL, Tucker JF, Kaplan AL, et al. Bedside multimarker testing for risk stratification in chest pain units: the chest pain evaluation by creatine kinase-MB, myoglobin, and troponin I (CHECKMATE) study. Circulation [Internet].2001 Apr 10 [cited 2015 Jan 29];103(14):1832-7. Available from: http://circ.ahajournals.org/content/103/14/1832.full.pdf+html

Ng SM, Krishnaswamy P, Morissey R, Clopton P, Fitzgerald R, Maisel AS. Ninety-minute accelerated critical pathway for chest pain evaluation. Am J Cardiol.2001 Sep 15;88(6):611-7.

Rogic D, Radic M, Fressl G, Fucek M. Evaluation of RAMP troponin I point of care assay. Point Care.2005 Mar;4(1):24-6.

Schilling UM.Clinical evaluation and cross-validation of the point-of-care system iStat at the emergency department versus central laboratory analysis.Point Care.2014 Mar;13(1):24-6.

Schilling UM. Time is money --the economic impact of point of care on the emergency department of a tertiary care university hospital. Point Care.2014 Mar;13(1):21-3.

Schneider HG, Ablitt P, Taylor J. Improved sensitivity of point of care troponin I values using reporting to below the 99th percentile of normals. Clin Biochem.2013 Aug;46(12):979-82.

Shoaibi A, Tavris DR, McNulty S. Gender differences in correlates of troponin assay in diagnosis of myocardial infarction. Transl Res.2009 Nov;154(5):250-6.

Soremekun OA, Datner EM, Banh S, Becker LB, Pines JM. Utility of point-of-care testing in ED triage. Am J Emerg Med.2013 Feb;31(2):291-6.

Svensson L, Axelsson C, Nordlander R, Herlitz J. Prognostic value of biochemical markers, 12-lead ECG and patient characteristics amongst patients calling for an ambulance due to a suspected acute coronary syndrome. J Intern Med.2004 Apr;255(4):469-77.

Tate JR, Ferguson W, Bais R, Kostner K, Marwick T, Carter A. The determination of the 99th centile level for troponin assays in an Australian reference population. Ann Clin Biochem.2008 May;45(Pt 3):275-88.

Volz KA, McGillicuddy DC, Horowitz GL, Sanchez LD. Creatine kinase-MB does not add additional benefit to a negative troponin in the evaluation of chest pain. Am J Emerg Med.2012 Jan;30(1):188-90.

Inappropriate Study Design

Antman EM, Grudzien C, Mitchell RN, Sacks DB. Detection of unsuspected myocardial necrosis by rapid bedside assay for cardiac troponin T. Am Heart J.1997 May;133(5):596-8.

Apple FS, Murakami MM, Jesse RL, Levitt MA, Berger AK, Pearce LA, et al. Near-bedside whole-blood cardiac troponin I assay for risk assessment of patients with acute coronary syndromes. Clin Chem [Internet].2002 Oct [cited 2015 Jan 30];48(10):1784-7. Available from: http://www.clinchem.org/content/48/10/1784.full.pdf+html

Baker K, Harrison C. Timely troponins avoid admissions: clinical assessment of undifferentiated chest pain. Scott Med J.2010;55(3).

Casagranda I, Boverio R, Baio R, Cecconi D, Marenco M. Chest pain unit and decentralized testing of cardiac markers. Clin Chim Acta.2001 Sep 15;311(1):63-6.

Collinson PO, Gaze DC, Thokala P, Goodacre S. Randomised Assessment of Treatment using Panel Assay of Cardiac markers--Contemporary Biomarker Evaluation (RATPAC CBE). Health Technol Assess [Internet].2013 [cited 2015 Jan 30];17(15):v-vi. Available from: http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0019/67042/FullReport-hta17150.pdf

Dadkhah S, Fisch C, Zonia C, Foschi A. Accelerated coronary reperfusion through the use of rapid bedside cardiac markers--case reports. Angiology.1999 Jan;50(1):55-62.

Kokar G, Tucker G, Mikhail S. Are we relying too much on bedside troponin estimation for the management of chest pains both in the country and city? Aust J Rural Health.2004 Dec;12(6):282-3.

Lippi G, Aloe R, Cervellin G. Point-of-care testing of cardiac biomarkers against standard core laboratory testing. Am J Emerg Med.2011;29(4):469-70.

Louie RF, Ferguson WJ, Curtis CM, Vy JH, Tang CS, Kost GJ. Effects of environmental conditions on point-of-care cardiac biomarker test performance during a simulated rescue: implications for emergency and disaster response. Am J Disaster Med.2013;8(3):205-12.

Pernet P, Benéteau-Burnat B, Hermand C, Vaubourdolle M. Point-of-care testing: false elevation of cardiac troponin I assayed in the emergency department. Am J Emerg Med.2008 Oct;26(8):969-2.

Radhakrishnan J. The use of point of care cardiac troponin (cTnI) measurement. Aust J Med Sci.2012;33(1):22-3.

Takakuwa KM, Ou FS, Peterson ED, Pollack CV, Jr., Peacock WF, Hoekstra JW, et al. The usage patterns of cardiac bedside markers employing point-of-care testing for troponin in non-ST-segment elevation acute coronary syndrome: results from CRUSADE. Clin Cardiol.2009 Sep;32(9):498-505.

Tirimacco R, Tideman P, Simpson P. Design, implementation, and outcomes for point-of-care pathological testing in a cardiac clinical network.Point Care.2009 Jun;8(2):56-60.

Zhang J, Kruss S, Hilmer AJ, Shimizu S, Schmois Z, De La Cruz F, et al. A rapid, direct, quantitative, and label-free detector of cardiac biomarker troponin T using near-infrared fluorescent single-walled carbon nanotube sensors.Advanced Healthcare Materials.2014 Mar;3(3):412-23.

Zhu J, Zou N, Zhu D, Wang J, Jin Q, Zhao J, et al. Simultaneous detection of high-sensitivity cardiac troponin I and myoglobin by modified sandwich lateral flow immunoassay: proof of principle. Clin Chem [Internet].2011 Dec [cited 2015 Jan 30];57(12):1732-8. Available from: http://www.clinchem.org/content/57/12/1732.full.pdf+html

Review

Aldous SJ. Cardiac biomarkers in acute myocardial infarction. Int J Cardiol.2013 Apr 15;164(3):282-94.

Amundson BE, Apple FS. Cardiac troponin assays: a review of quantitative point-of-care devices and their efficacy in the diagnosis of myocardial infarction. Clin Chem Lab Med.2014 Oct 15.

Bassand JP. [Classification of acute coronary syndromes]. Rev Prat.2003 Mar 15;53(6):597-601. French.

Bhoi S, Verma P, Vankar S, Galwankar S. High sensitivity troponins and conventional troponins at the bedside. Int J Crit Illn Inj Sci [Internet].2014 Jul [cited 2015 Jan 30];4(3):253-6. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4200553

Bingisser R, Cairns C, Christ M, Hausfater P, Lindahl B, Mair J, et al. Cardiac troponin: a critical review of the case for point-of-care testing in the ED. Am J Emerg Med.2012 May 23.

Chopra V, Eagle KA. PRACTITIONERS SECTION: Cardiac biomarkers in the diagnosis, prognosis and management of coronary artery disease: a primer for internists. Indian J Med Sci.2010;64(12):564-76.

Choudhary R, Iqbal N, Khusro F, Higginbotham E, Green E, Maisel A. Heart failure biomarkers. J Cardiovasc Transl Res.2013;6(4):471-84.

Christenson ES, Collinson PO, DeFilippi CR, Christenson RH. Heart failure biomarkers at point-of-care: current utilization and future potential. Expert Rev Mol Diagn.2014 Mar;14(2):185-97.

Christenson RH, Azzazy HM. Cardiac point of care testing: a focused review of current National Academy of Clinical Biochemistry guidelines and measurement platforms. Clin Biochem.2009 Feb;42(3):150-7.

Christenson RH, Duh SH. Methodological and analytic considerations for blood biomarkers. Prog Cardiovasc Dis.2012;55(1):25-33.

Clark M, Payne J. Elevated cardiac troponins: their significance in acute coronary syndrome and noncardiac conditions. J Okla State Med Assoc.2006 Jun;99(6):363-7.

Collinson PO. Troponin T or troponin I or CK-MB (or none?). Eur Heart J.1998 Nov;19 Suppl N:N16-24, 1998 Nov.:-24.

Collinson PO. The need for a point of care testing: an evidence-based appraisal. Scand J Clin Lab Invest Suppl.1999;230:67-73.

Collinson PO. Testing for cardiac markers at the point of care. Clin Lab Med.2001 Jun;21(2):351-62.

Collopy KT, Kivlehan SM, Snyder SR. What's the point of point-of-care testing? EMS World [Internet].2014 Feb [cited 2015 Jan 30];43(2):34-42. Available from: http://media.cygnus.com/files/cygnus/document/EMSR/2014/FEB/ce-article-february-2014_11308016.pdf

Conrad MJ, Jarolim P. Cardiac troponins and high-sensitivity cardiac troponin assays. Clin Lab Med.2014;34(1):59-73.

Dadkhah S, Sharain K, Sharain R, Kiabayan H, Foschi A, Zonia C, et al. The value of bedside cardiac multibiomarker assay in rapid and accurate diagnosis of acute coronary syndromes. Crit Pathw Cardiol.2007 Jun;6(2):76-84.

Daniels LB. Making sense of high sensitivity troponin assays and their role in clinical care. Curr Cardiol Rep.2014 Apr;16(4):471, 2014.

De Lemos JA. Increasingly sensitive assays for cardiac troponins: a review. JAMA.2013 Jun 5;309(21):2262-9.

Di Somma S, Zampini G, Vetrone F, Soto-Ruiz KM, Magrini L, Cardelli P, et al. Opinion paper on utility of point-of-care biomarkers in the emergency department pathways decision making. Clin Chem Lab Med.2014 Oct;52(10):1401-7.

Eriksson S, Wittfooth S, Pettersson K. Present and future biochemical markers for detection of acute coronary syndrome. Critical Reviews in Clinical Laboratory Sciences.2006;43(5-6):427-95.

Friess U, Stark M. Cardiac markers: a clear cause for point-of-care testing. Anal Bioanal Chem.2009 Mar;393(5):1453-62.

Fuller F. Just point and click. Is your system ready for point-of-care testing? Ems mag.2008 Aug;37(8):84-9.

Gaze DC. The perils, pitfalls and opportunities of using high sensitivity cardiac troponin. Curr Med Chem.2011;18(23):3442-5.

Giannitsis E, Katus HA. Biomarkers: pros and cons of high-sensitivity assays for cardiac troponin. Nature Reviews Cardiology.2012;9(11):616-8.

Hearty S, O'Kennedy R. Exploiting recombinant antibodies in point-of-care (POC) diagnostics: the combinatorial advantage. Bioeng Bugs.2011 May;2(3):182-6.

Hudson MP, Christenson RH, Newby LK, Kaplan AL, Ohman EM. Cardiac markers: point of care testing. Clin Chim Acta.1999 Jun 30;284(2):223-37.

Jeremias A, Gibson CM. Narrative review: alternative causes for elevated cardiac troponin levels when acute coronary syndromes are excluded. Ann Intern Med.2005 May 3;142(9):786-91.

Kelley WE, Januzzi JL, Christenson RH.Increases of cardiac troponin in conditions other than acute coronary syndrome and heart failure. Clin Chem [Internet].2009 Dec [cited 2015 Jan 30];55(12):2098-112. Available from: http://www.clinchem.org/content/55/12/2098.full.pdf+html

Knight CJ, Timmis AD. Almanac 2011: Acute coronary syndromes. The national society journals present selected research that has driven recent advances in clinical cardiology.Turk Kardiyoloji Dernegi Arsivi.2011;39(8):704-16.

Kost GJ, Kost LE, Suwanyangyuen A, Cheema SK, Curtis C, Sumner S, et al. Emergency cardiac biomarkers and point-of-care testing: optimizing acute coronary syndrome care using small-world networks in rural settings. Point Care [Internet].2010 Jun [cited 2015 Feb 25];9(2):53-64. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2888163/pdf/nihms190092.pdf

Kost GJ, Tran NK. Point-of-care testing and cardiac biomarkers: the standard of care and vision for chest pain centers. Cardiol Clin.2005 Nov;23(4):467-90.

Layfield C, Rose J, Alford A, Snyder SR, Apple FS, Chowdhury FM, et al. Effectiveness of practices for improving the diagnostic accuracy of Non ST Elevation Myocardial Infarction in the Emergency Department: A Laboratory Medicine Best Practices systematic review. Clin Biochem.2015 Feb 7.

Lewandrowski K, Flood JG, Tochka L, Lee-Lewandrowski E. Implementation of a point-of-care satellite laboratory (kiosk) in the emergency department of an academic medical center: an 8-year experience at the Massachusetts General Hospital. Point Care.2011 Jun;10(2):93-7.

Lewandrowski KB. Cardiac markers of myocardial necrosis: a history and discussion of milestones and emerging new trends. Clin Lab Med.2014 Mar;34(1):31-41.

Louie RF, Ferguson WJ, Curtis CM, Vy JH, Kost GJ. Vulnerability of point-of-care test reagents and instruments to environmental stresses: Implications for health professionals and developers. Clin Chem Lab Med.2014;52(3):325-35.

Mahajan VS, Jarolim P. How to interpret elevated cardiac troponin levels. Circulation [Internet].2011 Nov 22 [cited 2015 Jan 29];124(21):2350-4. Available from: http://circ.ahajournals.org/content/124/21/2350.full.pdf+html

Mair J. High-sensitivity cardiac troponins in everyday clinical practice.World Journal of Cardiology [Internet].2014 [cited 2015 Jan 29];6(4):175-82. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3999337/pdf/WJC-6-175.pdf

Males RG, Stephenson J, Harris P. Cardiac markers and point-of-care testing: a perfect fit. Crit Care Nurs Q.2001 May;24(1):54-61.

Mant J, McManus RJ, Oakes RA, Delaney BC, Barton PM, Deeks JJ, et al. Systematic review and modelling of the investigation of acute and chronic chest pain presenting in primary care. Health Technol Assess [Internet].2004 Feb;8(2):iii, 1-iii158.

McDonnell B, Hearty S, Leonard P, O'Kennedy R. Cardiac biomarkers and the case for point-of-care testing. Clin Biochem.2009;42(7-8):549-61.

McLean AS, Huang SJ, Salter M. Bench-to-bedside review: the value of cardiac biomarkers in the intensive care patient. Crit Care [Internet].2008 [cited 2015 Jan 30];12(3):215, 2008. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2481437

McPartlin DA, O'Kennedy RJ. Point-of-care diagnostics, a major opportunity for change in traditional diagnostic approaches: Potential and limitations. Expert Rev Mol Diagn.2014;14(8):979-98.

Mohammed MI, Desmulliez MPY. Lab-on-a-chip based immunosensor principles and technologies for the detection of cardiac biomarkers: A review. Lab on a Chip - Miniaturisation for Chemistry and Biology.2011;11(4):569-95.

Muthu V, Kozman H, Liu K, Smulyan H, Villarreal D. Cardiac troponins: bench to bedside interpretation in cardiac disease. Am J Med Sci.2014 Apr;347(4):331-7.

Panteghini M. Assay-related issues in the measurement of cardiac troponins. Clin Chim Acta.2009;402(1-2):88-93.

Pascual-Figal DA, Caballero L, Sanchez-Mas J, Lax A. Prognostic markers for acute heart failure. Expert Opin Med Diagn.2013 Jul;7(4):379-92.

Patil H, Vaidya O, Bogart D. A review of causes and systemic approach to cardiac troponin elevation. Clin Cardiol [Internet].2011 Dec [cited 2015 Jan 30];34(12):723-8. Available from: http://onlinelibrary.wiley.com/doi/10.1002/clc.20983/pdf

Plebani M, Zaninotto M. Cardiac markers: present and future. Int J Clin Lab Res.1999;29(2):56-63.

Pribul V, Woolley T. Point of care testing.Surgery (United Kingdom).2013;31(2):84-6.

Price CP. Point-of-care testing for cardiac markers: applications and outcomes. Point Care.2008 Dec;7(4):261-4.

Price CP, John A, Christenson RH. Testing at the point-of-care: errors of omission in the patient care pathway.Point Care.2011 Dec;10(4):182-5.

Proud TA. Point-of-care highly sensitive troponin: saving lives, time, and money. MLO Med Lab Obs.2013 Aug;45(8):38-9.

Ramlawi M, Delemont C. [Emergency department point of care testing: what are the benefits and for which patients?]. Rev Med Suisse.2011 Aug 24;7(305):1584-7. French.

Reinemund B. Cardiac point-of-care systems: an overview. J Clin Eng.2011;36(3):109-12.

Roberts R. Early diagnosis of myocardial infarction with MB CK isoforms.Clin Chim Acta.1998 Apr 6;272(1):33-45.

Sarko J, Pollack CV Jr. Cardiac troponins. J Emerg Med.2002 Jul;23(1):57-65.

Searle J, Möckel M. Cardiac biomarkers: Troponin, BNP and more. Med Welt.2012;63(6):317-23.

Sharma R. Troponin T: Newer magnetic immunoassay method of troponins as point-of-care detection of acute myocardial infarction. World Heart Journal.2010;3(1):17-29.

Shebuski RJ. Utility of point-of-care diagnostic testing in patients with chest pain and suspected acute myocardial infarction.Curr Opin Pharmacol.2002 Apr;2(2):160-4.

Sluss PM. Cardiac markers: current technologies for their measurement at points of care. Point Care.2006 Mar;5(1):38-46.

Storrow AB, Gibler WB. The role of cardiac markers in the emergency department.Clin Chim Acta.1999 Jun 30;284(2):187-96.

Storrow AB, Lyon JA, Porter MW, Zhou C, Han JH, Lindsell CJ.A systematic review of emergency department point-of-care cardiac markers and efficiency measures.Point Care.2009 Sep;8(3):121-5.

Stubbs P, Collinson PO. Point-of-care testing: a cardiologist's view. Clin Chim Acta.2001;311(1):57-61.

Tideman P, Simpson P, Tirimacco R. Integrating PoCT into Clinical Care. Clin Biochem Rev [Internet].2010 Aug [cited 2015 Jan 29];31(3):99-104. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2924130/pdf/cbr31_3_pg99.pdf

Van Der Laarse A, Cobbaert CM, Gorgels AP, Swenne CA. Will future troponin measurement overrule the ECG as the primary diagnostic tool in patients with acute coronary syndrome? J Electrocardiol.2013 Jul;46(4):312-7.

Vaughan L. Biomarkers in acute medicine. Medicine (United Kingdom).2013;41(3):136-41.

Wu AH.Use of cardiac markers as assessed by outcomes analysis. Clin Biochem.1997 Jun;30(4):339-50.

Wu AH.A comparison of cardiac troponin T and cardiac troponin I in patients with acute coronary syndromes. Coron Artery Dis.1999;10(2):69-74.

Wu AH.Point-of-care testing for conventional cardiac markers.Point Care.2006 Mar;5(1):20-4.

Wu AHB, Feng YJ. Biochemical differences between cTnT and cTnI and their significance for diagnosis of acute coronary syndromes. Eur Heart J.1998;19(Suppl N):N25-N29.

Ziebig R, Schimke I. [Laboratory medicine in Acute Coronary Syndrome and heart failure].Med Welt.2012;63(6):300-9. German.

Other (E.g., Abstract, Letter, Duplicate)

Apple FS, Jaffe AS. Bedside multimarker testing for risk stratification in chest pain units: the chest pain evaluation by creatine kinase-MB, myoglobin, and troponin I (CHECKMATE) study. Circulation.2001 Nov 27;104(22):E125-E126.

Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, Fernandez-Aviles F, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology. Eur Heart J [Internet].2007 [cited 2015 Jan 30];28(13):1598-660. Available from: http://eurheartj.oxfordjournals.org/content/ehj/28/13/1598.full.pdf

Baxter MS, Brogan J, Harchelroad J, Knoop KJ, Zackowski SW, Ryan RJ, et al. Evaluation of a bedside whole-blood rapid troponin T assay in the emergency department. Acad Emerg Med.1997;4(11):1018-24.

Blick KE. Economics of point-of-care (POC) testing for cardiac markers and B-Natriuretic Peptide (BNP).Point Care.2005 Mar;4(1):11-4.

Bradburn M, Goodacre SW, Fitzgerald P, Coats T, Gray A, Hassan T, et al. Interhospital variation in the RATPAC trial (Randomised Assessment of Treatment using Panel Assay of Cardiac markers). Emerg Med J.2012 Mar;29(3):233-8.

Buescher JJ, Kane KY. Can a bedside blood test predict death or myocardial infarction (MI) in patients with chest pain? J Fam Pract.2001 Sep;50(9):800.

Cals JW, Schols AM, Van Weert HC, Stevens F, Zeijen CG, Holtman G, et al. Point-of-care testing in family practices: present use and need for tests in the future. Ned Tijdschr Geneeskd.2014;158:A8210.

Cappelletti P, Galli GA, Malloggi L, Stenner E, Moretti M, Morandini M, et al. [State of the art of cardiac markers in Italy: III survey of GdS MM SIMeL]. Rivista Italiana della Medicina di Laboratorio.2014;10(4):212-23.

Christenson RH. Insights into development of the National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for point-of-care testing for biomarkers of cardiac injury.Point Care.2006 Mar;5(1):13-9.

Collinson P, Goodacre S, Gaze D, Gray A, RATPAC Research Team. Very early diagnosis of chest pain by point-of-care testing: comparison of the diagnostic efficiency of a panel of cardiac biomarkers compared with troponin measurement alone in the RATPAC trial. Heart.2012 Feb;98(4):312-8.

Descatha A, Derian S, Groizard C. Rapid diagnostic protocol for patients with chest pain. The Lancet.2011;378(9789):398-August.

Fitzgerald P, Goodacre SW, Cross E, Dixon S. Cost-effectiveness of point-of-care biomarker assessment for suspected myocardial infarction: the randomized assessment of treatment using panel Assay of cardiac markers (RATPAC) trial. Acad Emerg Med.2011 May;18(5):488-95.

FitzGibbon F, Huckle D, Meenan BJ. Barriers affecting the adoption of point-of-care technologies used in chest pain diagnosis within the UK National Health Service: part 2-manufacturer pricing and reimbursement policy issues. Point Care.2010 Jun;9(2):80-90.

FitzGibbon F, Meenan BJ, Brown A, Dixon D. User perspectives of cardiac marker point-of-care testing for hospital-based chest pain diagnosis. Point Care.2008 Jun;7(2):47-53.

Gómez Gerique JA, Izquierdo F, Galán A, Laporta P, Garnacho N, Ekizoglou N. [Evaluation of the troponin I on the Pathfast® analyzer]. Revista del Laboratorio Clinico [Internet].2009 [cited 2015 Jan 30];2(3):131-8. Available from: http://apps.elsevier.es/watermark/ctl_servlet?_f = 10&pident_articulo = 13140221&pident_usuario = 0&pcontactid = &pident_revista = 282&ty = 68&accion = L&origen = zonadelectura&web = www.elsevier.es&lan = es&fichero = 282v02n03a13140221pdf001.pdf Spanish.

Heeschen C, Hamm CW, Goldmann BU, Moeller RH, Meinertz T. [Cost-effectiveness of a rapid test for troponin in emergency admissions].Dtsch Med Wochenschr.1998 Oct 16;123(42):1229-34. German.

Higuchi K, Abe S, Matsuoka T, Nakajima H, Toda H, Akazaki Y, et al. [Usefulness of rapid quantitative cardiac troponin T and myoglobin assays for the diagnosis of acute myocardial infarction]. J Cardiol.2003 Feb;41(2):55-62. Japanese.

Jalal S, Habib K, Rauoof MA. Prognostic significance of rapid bedside cardiac troponin T testing in unstable angina. Indian Heart J.2002 Mar;54(2):220, 2002-220, 2Apr.

Juárez Herrera U, Ojeda LA, Rosas Peralta M, Luna Guerra J, Lopez Rodriguez MC, Chuquiure Valenzuela E, et al. [The utility of rapid qualitative determination of troponin T, the MB fraction of creatine phosphokinase and myoglobin in acute ischemic coronary syndromes]. Arch Inst Cardiol Mex.1998 Nov;68(6):473-81. Spanish.

Kashlova S, Boncheva M, Madjova V. [Review of modern POCT tests and systems]. General Medicine.2011;13(1):28-35. Bulgarian.

Kellett J, Hirschl MM, Derhaschnig U, Collinson PO, Gaze D, Haass M, et al. Bedside testing of cardiac troponin T and myoglobin for the detection of acute myocardial infarction in patients with a nondiagnostic electrocardiogram in the emergency department. Point Care.2004 Dec;3(4):159-61.

Kuwabara Y, Sato Y, Fujiwara H, Takatsu Y, Kita T. [Bedside rapid measuring instrument--PATHFAST]. Nippon Rinsho.2007 Apr 28;65 Suppl 4:460-4, 2007 Apr 28.:-4. Japanese.

Li F, Clark R, Versace V, Newman P. The association between point-of-care testing of Troponin and the management of patients with chest pain suspected of acute coronary syndrome: a systematic review protocol. JBI Database of Systematic Reviews & Implementation Reports.2014;12(3):99-112.

Lippi G, Mattiuzzi C, Cervellin G. Point of care troponin testing: rules and regulations [letter]. J Electrocardiol.2013 Nov;46(6):727-8.

Liu YC, Chen CH, Ding PY. Usefulness of a rapid cardiac troponin I test kit in patients with non-diagnostic chest pain or elevated CK enzyme in a Coronary Care Unit. Int J Cardiol.2000 Jan 15;72(2):193-4.

Luiz T, Ellinger K, Budde A, Hechler C, Klar H, Riester T. [Evaluation of a rapid qualitative test for cardiac troponin T in clinical diagnosis of patients with acute coronary syndrome]. Z Kardiol.1998 Apr;87(4):267-75. German.

Mah G, Wong K, Dubinsky I. Is a rapid bedside troponin T assay predictive of outcomes in unstable angina? Am J Emerg Med.1999 Nov;17(7):740-1.

Martin Calderon JL, Varona PJ, Bustos GF, Sanchez Gomez JC. Comparison of the new point of care method for measuring cardiac troponin i in whole blood versus two plasma immunoassays. Revista del Laboratorio Clinico.2013;6(4):140-4.

McCord J, Nowak RM. Ninety-minute exclusion of acute MI using cardiac markers.Cardiology Review.2002;19(6):22-5.

Meinertz T, Hamm CW. Rapid testing for cardiac troponins in patients with acute chest pain in the emergency room. Eur Heart J.1998 Jul;19(7):973-4.

Meraz Soria CA, Camarena Alejo G, Elizalde González JJ, Aguirre Sánchez J, Martinez Sánchez J. Utilidad de la determinación cualitativa de troponina I y creatinfosfocinasa isoenzima MB en los síndromes isquémicos coronarios agudos [Usefulness of rapid bedside assay of cardiac troponin I and creatine phosphokinase-MB in acute ischemic coronary syndromes]. Arch Cardiol Mex.2006 Jan;76(1):37-46. Spanish.

Miguel MJ, Amaral T, Loureiro J, Brito B, Pego J, Machado HC, et al. [Cardiac troponin-T. Diagnostic efficacy in acute myocardial infarction.Clinical and laboratory assessment]. Rev Port Cardiol.1998 Apr;17(4):339-43. Portuguese.

Monneret D, Abbes RA, Omarjee R, Devilliers C, Le MY, Raux M, et al. Analytical comparison of the new point-of-care troponin T immunoassay on AQT90Flex analyzer (Radiometer) and the high-sensitivity troponin T immunoassay on ModularE170 (Roche Diagnostics). Clin Chem Lab Med.2014 Dec;52(12):e279-e282.

Mutrie D.A new chest pain strategy in Thunder Bay. CJEM.1999 Apr;(1):57-61.

Nilsson S, Andersson A, Janzon M, Karlsson JE, Levin LÅ. Cost consequences of point-of-care troponin T testing in a Swedish primary health care setting. Scand J Prim Health Care [Internet].2014 Dec [cited 2015 Feb 18];32(4):241-7. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4278399/pdf/pri-32-241.pdf

Ogawa M, Abe S, Saigo M, Kozono T, Yamaguchi K, Toda H, et al. [Usefulness of rapid bedside cardiac troponin T assay for the diagnosis of acute myocardial infarction]. J Cardiol.2000 Mar;35(3):157-64. Japanese.

Ohman EM, Armstrong PW, White HD, Granger CB, Wilcox RG, Weaver WD, et al. Risk stratification with a point-of-care cardiac troponin T test in acute myocardial infarction.GUSTOIII Investigators. Global Use of Strategies To Open Occluded Coronary Arteries. Am J Cardiol.1999 Dec 1;84(11):1281-6.

Pagani F, Serena C, Bosio C, Cuccia C, Panteghini M. Evaluation of a rapid bedside immunochromatographic assay for detection of cardiac troponin I in whole blood. Clin Chem Lab Med.2001 May;39(5):458-9.

Scholz J, Fassmann M, Schuchert A, Klimmeck S, Goldmann B, Hamm CW, et al. [Troponin T quick test in emergency medical care]. Unfallchirurgie.1999;25(2):78-83. German.

Seino Y, Nejima J, Takayama M, Takano T, Ohbayashi K. [Evaluation of whole blood rapid troponin T assay: cooperative study of general practitioners and office cardiologists in Tokyo]. J Cardiol.1998 May;31(5):281-7. Japanese.

Singh J, Akbar MS, Adabag S. Discordance of cardiac troponin I assays on the point-of-care i-STAT and Architect assays from Abbott Diagnostics. Clin Chim Acta.2009 May;403(1-2):259-60.

Soria CAM, Alejo GC, Gonzalez JJE, Sanchez JA, Sanchez JM. Usefulness of rapid bedside assay of cardiac troponin I and creatine phosphokinase-MB in acute ischemic coronary syndromes. Arch Cardiol Mex.2006;76(1):37-46.

Stengaard C, Thorsted SJ, Terkelsen CJ. [Prehospital point of care testing of biomarkers has diagnostic value in relation to acute myocardial infarction]. Ugeskr Laeger.2013 Jan 21;175(4):186-9. Danish.

Storrow AB, Apple FS, Wu AH, Jesse RL, Francis GS, Christenson RH, et al. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: point of care testing, oversight, and administration of cardiac biomarkers for acute coronary syndromes. Point Care.2007 Dec;6(4):215-22.

Svensson L, Axelsson C, Nordlander R, Herlitz J. Elevation of biochemical markers for myocardial damage prior to hospital admission in patients with acute chest pain or other symptoms raising suspicion of acute coronary syndrome. J Intern Med.2003 Mar;253(3):311-9.

Szantho E, Szabo Z, Varga J, Paragh G, Olah V. [Interpretation of highly sensitive troponin assays: acute or chronic myocardial damage?]. Orv Hetil.2011 Sep 18;152(38):1528-34. Hungarian.

Wilgen U, Pretorius CJ, Ungerer JP. Improved sensitivity of point of care troponin I values using reporting to below 99th percentile of normals. Schneider HG et al. Clin Biochem.2013 Nov;46(16-17):1774-5.

Wu AH, Smith A, Christenson RH, Murakami MM, Apple FS. Evaluation of a point-of-care assay for cardiac markers for patients suspected of acute myocardial infarction. Clin Chim Acta [Internet].2004 Aug 16 [cited 2015 Jan 30];346(2):211-9. Available from: http://responsebio.com/uploads/publications/Cardiac_Wu_2007.pdf

Wu AH, Smith A, Christenson RH, Murakami MM, Apple FS. Erratum: Evaluation of a point-of-care assay for cardiac markers for patients suspected of acute myocardial infarction. Clin Chim Acta [Internet].2005 [cited 2015 Jan 30];355:219. Available from: http://ac.els-cdn.com/S0009898105000197/1-s2.0-S0009898105000197-main.pdf?_tid = 938e572e-a89c-11e4-a03e-00000aacb362&acdnat = 1422635297_c674fe28ac2bd54655f5280590f4b684

Appendix 6: Study Characteristics

Table 14: Study Characteristics

First Author, Year Country of Origin Study Design	Funding Source Conflicts of interest	Study Setting Study Duration	Inclusion Criteria	Exclusion Criteria	AMI Definition	POC Device/ Manufacturer Troponin Test Test Protocol	Health Personnel Conducting POC Test	Central Laboratory Instrument/Manufacturer Troponin Test Test Protocol	Clinical Adjudication for Final MI Diagnosis (Diagnostic-Accuracy Studies Only)
Diagnostic-Accuracy Studies									
Aldous, 2014[16] New Zealand Prospective observational study	Research group plus industry funding Some authors had received funding from industry	Hospital ED 29 months (Nov. 2007 to Apr. 2010)	Symptoms suggestive of cardiac ischemia (acute chest, epigastric, neck, jaw, or arm pain, or discomfort or pressure without an apparent non-cardiac source)	< 18 years of age, not able to provide consent, not willing to participate, not available for follow-up	Universal definition: rise and/or fall of cTn with at least one value about the 99th percentile, with symptoms of ischemia	Cardio3/Alere cTnI At presentation (0 h), and 2 h	NR	Architect Troponin I/Abbott cTnI At presentation (0 h) and at least 6 h later. Additional sample taken at 2 h post-presentation for study laboratory cTnI measurement, at 0 h and 2 h for freezing for later analysis using other cTn assays	Diagnoses on admission and at follow-up were determined independently by a cardiologist and a cardiology research clinician who were blinded to the results of the test assays. A second cardiologist was involved in cases of discrepancy.
Di Serio, 2005[23] Italy Prospective observational study	Funding NR Conflicts of interest NR	Hospital ED Duration NR	Patients presenting to ED with chest pain	STEMI	ESC/ACC criteria	Stratus CS/ Dade Behring cTnI On admission, 6 h, 12 h, 24 h	ED/ cardiology department staff	Dimension RxL/ Dade Behring cTnI On admission, 6 h, 12 h, 24 h	Final diagnosis of AMI in the ICU was made according to ESC/ACC diagnostic criteria by ICU cardiologists
Di Serio, 2007;[24] Amodio, 2007[25] Italy Prospective observational with retrospective data analysis	Funding NR Conflicts of interest NR	Hospital ED 7 months (Feb. to Sept. 2005)	Patients presenting to ED with chest pain and suspected clinical angina or AMI	STEMI or left bundle-brunch block of recent onset	ESC/ACC diagnostic criteria	Stratus CS/ Dade Behring cTnI Within 15 min of admission, then patients with cTnI > 0.07 mcg/L followed up every 6 h, and patients with cTnI ≤ 0.07 mcg/L followed up every 3 h	NR	Dimension RxL/ Dade Behring cTnI Within 15 min of admission, then patients with cTnI > 0.07 mcg/L followed up every 6 h; patients with cTnI ≤ 0.07 mcg/L followed up every 3 h	Final diagnosis of AMI was assessed according to ESC/ACC diagnostic criteria; cardiac marker follow-up after hospital admission was performed in a CL

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Diercks, 2012[19] US Secondary analysis of a multi-centre blinded observational study	Industry funding Conflicts of interest NR	18 hospital EDs 13 months (May 2006 to Jun. 2007)	Adults > 18 years, presenting to the ED with chest pain or ischemic symptoms that had been occurring for at least 30 min but not more than 8 h before blood sampling	NR	Standard ACC/AHA definition	Triage Cardio 3/ Biosite cTnI At presentation, 90 min, 3 h, and 6 h	NR	DxI AccuTnI/Beckman Coulter cTnI At presentation, 90 min, 3 h, and 6 h	Diagnoses were determined by 1 or 2 experienced clinicians using all available medical records per ACC/AHA criteria using local biomarker results. Reviewers were blinded to the POC cTnI findings.
Hjortshoj, 2011[21] Denmark Retrospective, observational study	Assays provided by industry Conflicts of interest NR	Hospital ED and CCUs 20 months (Feb. 2003 to Oct. 2004)	Chest pain and suspected ACS	Documented MI within the week before admission, or admitted with STEMI	New universal definition; detection of rise and/or fall of cTnT > 0.03 mcg/L together with signs indicative of ischemia (clinical symptoms, ECG)	AQT90 FLEX/ Radiometer cTnI At arrival, 6 h to 9 h, and 12 h to 24 h; samples were taken at these points, then frozen for later analysis	Trained laboratory staff	Access AccuTnI/Beckman Coulter AxSYM ADV assay/ Abbott At arrival, 6 h to 9 h, and 12 h to 24 h; samples were taken at these points, then frozen for later analysis	Patients were diagnosed with AMI according to the new universal definition of AMI.
Ivandic, 2014[17] Germany Prospective, observational study	Funding from industry 2 authors employed by a group that consulted for industry	Hospital ED 16 months (Mar. 2009 to Jun. 2010)	New-onset chest pain and NSTEMI	Patients with chest pain of non-cardiac origin, or patients with STEMI	Chest pain with cTnT ≥ 30 ng/L in at least 1 sample during the first 6 h after admission	AQT90 FLEX/ Radiometer GmbH cTnI At admission, 3 h and 6 h	NR	Elecsys 2010 Cobas e 411/ Roche cTnT At admission, 3 h, and 6 h	The final discharge diagnosis was made in agreement with coronary angiography, when available.
Lee-Lewandrowski, 2011[20] US Prospective, observational study	Partially funded by industry 2 authors had received funding from industry	Hospital ED 18 days	Symptoms of ACS	NR	Universal criteria	i-STAT/Abbott and Triage Cardiac Reader/Inverness Biosite cTnI Protocol NR	Medical technologists	Elecsys E170/Roche Protocol NR	Using the available laboratory data, ECG results and clinical findings, ED physicians (or in-patient, hospital-based physicians) determined the final diagnosis

First Author, Year Country of Origin Study Design	Funding Source Conflicts of interest	Study Setting Study Duration	Inclusion Criteria	Exclusion Criteria	AMI Definition	POC Device/ Manufacturer Troponin Test Test Protocol	Health Personnel Conducting POC Test	Central Laboratory Instrument/Manufacturer Troponin Test Test Protocol	Clinical Adjudication for Final MI Diagnosis (Diagnostic-Accuracy Studies Only)
Nilsson, 2013;[61] Andersson, 2015[1] Sweden Prospective, observational, cross-sectional study	Government funding No conflicts of interest declared	7 primary health care settings 20 months (May 2009 to Jan. 2011)	Chest pain, dyspnea on exertion unexplained weakness, and/or fatigue; symptoms commenced or worsened during the last 7 days; age ≥ 35 years	NR	NR	Cobas h232/ Roche cTnT Protocol NR	NR	No CL testing	The cases of AMI and UA in the study were diagnosed in conjunction with the first GP visit. The diagnoses of AMI and UA were based on the current definitions.
Palamalai, 2013[18] US Prospective, observational study	Partially funded by industry Conflicts of interest NR	Hospital ED Duration NR	Symptoms suggestive of ACS	NR	Clinical symptoms of ischemia with increasing cTnI, with at least one cTn value above the 99th percentile	GEM Immuno/ Instrumentation Laboratory; AQT90 FLEX/ Radiometer Medical; i-STAT/ Abbott; PATHFAST/ Mitsubishi Chemical Medience cTnI At presentation, 3 h and 6 h (samples were frozen and later thawed for evaluations)	Research laboratory technologists	Vitros ECi ES/Ortho-Clinical Diagnostics cTnI At presentation, 3 h and at 6 h (samples were frozen and later thawed for evaluations)	Diagnosis of MI was determined by attending clinicians (internal medicine or emergency medicine) caring for each patient according to the Universal Definition of Myocardial Infarction recommendations
Stengaard, 2013[62] Denmark Prospective, observational study	University, foundation, and industry funding 2 authors had received fees or grants from industry	Ambulance and EDs 12 months (May 2010 to May 2011)	Ongoing or prolonged periods of chest discomfort within the past 12 h, acute dyspnea in the absence of known pulmonary disease, or a clinical suspicion of AMI	Subjects were only included once in survival analysis at first admission if they had first admission if they had pre-hospital POC cTnT analysis performed on more occasions	Universal Definition of Myocardial Infarction using the 99th percentile URL as diagnostic cut point	Cobas h232/Roche cTnT Heparinized blood taken in ambulance	Paramedics in ambulance	Roche (Instrument NR) Protocol NR	All admissions were evaluated by any 2 of 3 primary adjudicators who were blinded to the decision of the other and the pre-hospital cTnT levels. The definitive diagnosis of AMI was established in accordance with the Universal Definition Of Myocardial Infarction.

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ter Avest, 2014[22] The Netherlands Prospective, observational study	Industry provided discounted assays No conflicts of interest declared	Medical centre ED 4 months (May to Aug. 2013)	Patients ≥ 18 years presenting to ED with at least 5 min of chest pain related to ACS	Patients presenting with only dyspnea, palpitations, fatigue, nausea, or dizziness; inter-hospital referrals; previously included patients; STEMI	Third universal definition of AMI: rise and/or fall of cardiac-biomarker values, with at least 1 value above the 99th percentile, with symptoms of ischemia, new significant ST-segment T-wave depression, new left bundle-branch block, or pathological Q waves on the ECG	AQT90 FLEX/ Radiometer cTnT On presentation in ED; 6 h later if patients presented to ED within 6 h of symptoms	NR	Modular E170/Roche cTnT On presentation in ED; 6 h later if patients presented to ED within 6 h of symptoms	The diagnosis of AMI was made during hospitalization by the treating cardiologist using Roche Modular E170 hs-cTnT results (URL 14 ng/L), and adjudicated through coronary angiography in the majority of patients diagnosed with AMI. The treating cardiologist was blinded to the POC test results, as these were provided only to the investigators.
Clinical-Utility Studies									
Altinier, 2001[33] Italy Prospective, observational study	Funding NR Conflicts of interest NR	Hospital ED Duration NR	Patients presenting to ED with chest pain and clinical findings suggesting ACS	NR	NR	Stratus CS/Dade Behring; and Triage Cardiac Panel/Biosite cTnI Protocol NR	NR	Dimension RxL/Dade Behring cTnI Protocol NR	
Apple, 2006[49] US Retrospective, observational, before/after study	Partly funded by industry Conflicts of interest NR	Hospital cardiology service 7 months before/ 3 months after POC	Symptoms of ACS	Patients for whom less than 2 blood samples were obtained and patients without at least one sample ≥ 8 h post-baseline	ESC, ACC, and AHA guidelines	Stratus CS/Dade Behring cTnI Baseline, 4 h, 8 h, and 12 h	Nurses	Dimension RxL/Dade Behring cTnI Baseline, 4 h, 8 h, and 12 h	

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Asha, 2014[41,57] Australia RCT	Government funding No conflicts of interest declared	Hospital ED 6 months (Dec. 2011 to May 2012)	Patients ≥ 18 years presenting to ED with suspected ACS	STEMI	NR	AQT90 FLEX/ Radiometer cTnT At initial assessment, then every 6 h if abnormal; at 6 h if normal. If pain onset at presentation > 6 h, only taken at presentation	NR	Cobas/Roche cTnT At initial assessment, then every 6 h if abnormal; at 6 h if normal. If pain onset at presentation > 6 h, only taken at presentation	
Caragher, 2002[32] US Prospective, observational study	Funding NR Conflicts of interest NR	Hospital ED 16 days	Patients presenting to ED with chest pain	NR	NR	Stratus CS/ Dade Behring cTnI Within 10 min of admission, then at 2 h, 6 h, and 9 h	Nurses	Stratus II/Dade Behring cTnI Within 10 min of admission, then at 2 h, 6 h, and 9 h	
Collinson, 2004[50] England RCT	Partly funded by government Conflicts of interest NR	Hospital CCU 8 months	Patients assessed in ED at high risk of ACS on clinical grounds	None	1. STEMI 2. NSTEMI with significant changes in serial cardiac biomarkers and symptoms suggestive of cardiac disease	CARDIAC T/ Roche cTnT 12 h after CCU admission	NR	Elecsys 1010/Roche Diagnostics cTnT 12 h after CCU admission	
Cramer, 2007[34] the Netherlands Prospective, observational study	Funding NR Conflicts of interest NR	Hospital ED 9 months (Jun. 2001 to Mar. 2002)	Patients presenting to ED with suspected ACS	STEMI	NR	Cardiac Reader/ Roche cTnT At presentation	Nurses	Immulite 2000/Diagnostic Products cTnI At presentation	
Cullen, 2012[44] Australia Prospective, observational study	Medical research foundation Reagents and AQT90 Flex instrument supplied by industry Authors had received fees and support from industry	Hospital ED Duration NR; 30-day follow-up	All adult patients (> 18 years) presenting to the ED with at least 5 min of chest pain suggestive of ACS	Pregnant, inter-hospital transfers	Defined under current guidelines. Along with symptoms suggestive of ACS, if there was a rise and/or fall of the CL cTn with one or more values above the 99th percentile (> 0.04 mg/L)	AQT90 FLEX/ Radiometer cTnI At presentation and 2 h	NR	Access AccuTnI/Beckman Coulter cTnI At presentation, and then at least 6 h afterwards	

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Deledda, 2011[42] US Retrospective, observational, before/after study	Funding NR Conflicts of interest NR	1 academic and 1 community centre ED 8 months (4 months before and 4 months after) (Nov. 2004 to Feb. 2005, and Nov. 2005 to Feb. 2006)	Patients presenting to ED with chief symptom of chest pain or other ACS symptoms, or who had hospital discharge diagnosis of ACS and had cTnI testing in the ED	NR	NR	Triage Profiler SOB/ Biosite cTnI Testing at 0 min, 90 min, 180 min	Trained ED paramedics and patient care assistants	Device NR cTnI Testing at 0 min, 90 min, 180 min	
Di Serio, 2003[31] Italy Retrospective, observational study	Funding NR Conflicts of interest NR	Hospital ED 4 years	Patients presenting to ED with chest pain	NR	NR	Triage/ Biosite cTnI On admission to ED; no other details provided	Nurses	Dimension RxL/Dade Behring cTnI On admission to ED; no other details provided	
Eggers, 2011[45] Sweden pooled analysis of two RCTs (FAST II and FASTER-I)	Some funding from industry All authors have affiliation with industry	Coronary care units of 4 hospitals FAST II was 10 months (May 2000 to Mar. 2001); FASTER-I was 10 months (Oct. 2002 to Aug. 2003)	Chest pain with ≥ 15 min duration within the last 8 h; patients were enrolled after being admitted to coronary care unit from the ED	Pathological STEMI leading to reperfusion therapy or consideration of reperfusion therapy	Troponin-based standard applying cTnI ≥ 0.1 mcg/L (Stratus CS; 10% CV level) within 24 h from admission for least 2 samples	Stratus CS/Siemens cTnI At admission to CCU, at 30 or 40 min, 90 or 80 min, then 2 h, 3 h, 6 h, 12 h, and 24 h	NR	AxSYM/ Abbott for the FAST II trial cTnI At admission to CCU, at 30 min or 40 min, 90 min or 80 min, then 2 h, 3 h, 6 h, 12 h, and 24 h	
Ezekowitz, 2015[55] Canada RCT	Government and industry funding One author has affiliation with industry	Ambulance; 19 months	Patients with chest pain activating pre-hospital emergency medical services	ST elevation or a previous diagnosis compatible with a non-cardiovascular cause	NR	Cadio2/Alere cTnI In ambulance	Emergency medical service personnel in ambulance	AccuTnI/ Beckman cTnI; At admission	
Fitzgibbon, 2010,[53] Fitzgibbon, 2007[58] UK (Northern Ireland) Survey	Government funding Conflicts of interest NR	5 health trusts Duration NR	POC device users in 10 major hospitals in Northern Ireland	NR	NR	i-STAT Abbott; Triage/Biosite; Stratus/Dade Behring; Cardiac Reader/Roche Troponin test NR Protocol NR	Clinicians, nurses, laboratory scientists	NA	

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Goodacre, 2011[39] UK Multi-centre RCT	Government funding No conflicts of interest declared	6 hospital EDs 2,658 days	Adults with chest pain due to suspected but not proven MI, and no other potentially serious alternative pathology or comorbidity	An obvious non-cardiac morbidity; known CHD; prolonged or recurrent episodes of typical cardiac-type pain; serious non-coronary pathology requiring diagnostic ECG changes for AMI or high-risk ACS comorbidity or social problems; presentation more than 12 h after the most significant episode of pain; previous participation in the RATPAC trial	Universal definition for acute, evolving or recent AMI, troponin level above the 99th percentile of the values for a reference control group; or STEMI on ECG	Stratus CS/Siemens cTnI At presentation and 90 min	Trained staff	Siemens Centaur XP/ Siemens; Modular E170 fourth-generation assay/ Roche; i2000SR/Architect; Access 2/Beckman Coulter cTnI Each hospital followed its own testing protocol. Some were 6 h, some were 12 h after onset of worst symptoms	

First Author, Year Country of Origin Study Design	Funding Source Conflicts of interest	Study Setting Study Duration	Inclusion Criteria	Exclusion Criteria	AMI Definition	POC Device/ Manufacturer Troponin Test Test Protocol	Health Personnel Conducting POC Test	Central Laboratory Instrument/Manufacturer Troponin Test Test Protocol	Clinical Adjudication for Final MI Diagnosis (Diagnostic-Accuracy Studies Only)
Guo, 2006[51] China Prospective, observational study	Hospital funding Conflicts of interest NR	Hospital CCU or cardiac department; 37 months (May 2001 to Jun. 2004)	Chest pain	NR	Either of the following two criteria: 1. a typical rise and gradual fall of troponin or more rapid rise and fall of CK-MB, with at least one of the following: ischemic symptoms, pathological Q waves on the ECG, STEMI, or coronary artery intervention 2. pathological findings of an AMI (cTnI, CK, and CK-MB)	Cardiac Reader/ Roche cTnT At admission, then after 6 and 12 h	Doctors or nurses of the cardiac department or coronary care unit	AccuTnI 33340/Beckman Coulter cTnI At admission, then every 6 h on day 1, and every 24 h for next 6 days	
Koehler, 2013[27] US Retrospective, observational, before/after study	Partially funded by industry 2 authors are speakers for industry	Hospital ED Pre-POC testing 4 days (Mar. 2010); post-POC testing 3 months (Apr. to May, Jul., and Sept. 2010)	Chest, abdominal, or shoulder pain with a cTn test ordered as part of the clinical workup	NR	NR	i-STAT/Abbott cTnI At admission and 2 h (at discretion of clinician)	Physicians, nurses, and ED technicians	ADVIA Centaur XP Immunoassay System, TnI Ultra Assay/Siemens cTnI At admission and 2 h (at discretion of clinician)	
Lee-Lewandrowski, 2002[37] US Retrospective, observational, before/after study	Funding NR Conflicts of interest NR	Hospital ED 12 month implementation of POC	NA	NA	NA	Spectral Status cTnI Protocol NR	NR	Elecsys 1010/ Roche cTnT Protocol NR	
Liikanen, 2005[54] Finland Survey	Funding NR Conflicts of interest NR	Health care units Duration NR	Health care units using POC testing	NA	NA	Devices NR cTnI and cTnT Protocol NR	Nurses, porters, secretaries, MLTs, physicians, home aids	NA	

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Loten, 2010[40] Australia RCT (cluster randomized)	Government funding Conflicts of Interest NR	2 hospital EDs 12 weeks (Nov 2007 to Jan 2008)	Adults > 25 years, admitted to ED with possible ACS, with troponin measurement taken	Transfer from another hospital with known ACS or known elevated troponin, ST elevation upon arrival, departure against medical advice	NR	i-STAT/Abbott cTnI At admission and at least 8 h after onset of symptoms	Medical and nursing staff	AccuTnI/Beckman Coulter At admission and at least 8 h after onset of symptoms	
Meek, 2012[28] Australia Prospective, observational, before/after study	Industry provided the POC device and testing materials No conflicts of interest declared	Hospital ED 81 days before POC 66 days after POC	Chest pain for which the physician ordered serial cardiac enzyme testing	Cardiac enzyme testing once only; diagnosed early with a STEMI (or other); ACS based on a diagnostic ECG and/or initial cardiac enzyme results; early transfer to either a critical care ward or another hospital or had an alternative non-cardiac diagnosis	NR	Triage MeterPro second generation/ Alere cTnI On arrival and at 2 h; high-risk patients had a third assay at 6 h	NR	Beckman Coulter (second generation)/Beckman Coulter On arrival and at 6 h; high-risk patients had a third cTnI assay at 10 h	
Mozina, 2010[35] Slovenia Prospective, observational study	Hospital funding tests donated by industry Conflicts of interest NR	Hospital ED Duration NR	Chest pain	NR	NR	PATHFAST/ Mitsubishi, Kagaku Iatron cTnI At admission	NR	LIAISON/DiaSorin cTnI At admission	
Nilsson, 2013, [61] Andersson, 2015[1] Sweden Prospective, observational, cross-sectional study	Government funding No conflicts of interest declared	7 primary health care settings 20 months (May 2009 to Jan 2011)	Chest pain, dyspnea on exertion; unexplained weakness and/or fatigue; symptoms commenced or worsened during the last 7 days; and age ≥ 35 years	NR	NR	Cobas h232/Roche cTnT Protocol NR	NR	No CL testing	

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Ordonez-Llanos, 2006[47] Spain, Great Britain, Germany, Austria, Ireland, Sweden Prospective, observational study	Funded by industry One author employed by industry	5 hospital EDs 17 months (Aug. 1998 to Jan. 2000)	Chest pain and suspected ACS	NR	cTnT ≥ 0.05 mcg/L or CK-MB ≥ 10 mcg/L within 24 h of admission; or new abnormal Q-wave on ECG or STEMI	Cardiac Reader/ Roche cTnT On admission, 1, 2, 4, 24, and 48 h	ED personnel	ELECSYS 1010 or 2010/ Roche cTnT On admission, 1, 2, 4, 24, and 48 h	
Renaud, 2008[29] France RCT	Reagents provided by industry One author has been supported by industry	Hospital ED 17 months (Nov. 2002 to Apr. 2004)	1. Adults ≥ 18 years in ED with symptoms suspicious of ACS 2. One of the above symptoms and either cTnI ≥ 0.1 mcg/L, or at least 2 of: ≥ 60 years, at least 3 cardiovascular risk factors, history of CAD, chest pain, or NSTEMI ECG changes indicating ischemia	Previous enrolment in study; STEMI	ESC/ACC guidelines	Stratus CS/Dade Behring cTnI Protocol NR	Nurses	Dimension RxL-HM/Dade Behring cTnI Protocol NR	
Ryan, 2009[26] US RCT	Funded in part by industry 2 authors had received research grants from industry	4 medical centre EDs 2 years	Patients ≥ 21 years, presenting to ED with symptoms suggestive of ACS	Tachydysrhythmia (ventricular tachycardia, supraventricular tachycardia, or rapid atrial fibrillation), or 12-lead ECG diagnostic of AMI	NR	i-STAT/Abbott cTnI Baseline, 90 min, 180 min, 360 min	NR	Device NR cTnI 3 sites used baseline, 90 min, 180 min, 360 min; 1 site used baseline, 8 h, 12 h	

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Shephard, 2014,[52] Shephard, 2012[56] Australia Implementation review	No funding received Conflicts of interest NR	Remote health centres First 4 years of program	Remote health centres	NR	NR	i-STAT/Abbott cTnI Protocol NR	Remote health centre staff	NA	
Singer, 2015[38] US Retrospective, observational, before/after study	Funding NR One author was a speaker for industry	Hospital ED Approx. 1 month	All ED patients triaged to critical care	NR	NR	i-STAT/Abbott cTnI Protocol NR	Nurses	NR	
Singer, 2005[30] US Retrospective, observational, before/after study	No funding received Conflicts of interest NR	Hospital ED 4 weeks (2 weeks each before and after)	Chest pain	STEMI; patients not being admitted to hospital	NR	Stratus/ Dade Behring cTnI Protocol NR	Nurses	Centaur/Bayer cTnI Protocol NR	
Sorensen, 2011[48] Denmark Prospective, observational study	Foundation and service company funding 2 authors are affiliated with one of the service companies providing funding	Pre-hospital setting (ambulance) 15 months (Jun. 2008 to Sept. 2009)	Patients transported by an ambulance equipped with POC troponin testing	NR	Universal definition of MI using a rise or fall of cTnT above the 99th percentile, together with symptoms of ischemia, or ECG changes indicative of new ischemia	TROPT/Roche cTnT Heparinized blood taken in ambulance	Trained paramedics	Elecsys/Roche cTnT On arrival at hospital	
Stengaard, 2013[62] Denmark Prospective, observational study	University, foundation and industry funding 2 authors have received fees or grants from industry	Ambulance and EDs 12 months (May 2010 to May 2011)	Ongoing or prolonged periods of chest discomfort within the past 12 h, acute dyspnea in the absence of known pulmonary disease, or a clinical suspicion of AMI	Subjects were only included once in survival analysis at first admission if they had pre-hospital POC cTnT analysis performed on more occasions	Universal Definition of Myocardial Infarction using the 99th percentile URL as diagnostic cut point	Cobas h232/Roche cTnT Heparinized blood taken in ambulance	Paramedics in ambulance	Roche (instrument NR) Protocol NR	

First Author, Year Country of Origin Study Design	Funding Source Conflicts of interest	Study Setting Study Duration	Inclusion Criteria	Exclusion Criteria	AMI Definition	POC Device/ Manufacturer Troponin Test Test Protocol	Health Personnel Conducting POC Test	Central Laboratory Instrument/Manufacturer Troponin Test Test Protocol	Clinical Adjudication for Final MI Diagnosis (Diagnostic-Accuracy Studies Only)
Storrow, 2006[36] US Prospective, observational study	Industry Conflicts of interest NR	1 teaching hospital ED + 1 community-based ED Duration NR; 30-day follow-up of patients	ED patients ≥ 21 years presenting with ACS symptoms; NSTEMI; enrolled within 1 h of ECG	Need for emergent catheterization or reperfusion therapy; hospitalized for ACS within past 4 weeks; trauma; presentation with a new left bundle-branch block or STEMI	NR	Cardiac Reader/ Roche cTnT Baseline; 3 h ± 2 h; 6 h ± 2 h; 12 ± 5 h; 24 h ± 7 h	Trained clinical research associates	Elecsys 2010/Roche cTnT Baseline; 3 ± 2 h; 6 h ± 2 h; 12 ± 5 h; 24 h ± 7 h	
Venge, 2013[43] Sweden Prospective, observational study	Partially funded by industry Authors had consultant or advisory roles with industry	Hospital ED 13 months (Nov 2004 to May 2005 and Oct 2006 to May 2007); deaths recorded over a 31-month period	Suspected MI plus troponin analysis requested by clinician	NR	NR	i-STAT/Abbott cTnI Whole blood by Stratus CS at the ED and/or in heparinized plasma by architect in the clinical chemistry laboratory	NR	Access AccuTnI/Beckman Architect cTnI/Abbott (VIDAS)/BioMerieux cTnI Whole blood was analyzed for cTnI by Stratus CS at the ED and/or in heparinized plasma by architect cTnI in the CL. Leftover heparinized whole blood was simultaneously analyzed for cTnI by i-STAT, and leftover heparinized plasma was frozen at–70 °C and analyzed at a later occasion in batches by Access AccuTnI or VIDAS cTnI	
Venge, 2010[46] Sweden Prospective, observational study	Assays provided by industry 2 authors affiliated with industry	Hospital ED 13 months (Nov 2004 to May 2005 and Oct 2006 to May 2007)	Admission to ED with a troponin analysis requested as part of the clinical workup	NR	NR	i-STAT/Abbott and Stratus CS/ Siemens cTnI Protocol NR	NR	Access AccuTnI/Beckman Coulter; Architect cTnI/ Abbott cTnI Protocol NR	

ACC = American College of Cardiology; ACS = acute coronary syndrome; AHA = American Heart Association; AMI = acute myocardial infarction; CAD = coronary artery disease; CCU = coronary care unit; CHD = coronary heart disease; CL = clinical laboratory; cTn = cardiac troponin; cTnI = cardiac troponin I; cTnT = cardiac troponin T; ECG = electrocardiogram; ED = emergency department; ESC = European Society of Cardiology; GP = general practitioner; h = hours; hs-cTnT = high-sensitivity cardiac troponin T; ICU = intensive care unit; MI = myocardial infarction; min = minutes; MLT = medical laboratory technologist; NA = not applicable; NR = not reported; NSTEMI = non-ST segment elevation myocardial infarction; POC = point of care; RCT = randomized controlled trial; STEMI = ST segment elevation myocardial infarction; UA = unstable angina; UK = United Kingdom; URL = upper reference limit; US = United States.

Appendix 7: Patient Characteristics

Table 15: Patient Characteristics

First Author, Year	Number of Patients Enrolled (N) Number Completed	Reasons for Withdrawal	Age (Years)	Sex	Symptoms	Comorbidities	Time From Symptom Onset
Diagnostic-Accuracy Studies							
Aldous, 2014[16]	N = 1,184 962 (81%) completed	NR	Median 66 (IQR 56 to 76)	59% male (n = 568)	Cardiac ischemia	• Diabetes,153 (15.9%) • Prior ischemic heart disease, 474 (49.3%) • Hypertension, 583 (60.6%) • Dyslipidemia, 539 (56.0%) • Current smoker, 141 (14.7%) • Previous smoker, 437 (45.4%)	NR
Di Serio, 2005[23]	N = 41 All completed	NR	Mean 61 ± SD 11.6	80% male (n = 33)	Chest pain	NR	Mean 6 h ± SD 4 h
Di Serio, 2007,[24] Amodio, 2007[25]	N = 516 All completed	NA	Mean 61	60% male (n = 308)	Chest pain	• Hypertension, 209 (40%); • Diabetes, 110 (21%) • Smoking, 109 (21%) • Previous, smoker, 200 (38%) • Previous MI, 120 (23%) • Congestive heart failure, 101 (19%)	Mean 5.0 h
Diercks, 2012[19]	N = 1,107 858 (78%) completed	48 with symptom onset > 8 hours before blood work 201 did not have all 3 samples drawn	Median 57.0 (IQR 48.0 to 67.0)	55.5% male (n = 476)	Chest pain or ischemic symptoms	• Diabetes mellitus, 224 (26.1%) • Hypertension, 575 (67%) • Hyperlipidemia, 482 (56.2%) • Renal insufficiency, 173 (20.2%) • Prior cardiac surgery, 328 (38.2%) • Prior MI, 230 (26.8%) • Smoker, 253 (29.5%)	Median 3.9 h (IQR 2.7 to 5.2 h)
Hjortshoj, 2011[21]	N = 458 Completed NR	NR	Median 63 (range 27 to 96)	64% male (n = 293)	Chest pain	• Angina pectoris, 167 (35%) • Previous MI, 48 (11%) • CABG, 20 (4%) • PCI, 27 (6%) • Diabetes, 55 (12%) • Hypertension, 188 (41%) • CHF, 33 (7%)	Median 2.20 h (range 0.75 to 6.00 h)
Ivandic, 2014[17]	N = 151 Completed NR	NR	Median 69 (range 37 to 90)	72% male (n = 109)	Chest pain	NR	NR

First Author, Year	Number of Patients Enrolled (N) Number Completed	Reasons for Withdrawal	Age (Years)	Sex	Symptoms	Comorbidities	Time From Symptom Onset
Lee-Lewandrowski, 2011[20]	N = 201 All completed	NA	Mean 61.7	53.9% male (n = 110)	Resting or exertional chest pain; arm, shoulder, or jaw pain; exertional dyspnea; palpitations; syncope; nausea and/or diaphoresis; and new ECG abnormalities	NR	NR
Nilsson, 2013[61] Andersson, 2015[1]	N = 196 POC: 128 All completed	NA	POC: mean 66 ± SD 14	POC: 56% male (n = 71)	POC: • chest pain 110 (86%) • weakness and/or dyspnea on exertion, no chest pain, 18 (14%)	POC: • angina pectoris, 22 (17%) • previous AMI, 20 (16%) • coronary revascularization, 16 (13%) • stroke, 5 (3.9%) • heart failure, 12 (9.4%) • aortic valve disease, 6 (4.7%) • potential causes of increase in troponin T in the absence of overt ischemic heart disease, 3 (2.3%)	NR
Palamalai, 2013[18]	N = 169 All completed	NA	Mean 58 ± SD16	60% male (n = 101)	Symptoms suggestive of ACS	NR	NR
Stengaard, 2013[62]	N = 985 924 completed	985 cases were 936 individual patients; 9 foreign citizens and 1 emigrant lost to follow-up; 2 patients had no status data	NR	NR	Chest pain within past 12 hours, acute dyspnea in absence of known pulmonary disease	Hypercholesterolemia, diabetes, hypertension, smoking (current and previous)	Median 70 min (range 35–180 min)
ter Avest, 2014[22]	N = 261 Completed NR	NR	Mean 62 (range 16 to 93)	61% male (n = 159)	Chest pain	NR	NR
Clinical-Utility Studies							
Altinier, 2001[33]	N = 100 Completed NR	NR	NR	NR	Chest pain	NR	NR
Apple, 2006[49]	N = 555 551 (99%) completed POC: N = 274 CL: N = 271	NR	POC: Median 51 CL: Median 54	POC: 56% male (n = 153) CL: 59% male (n = 160)	NR	Diabetes, renal disease, coronary artery disease (POC, 29%; CL, 48%) Previous MI (POC, 23%; CL, 33%)	NR
Asha, 2014[41,57]	N = 487 452 (93%) completed POC: N = 235 229 (97%) completed CL: N = 233 223 (96%) completed	19 enrolment forms not returned; 10 enrolled twice; 1 enrolled 3 times; 1 enrolled 5 times	POC: mean 61.9 ± SD16.6 CL: mean 61.7 ± SD 16.6	POC: 53% male (n = 122) CL: 52% male (n = 117)	NR	NR	NR
Caragher, 2002[32]	N = 205 Completed NR	NR	NR	NR	Chest pain	NR	NR

First Author, Year	Number of Patients Enrolled (N) Number Completed	Reasons for Withdrawal	Age (Years)	Sex	Symptoms	Comorbidities	Time From Symptom Onset
Collinson, 2004[50]	N = 263 All completed	NA	All: median 65.3 (IQR 27 to 88) POC: median 64.9 (IQR 39 to 88) CL: median 65.8 (IQR 26 to 87)	All: 67% male (n = 177) POC: 70% male (n = 92) CL: 64% male (n = 85)	NR	POC: • smoker, 23 (18%) • previous smoker, 46 (35%) • diabetes, 23 (18%) • previous history of ischemic heart disease, 66 (50%) • hypertension, 54 (41%) • hypercholesterolemia, 26 (20%) • dysrhythmia, 10 • unstable angina pain, 24 • non-ischemic chest pain, 9 CL: • smoker, 30 (23%) • previous smoker, 45 (34%) • diabetes, 18 (14%) • previous history of ischemic heart disease, 72 (54%) • hypertension, 47 (36%) • hypercholesterolemia, 3 (24%) • dysrhythmia, 22 • unstable angina pain, 30 • non-ischemic chest pain, 10	POC: median 6.5 h CL: median 5.0 h
Cramer, 2007[34]	N = 358 Completed NR	NR	Mean 64 ± SD 14	58% male (n = 208)	NR	NR	NR
Cullen, 2012[44]	N = 976 704 (72%) completed	272 patients did not have index blood drawn at appropriate time	Median 53 (IQR: 44 to 65)	62.1% male (n = 606)	Chest pain	Hypertension, diabetes, dyslipidemia, smoking or prior angina, coronary artery disease, chronic heart failure, stroke, coronary artery bypass graft, or percutaneous cardiac intervention	NR
Deledda, 2011[42]	All: N = 4,886 All completed POC: N = 2,446 CL: N = 2,440	NA	POC: mean 56.3 ± SD 15.7 CL: mean 57.4 ± SD 16.0	POC: 48.1% male (n = 1,177) CL: 46.1% male (n = 1,124)	Chest pain or other symptoms of ACS	NR	NR
Di Serio, 2003[31]	NR	NR	NR	NR	Chest pain	NR	NR

First Author, Year	Number of Patients Enrolled (N) Number Completed	Reasons for Withdrawal	Age (Years)	Sex	Symptoms	Comorbidities	Time From Symptom Onset
Eggers, 2011[45]	N = 454 Completed NR	NR	Median 65 (IQR 57 to 76)	69.5% male (n = 299)	Acute chest pain	• Hypertension, 187 (41.2%) • Diabetes, 78 (17.2%) • Hyperlipidemia, 165 (36.3%) • Previous AMI, 155 (34.1%) • Congestive heart failure, 76 (16.7%) • Previous revascularization, 132 (29.1%) • Smoker: 80 (17.6%) • Previous smoker, 195 (43.0%)	NR
Ezekowitz, 2015[55]	N = 601 544 (91%) completed per protocol analysis	2 patients allocated to usual care received POC; 55 patients allocated to POC did not receive POC testing	All: median 66 (IQR 53 to 79) Usual care: median 68 (IQR 53 to 79) POC: median 64 (IQR 53 to 76)	All: 56.6% (n = 340) Usual care: 54% male (n = 160) POC: 59% male (n = 180)	Acute chest pain	POC: • previous MI, 96 (31.5%) • heart failure, 21 (6.9%) • diabetes, 80 (26.2%) Usual care: • previous MI, 82 (27.7%) • heart failure, 29 (9.8%) • diabetes, 72 (24.3%) • hypertension, 181 (61.1%)	NR
Fitzgibbon, 2010,[53] Fitzgibbon, 2007[58]	100 health care personnel at 10 major hospitals responded to survey	NA	NA	NA	NA	NA	NA
Goodacre, 2011[39]	N = 2,263 2,243 (99%) completed	12 not adequate consent 2 consent withdrawn; 6 recruited in error and not followed up	Mean 54.5 ± SD14.1	58% male (n = 1,307)	• Indigestion/ burning, 154 (7%) • Stabbing/sharp chest pain, 459 (21%) • Aching/dull chest pain, 567 (26%) • Gripping/crushing/ heavy chest pain, 794 (36%) • Non-specific/other chest pain, 239 (11%)	• Known coronary artery disease, 269 (12%) • Diabetes, 178 (8%) • Hypertension, 737 (33%) • Hyperlipidemia, 553 (27%) • Smoker, 626 (28%) • Previous smoker, 273 (13%) • Cocaine use, 16 (1%)	All: mean 230 min ± SD 425 POC: 241 min ± SD 504 CL: 219 min ± 325 SD
Guo, 2006[51]	N = 551 502 (91%) completed	NR	NR	NR	Chest pain	Hypertension, diabetes, renal failure, tumour, stroke, or previous MI	Onset of chest pain ranged from 0.5 h to 24 h before hospital admission
Koehler, 2013[27]	N =, 201; Completed NR	NR	NR	NR	Chest, abdominal, or shoulder pain	NR	NR

First Author, Year	Number of Patients Enrolled (N) Number Completed	Reasons for Withdrawal	Age (Years)	Sex	Symptoms	Comorbidities	Time From Symptom Onset
Lee-Lewandrowski, 2002[37]	NR	NR	NR	NR	NR	NR	NR
Liikanen, 2005[54]	401 surveys sent 301 (75%) responses	NA	NA	NA	NA	NA	NA
Loten, 2010[40]	N = 912 All completed	NA	POC: median 60 (range 25 to 101) CL: median 62 (range 25 to 99)	POC: 52.2% male (n = 244) CL: 49.7% male (n = 221)	Symptoms suggestive of ACS	NR	NR
Meek, 2012[28]	N = 671 All completed	NR	POC: median 62 (IQR 50 to 73) CL: median 63 (IQR 52 to 77)	POC: 52.7% male (n = 136) CL: 56.7% male (n = 234)	Chest pain	NR	NR
Mozina, 2010[35]	N = 31 All completed	NA	NR	NR	Chest pain	NR	NR
Nilsson, 2013[61] Andersson, 2015[1]	N = 196 POC: 128 All completed	NA	POC: mean 66 ± SD 14	POC: 56% male (n = 71)	POC: • chest pain, 110 (86%) • weakness and/or dyspnea on exertion, no chest pain, 18 (14%)	POC: • angina pectoris, 22 (17%) • previous AMI, 20 (16%) • coronary revascularization, 16 (13%) • stroke, 5 (3.9%) • heart failure, 12 (9.4%) • aortic valve disease, 6 (4.7%) • potential causes of increase in troponin T in the absence of overt ischemic heart disease, 3 (2.3%)	NR
Ordonez-Llanos, 2006[47]	N = 1,410 Completed NR	NR	Mean 63 ± SD 14.6	64% male (n = 906)	Chest pain	NR	Median 285 min

First Author, Year	Number of Patients Enrolled (N) Number Completed	Reasons for Withdrawal	Age (Years)	Sex	Symptoms	Comorbidities	Time From Symptom Onset
Renaud, 2008[29]	N = 833 Completed NR	NR	POC: median 62 (IQR 49 to 75) CL: median 64 (IQR 50 to 77)	POC: 62% male (n = 260) CL: 58.4% male (n = 242)	POC: • chest pain (58%) • left arm pain (13%) • general malaise (19%) • dyspnea (32%) • epigastric pain (8%) CL: • chest pain (56%) • left arm pain (16%) • general malaise (24%) • dyspnea (33%) • epigastric pain (8%)	POC: • high BMI, 59% • hypertension, 49% • diabetes, 21% • hyperlipidemia, 33% • history of smoking, 52% history of atherosclerosis, 47% CL: • high BMI, 59% • hypertension, 49% • diabetes, 21% • hyperlipidemia, 36% • history of smoking, 48% • history of atherosclerosis, 48%	NR
Ryan, 2009[26]	N = 2,134 2,000 (94%) completed	62 met exclusion criteria, 24 unable to obtain blood, 14 process or assay error, 15 withdrew consent, 10 left ED prior to data collection, 6 unable to consent, 2 no patient data available, 1 physician refused further participation	POC: mean 60 ± SD 16 CL: mean 59 ± SD16	POC: 47.4% male (n = 474) CL: 49.7% male (n = 497)	POC: • dyspnea, 524 (52%) • diaphoresis, 216, (22%) • nausea, 255 (26%) • weakness, 310 (31%) • dizziness, 236 (24%) • palpitations, 166 (17%) CL: • dyspnea, 481 (48%) • diaphoresis, 213 (21%) • nausea, 260 (26%) • weakness, 320 (32%) • dizziness, 243 (24%) • palpitations, 147 (15%)	POC: • Current smoker, 251 (25%) • Current cocaine user, 14 (1%) • hypertension, 625 (62%) • diabetes, 209 (21%) • previous MI, 181 (18%) • previous arrhythmia, 198 (20%) • hyperlipidemia, 436 (44%) • previous PCI, 273 (27%) • previous CABG, 115 (12%) CL: • current smoker, 253 (25%) • current cocaine user, 14 (1%) • hypertension, 606 (61%) • diabetes, 204,(20%) • previous MI, 205 (20%) • previous arrhythmia, 177 (18%) • hyperlipidemia, 428 (43%) • previous PCI, 265 (26%) • previous CABG, 117 (12%)	POC: • < 1 h, 148 (15%) • ≥ 1 h to < 3 h, 217 (22%) • ≥ 3 h to < 6 h, 125 (12%) • ≥ 6 h: 509 (51%) CL: • < 1 h, 150 (15%) • ≥ 1 h to < 3 h, 221 (22%) • ≥ 3 h to < 6 h, 112 (11%) • ≥ 6 h, 516 (52%)

First Author, Year	Number of Patients Enrolled (N) Number Completed	Reasons for Withdrawal	Age (Years)	Sex	Symptoms	Comorbidities	Time From Symptom Onset
Shephard, 2014,[52] Shephard, 2012[56]	33 remote health centres; 3 aboriginal community health centres; 506 trained staff	NA	NA	NA	NA	NA	NA
Singer, 2015[38]	N = 2,386 All completed POC: 190 cTn tests CL: 845 cTn tests	NA	NR	NR	NR	NR	NR
Singer, 2005[30]	N = 366 All completed	NA	All: mean 63 ± SD 16 POC: mean 60.8 ± SD16.9 CL: mean 64.2 ± SD15.5	All: 56% male (n = 205) POC: 58% male (n = 77) CL: 54% male (n = 126)	Chest pain	POC: • hypertension, 41 (32%) • history of smoking, 34, (31%) • diabetes, 22 (20%) • hypercholesterolemia, 29 (26%) CL: • hypertension, 77 (35%) • history of smoking, 41 (22%) • diabetes, 47 (26%) • hypercholesterolemia, 48 (26%) • cocaine use, 2 (1%)	NR
Sorensen, 2011[48]	N = 4,905, Completed NR POC: N = 958; 928 (97%) completed CL: N = 3,947 Completed NR	• 5 failure of test kit • 18 inability to draw blood • 9 short transport distance	• POC: median 66 (IQR 55 to 78) • • CL: median 67 (IQR 55 to 79)	• POC: 59% male (n = 565) • • CL: 60% male (n = 2,380)	Chest pain	POC: • previous MI, 226 (25%) • previous PCI or CABG, 218 (24%) • diabetes, 111 (12%) CL: • previous MI, 980 (26%) • previous PCI or CABG, 831 (23%) • diabetes, 397 (11%)	POC: median 83 min (IQR 46 to 167 min) CL: 165 min (110 to 276 min)
Stengaard, 2013[62]	N = 985 924 completed	985 cases were 936 individual patients; 9 foreign citizens and 1 emigrant lost to follow-up; 2 patients had no status data	NR	NR	Chest pain within past 12 hours, acute dyspnea in absence of known pulmonary disease	Hypercholesterolemia, diabetes, hypertension, smoking (current and previous)	Median 70 min (range 35 to 180 min)
Storrow, 2006[36]	N = 253 223 (88%) completed	24 chose to withdraw after baseline blood work; 2 left ED; 2 were excluded by treating physician; 17 were lost to follow-up; 1 had laboratory markers drawn pre-ED; 5 lacked documented ED arrival time	Mean 57.1 ± SD 14.6	52.5% male (n = 117)	Symptoms suggestive of ACS	NR	NR

First Author, Year	Number of Patients Enrolled (N) Number Completed	Reasons for Withdrawal	Age (Years)	Sex	Symptoms	Comorbidities	Time From Symptom Onset
Venge, 2013[43]	N = 508 All completed	NA	Male: mean 68.8 ± 17.8 SD Female: mean 70.2 ± SD17.8	51% male (n = 259)	NR	NR	NR
Venge, 2010[46]	N = 1,069 851 (80%) completed (outcome available for this number)	NR	Male: mean 70.1 ± SD18.1 Female: mean 72.8 ± SD 17.7	53% male (n = 567)	NR	NR	NR

ACS = acute coronary syndrome; AMI = acute myocardial infarction; BMI = body mass index; CABG = coronary artery bypass graft; CHF = congestive heart failure; CL = clinical laboratory; ECG = electrocardiogram; ED = emergency department; h = hours; IQR = interquartile ratio; MI = myocardial infarction; min = minutes; N = number; NA = not applicable; NR = not reported; PCI = percutaneous coronary intervention; POC = point of care; SD = standard deviation.

Appendix 8: Critical Appraisal

Table 16: Critical Appraisal of Diagnostic-Accuracy Studies (QUADAS-2)

First Author, Publication Date	Strengths	Limitations
Aldous, 2014[16]	Patient selection: • case-control design avoided • the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: low) • concern that the included patients did not match the review question (concern: low) Reference standard: • the reference standard was likely to correctly classify the target condition • the reference-standard results were interpreted without knowledge of the results of the index test • the reference standard, its conduct, or its interpretation could have introduced bias (risk: low) • concern that the reference-standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • there was an appropriate interval between index test and reference standard • all patients received a reference standard • all patients received the same reference standard • the patient flow could have introduced bias (risk: low)	Patient selection: • unclear if consecutive sample of patients were enrolled Index tests: • unsure if the index test results were interpreted without knowledge of the results of the reference standard • the conduct or interpretation of the index test could have introduced bias (risk: unclear) • concern that the index test, its conduct, or interpretation differs from the review question (concern: unclear) Flow and timing: • not all patients were included in the analysis
Di Serio, 2005[23]	Patient selection: • case-control design avoided • concern that the included patients did not match the review question (concern: low) Index tests: • concern that the index test, its conduct, or interpretation differs from the review question (concern: low) Reference standard: • the reference standard was likely to correctly classify the target condition • concern that the reference standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • all patients received a reference standard • all patients received the same reference standard	Patient selection: • unclear if consecutive sample of patients were enrolled • unclear if the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: uncertain) Index tests: • unsure if the index test results were interpreted without knowledge of the results of the reference standard • the conduct or interpretation of the index test could have introduced bias (risk: unclear) Reference standard: • unsure if the reference-standard results were interpreted without knowledge of the results of the index test • the reference standard, its conduct, or its interpretation could have introduced bias (risk: unclear)

First Author, Publication Date	Strengths	Limitations
		Flow and timing: • unclear if there was an appropriate interval between index test and reference standard • unsure if all patients were included in the analysis • the patient flow could have introduced bias (risk: uncertain)
Di Serio, 2007;[24] Amodio, 2007[25]	Patient selection: • consecutive sample of patients enrolled • case-control design avoided • the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: low) • concern that the included patients did not match the review question (concern: low) Index tests: • concern that the index test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • all patients were included in the analysis • the patient flow could have introduced bias (risk: low)	Reference standard: • there was no reference standard done
Diercks, 2012[19]	Patient selection: • case-control design avoided • the study avoided inappropriate exclusions • concern that the included patients did not match the review question (concern: low) Reference standard: • the reference standard was likely to correctly classify the target condition • concern that the reference-standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • all patients received a reference standard • all patients received the same reference standard	Patient selection: • unclear if consecutive sample of patients were enrolled • the selection of patients could have introduced bias (risk: unclear) Index tests: • unsure if the index test results were interpreted without knowledge of the results of the reference standard • concern that the index test, its conduct, or interpretation differs from the review question (concern: uncertain) • the conduct or interpretation of the index test could have introduced bias (risk: unclear) Reference standard: • unclear if the reference-standard results were interpreted without knowledge of the results of the index test • the reference standard, its conduct, or its interpretation could have introduced bias (risk: unclear) Flow and timing: • unclear if there was an appropriate interval between index test and reference standard • not all patients were included in the analysis • the patient flow could have introduced bias (risk: uncertain)

First Author, Publication Date	Strengths	Limitations
Hjortshoj, 2011[21]	Patient selection: • case-control design avoided • concern that the included patients did not match the review question (concern: low) Reference standard: • the reference standard was likely to correctly classify the target condition • concern that the reference-standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • there was an appropriate interval between index test and reference standard • all patients received a reference standard • all patients received the same reference standard • all patients were included in the analysis • the patient flow could have introduced bias (risk: low)	Patient selection: • unclear if consecutive sample of patients were enrolled • unclear if the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: unclear) Index tests: • unsure if the index test results were interpreted without knowledge of the results of the reference standard • concern that the index test, its conduct, or interpretation differs from the review question (concern: uncertain) • the conduct or interpretation of the index test could have introduced bias (risk: unclear) Reference standard: • unsure if the reference-standard results were interpreted without knowledge of the results of the index test • the reference standard, its conduct, or its interpretation could have introduced bias (risk: low)
Ivandic, 2014[17]	Patient selection: • consecutive sample of patients enrolled • case-control design avoided • the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: low) • concern that the included patients did not match the review question (concern: low) Index tests: • concern that the index test, its conduct, or interpretation differs from the review question (concern: low) Reference standard: • the reference standard was likely to correctly classify the target condition • concern that the reference-standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • all patients were included in the analysis	Index tests: • unsure if the index test results were interpreted without knowledge of the results of the reference standard • the conduct or interpretation of the index test could have introduced bias (risk: unclear) Reference standard: • unsure if the reference-standard results were interpreted without knowledge of the results of the index test • the reference standard, its conduct, or its interpretation could have introduced bias (risk: unclear) Flow and timing: • unclear if there was an appropriate interval between index test and reference standard • unclear if all patients received a reference standard • the patient flow could have introduced bias (risk: unclear)

First Author, Publication Date	Strengths	Limitations
Lee-Lewandrowski, 2011[20]	Patient selection: • case-control design avoided • concern that the included patients did not match the review question (concern: low) Index tests: • the index test results were interpreted without knowledge of the results of the reference standard • the conduct or interpretation of the index test could have introduced bias (risk: low) • concern that the index test, its conduct, or interpretation differs from the review question (concern: low) Reference standard: • the reference standard was likely to correctly classify the target condition • the reference standard, its conduct, or its interpretation could have introduced bias (risk: low) • concern that the reference-standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • there was an appropriate interval between index test and reference standard • all patients received a reference standard • all patients received the same reference standard • the patient flow could have introduced bias (risk: low)	Patient selection: • unclear if consecutive sample of patients were enrolled • unclear if the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: unclear) Reference standard: • unclear if the reference standard results were interpreted without knowledge of the results of the index test Flow and timing: • not all patients were included in the analysis
Nilsson, 2013;[61] Andersson, 2015[1]	Patient selection: • case-control design avoided • the study avoided inappropriate exclusions • concern that the included patients did not match the review question (concern: low) Index tests: • concern that the index test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • all patients were included in the analysis	Patient selection: • unclear if consecutive sample of patients were enrolled • the selection of patients could have introduced bias (risk: unclear) Index tests: • unsure if the index test results were interpreted without knowledge of the results of the reference standard • the conduct or interpretation of the index test could have introduced bias (risk: unclear) Flow and timing: • unclear if there was an appropriate interval between index test and reference standard • not all patients received a reference standard • the patient flow could have introduced bias (risk: unclear)

First Author, Publication Date	Strengths	Limitations
Palaimalai, 2013[18]	Patient selection: • consecutive sample of patients enrolled • case-control design avoided • concern that the included patients did not match the review question (concern: low) Reference standard: • the reference standard was likely to correctly classify the target condition • concern that the reference-standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • there was an appropriate interval between index test and reference standard • all patients received a reference standard • all patients received the same reference standard • all patients were included in the analysis • the patient flow could have introduced bias (risk: low)	Patient selection: • unclear if the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: unclear) Index tests: • unsure if the index test results were interpreted without knowledge of the results of the reference standard • concern that the index test, its conduct, or interpretation differs from the review question (concern: uncertain) • the conduct or interpretation of the index test could have introduced bias (risk: unclear) Reference standard: • unsure if the reference-standard results were interpreted without knowledge of the results of the index test • the reference standard, its conduct, or its interpretation could have introduced bias (risk: unclear)
Stengaard, 2013[62]	Patient selection: • consecutive sample of patients enrolled • case-control design avoided • the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: low) • concern that the included patients did not match the review question (concern: low) Index tests: • the index test results were interpreted without knowledge of the results of the reference standard • concern that the index test, its conduct, or interpretation differs from the review question (concern: low) Reference standard: • the reference standard was likely to correctly classify the target condition • concern that the reference-standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • all patients received a reference standard • all patients received the same reference standard	Index tests: • the conduct or interpretation of the index test could have introduced bias (risk: unclear) Reference standard: • unsure if the reference-standard results were interpreted without knowledge of the results of the index test • the reference standard, its conduct, or its interpretation could have introduced bias (risk: unclear) Flow and timing: • unclear if there was an appropriate interval between index test and reference standard • not all patients were included in the analysis • the patient flow could have introduced bias (risk: uncertain)

First Author, Publication Date	Strengths	Limitations
ter Avest, 2014[22]	Patient selection: • case-control design avoided • the study avoided inappropriate exclusions • the selection of patients could have introduced bias (risk: low) • concern that the included patients did not match the review question (concern: low) Index tests: • concern that the index test, its conduct, or interpretation differs from the review question (concern: low) Reference standard: • the reference-standard results were interpreted without knowledge of the results of the index test • the reference standard was likely to correctly classify the target condition • concern that the reference-standard test, its conduct, or interpretation differs from the review question (concern: low) Flow and timing: • there was an appropriate interval between index test and reference standard • all patients received a reference standard • all patients received the same reference standard • the patient flow could have introduced bias (risk: low)	Patient selection: • unclear if consecutive sample of patients were enrolled Index tests: • the index test results were interpreted with knowledge of the results of the reference standard • the conduct or interpretation of the index test could have introduced bias (risk: uncertain) Reference standard: • the reference standard, its conduct, or its interpretation could have introduced bias (risk: low) Flow and timing: • unclear if all patients were included in the analysis

Table 17: Critical Appraisal of Clinical-Utility Studies (Downs and Black)

First Author, Publication Date	Strengths	Limitations
Randomized Controlled Trials		
Asha, 2014[41,57]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distribution of principal confounders in each group of subjects to be compared was clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were described.	• No attempt was made to blind study subjects to the intervention they received. • No attempt was made to blind those measuring the main outcomes of the intervention. • Compliance with the intervention (regarding patient enrolment) was not reliable. • The study may not have had sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was < 5%.

First Author, Publication Date	Strengths	Limitations
	• Actual probability values were reported (except where *P* is less than 0.001). • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • Study subjects were randomized to intervention groups. • The randomized intervention assignment was concealed from both patients and health care staff until recruitment was complete and irrevocable. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were taken into account.	
Collinson, 2004[50]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distributions of principal confounders in each group of subjects to be compared was clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were described. • Actual probability values were reported (except where $P < 0.001$). • The subjects asked to participate in the study were representative of the entire population from which they were recruited.	• No attempt was made to blind study subjects to the intervention they received. • No attempt was made to blind those measuring the main outcomes of the intervention. • It is unclear if the time period between the intervention and outcome was the same for cases and controls.

First Author, Publication Date	Strengths	Limitations
	• The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • Statistical tests used to assess the main outcomes were appropriate. • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • Study subjects were randomized to intervention groups. • The randomized intervention assignment was concealed from both patients and health care staff until recruitment was complete and irrevocable. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were taken into account. • The study had sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was < 5%.	
Ezekowitz, 2015[55]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • Study subjects were randomized to intervention group. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • Those measuring the main outcomes of the intervention were blinded to the allocation. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of	• It could not be determined whether the study had sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was < 5%.

First Author, Publication Date	Strengths	Limitations
	the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn.	
Goodacre, 2011[39]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • An attempt was made to blind those measuring the main outcomes of the intervention. • All important adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were described. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • Study subjects were randomized to intervention group. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn.	• No attempt was made to blind study subjects to the intervention they received. • It is unclear if compliance with the intervention was reliable. • It could not be determined whether the randomized intervention assignment was concealed from both patients and health care staff until recruitment was complete and irrevocable. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited.

First Author, Publication Date	Strengths	Limitations
	• Losses of patients to follow-up were taken into account. • The study had sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was < 5%.	
Loten, 2010[40]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • The characteristics of patients lost to follow-up were described. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • Study subjects were randomized to intervention group. • Losses of patients to follow-up were taken into account. • The study had sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was < 5%.	• The characteristics of the patients included in the study were not clearly described. • The distributions of principal confounders in each group of subjects to be compared were not described. • Adverse events that may have been a consequence of the intervention were reported. • Compliance with the intervention was not reliable. • It could not be determined whether an attempt was made to blind study subjects to the intervention they received. • It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • It could not be determined whether randomized intervention assignment was concealed from both patients and health care staff until recruitment was complete and irrevocable. • It could not be determined if there was adequate adjustment for confounding in the analyses from which the main findings were drawn. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited
Renaud, 2008[29]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distribution of principal confounders in each group of subjects to be compared was clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have	• The number and characteristics of patients lost to follow-up were not described. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive, except that the study only occurred on weekdays, which may differ from weekend processes and procedures. • No attempt was made to blind study subjects to the intervention they received. • Some attempt was made to blind those measuring the main outcomes of the intervention, but those performing the testing and treating patients directly were not blinded. • It is unclear if losses of patients to follow-up were taken into account.

First Author, Publication Date	Strengths	Limitations
	been a consequence of the intervention were reported. • Actual probability values were reported (except where $P < 0.001$). • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • Study subjects were randomized to intervention groups. • The randomized intervention assignment was concealed from both patients and health care staff until recruitment was complete and irrevocable. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • The study had sufficient power to detect a clinically important effect (except for mortality) when the probability value for a difference being due to chance was < 5%.	
Ryan, 2009[26]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • The characteristics of patients lost to follow-up were described. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and	• Actual probability values were not reported. • Adverse events that may have been a consequence of the intervention were not reported. • The subjects asked to participate in the study were not completely representative of the entire population from which they were recruited, as this was a convenience sample. • It could not be determined whether an attempt was made to blind study subjects to the intervention they received. • It could not be determined whether randomized intervention assignment was concealed from both patients and health care staff until recruitment was complete and irrevocable. • It is unclear if an attempt was made to blind those measuring the main outcomes of the intervention. • Compliance with the intervention was not reliable.

First Author, Publication Date	Strengths	Limitations
	outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • Study subjects were randomized to intervention group. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were taken into account. • The study had sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was < 5%.	
Observational Studies		
Altinier, 2001[33]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • Actual probability values were reported (except where *P* < 0.001). • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • The study had sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was < 5%.	• The characteristics of the patients included in the study were not described. • Adverse events that may have been a consequence of the intervention were not reported. • The characteristics of patients lost to follow-up were not described. • No attempt was made to blind those measuring the main outcomes of the intervention. • It was not made clear if any of the results of the study were based on data dredging. • It is unclear if compliance with the intervention was reliable. • Study subjects were not randomized to intervention groups. • Losses of patients to follow-up were not reported.

First Author, Publication Date	Strengths	Limitations
Apple, 2006[49]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distribution of principal confounders in each group of subjects to be compared was clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • Actual probability values were reported (except where $P < 0.001$). • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population.	• The characteristics of patients lost to follow-up were not described. • The staff, places, and facilities where the patients were treated were not completely representative of the treatment the majority of patients receive (patients were selected from a cardiology service, not a hospital ED). • No attempt was made to blind study subjects to the intervention they received. • No attempt was made to blind those measuring the main outcomes of the intervention. • The cases and controls were not recruited over the same time, as this was a pre/post study. • Study subjects were not randomized to intervention groups. • There was not adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were taken into account. • It is unclear if losses of patients to follow-up were taken into account. • The study did not have sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was< 5%.
Caragher, 2002[32]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • All important adverse events that may have been a consequence of the intervention were reported. • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and	• The characteristics of the patients included in the study were not described. • The study did not provide estimates of the random variability in the data for the main outcomes. • The characteristics of patients lost to follow-up were not described. • Actual probability values were not reported. • No attempt was made to blind those measuring the main outcomes of the intervention. • It is unclear if statistical tests used to assess the main outcomes were appropriate. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were not reported. • It is unclear if the study had sufficient power to

First Author, Publication Date	Strengths	Limitations
	controls. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time.	detect a clinically important effect when the probability value for a difference being due to chance was < 5%.
Cramer, 2007[34]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • All important adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were described. • Actual probability values were reported (except where $P < 0.001$). • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • The study had sufficient power to detect a clinically important effect when the probability value for a difference being due to chance was < 5%.	• The characteristics of the patients included in the study were not clearly described. • The study did not provide estimates of the random variability in the data for the main outcomes. • It is unclear if the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It is unclear if the staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • No attempt was made to blind those measuring the main outcomes of the intervention. • It is unclear if compliance with the intervention (regarding patient enrolment) was reliable. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in the analyses from which the main findings were drawn. • It is unclear if losses of patients to follow-up were taken into account.

First Author, Publication Date	Strengths	Limitations
Cullen, 2012[44]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • The characteristics of the patients included in the study were clearly described. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • It was made clear if any of the results of the study were based on data dredging. • An attempt was made to blind those measuring the main outcomes of the intervention. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The time period between the intervention and outcome was the same for cases and controls. • The cases and controls were recruited from the same population.	• The characteristics of patients lost to follow-up were not described. • It could not be determined if compliance with the intervention was reliable. • Study subjects were not randomized to intervention group. • It could not be determined if there was adequate adjustment for confounding in the analyses from which the main findings were drawn. • It is unclear whether losses of patients to follow-up were not taken into account. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.
Deledda, 2011[42]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distribution of principal confounders in each group of subjects to be compared was clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive.	• Adverse events that may have been a consequence of the intervention were not reported. • The characteristics of patients lost to follow-up were not described. • Probability values were not reported. • No attempt was made to blind study subjects to the intervention they received. • No attempt was made to blind those measuring the main outcomes of the intervention. • It is unclear if compliance with the intervention was reliable. • The cases and controls were not recruited from the same population. • The cases and controls were not recruited over the same time. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in the analyses from which the main findings

First Author, Publication Date	Strengths	Limitations
	• It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.	were drawn. • The authors indicated the main outcome measures used were a limitation. • Losses of patients to follow-up were not taken into account.
Di Serio, 2003[31]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • One probability value was reported. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.	• The characteristics of the patients included in the study were not described. • No adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were not described. • It is unclear if subjects asked to participate in the study were representative of the entire population from which they were recruited. • It is unclear if the staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • No attempt was made to blind those measuring the main outcomes of the intervention. • It was not clear if any of the results of the study were based on data dredging. • It is not clear if compliance with the intervention was reliable. • It is not clear if the cases and controls were recruited from the same population. • It is not clear if the cases and controls were recruited over the same time. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were not taken into account.
Eggers, 2011[45]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random	• The characteristics of patients lost to follow-up were not described. • It could not be determined if compliance with the intervention was reliable. • It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention group. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It is unclear if losses of patients to follow-up were taken into account.

First Author, Publication Date	Strengths	Limitations
	variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn.	• It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.
Guo, 2006[51]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were described. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population.	• The characteristics of all patients included in the study were not clearly described. • It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention group. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.

First Author, Publication Date	Strengths	Limitations
	• The cases and controls were recruited over the same time. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were taken into account.	
Koehler, 2013[27]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable).	• The characteristics of the patients included in the study were not clearly described. • The distributions of principal confounders in each group of subjects to be compared were not clearly described. • No attempt was made to blind study subjects to the intervention they received. • It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • The time period between the intervention and outcome was not the same for cases and controls. • Adverse events that may have been a consequence of the intervention were reported. • It is unclear if compliance with the intervention was reliable. • The cases and controls were not recruited from the same population. • It could not be determined if there was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Study subjects were not randomized to intervention group. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.
Lee-Lewandrowski, 2002[37]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • Actual probability values were reported (except where *P* is less than 0.001). • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • An attempt was made to blind those measuring the main outcomes of the intervention. • It was made clear if any of the results of the study were based on data dredging.	• The characteristics of the patients included in the study were not described. • The distributions of principal confounders in each group of subjects to be compared was not described. • The study did not provide estimates of the random variability in the data for the main outcomes. • Adverse events that may have been a consequence of the intervention were not reported. • It is unclear if the subjects measured in the study were representative of the entire population from which they were recruited because there was no patient information. • The characteristics of patients lost to follow-up were not described. • It is unclear if statistical tests used to assess

First Author, Publication Date	Strengths	Limitations
	• The time period between the intervention and outcome was the same for cases and controls. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.	the main outcomes were appropriate. • The cases and controls were not recruited over the same time. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in the analyses from which the main findings were drawn.
Meek, 2012[28]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.	• The characteristics of the patients included in the study were not clearly described. • The distributions of principal confounders in each group of subjects to be compared were not clearly described. • The time period between the intervention and outcome was not the same for cases and controls. • The cases and controls were not recruited from the same population. • The characteristics of patients lost to follow-up were not described. • It could not be determined if compliance with the intervention was reliable. • It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention group. • It could not be determined if there was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were not taken into account. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited.
Mozina, 2010[35]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • Actual probability values were reported (except where $P < 0.001$). • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive.	• The characteristics of the patients included in the study were not described. • No adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were not described. • It is not clear if the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It is not clear if the staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • No attempt was made to blind those

First Author, Publication Date	Strengths	Limitations
	• It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • The study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.	measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were not reported.
Nilsson, 2013[61]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for 2 main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were described. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited over the same time. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were taken into account.	• It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention group. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.

First Author, Publication Date	Strengths	Limitations
Ordonez, Llanos, 2006[47]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • All important adverse events that may have been a consequence of the intervention were reported. • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time.	• The characteristics of the patients included in the study were not clearly described. • The distribution of principal confounders in each group of subjects to be compared was not clearly described. • The study did not provide estimates of the random variability in the data for the clinical-utility outcomes. • The characteristics of patients lost to follow-up were not described. • Actual probability values were not reported. • No attempt was made to blind study subjects to the intervention they received. • No attempt was made to blind those measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were not taken into account. • It was not stated if the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.
Singer, 2015[38]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distribution of principal confounders in each group of subjects to be compared was clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • Actual probability values were reported (except where *P* < 0.001). • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • It was made clear if any of the results of the study were based on data dredging. • Statistical tests used to assess the main outcomes were appropriate. • The study had sufficient power to detect a	• Adverse events that may have been a consequence of the intervention were not reported. • The characteristics of patients lost to follow-up were not described. • No attempt was made to blind study subjects to the intervention they received. • No attempt was made to blind those measuring the main outcomes of the intervention. • The time period between the intervention and outcome was not the same for cases and controls. • The authors indicated the main outcome measures used were not accurate (valid and reliable). • Compliance with the intervention was not reliable. • The cases and controls were not recruited from the same population. • The cases and controls were not recruited over the same time. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in

First Author, Publication Date	Strengths	Limitations
	clinically important effect where the probability value for a difference being due to chance < 5%.	the analyses from which the main findings were drawn. • Losses of patients to follow-up were not taken into account.
Singer, 2005[30]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distribution of principal confounders in each group of subjects to be compared was clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • The subjects asked to participate in the study were representative of the entire population from which they were recruited. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. Statistical tests used to assess the main outcomes were appropriate. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • The study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.	• No adverse events that may have been a consequence of the intervention were reported. • Patients lost to follow-up were not reported. • Actual probability values were not reported. • No attempt was made to blind study subjects to the intervention they received. • No attempt was made to blind those measuring the main outcomes of the intervention. • The cases and controls were not recruited over the same time, as this was a pre/post study. • Study subjects were not randomized to intervention groups. • Losses of patients to follow-up were not reported.
Sorensen, 2011[48]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • The main findings of the study were clearly described.	• The time period between the intervention and outcome was not the same for cases and controls. • It could not be determined if compliance with the intervention was reliable. • The cases and controls were not recruited from the same population. • It could not be determined if losses of patients to follow-up were taken into account. • It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention group.

First Author, Publication Date	Strengths	Limitations
	• The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were described. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • There was adequate adjustment for confounding in the analyses from which the main findings were drawn.	• It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.
Stengaard, 2013[62]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The distributions of principal confounders in each group of subjects to be compared were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • The characteristics of patients lost to follow-up were described. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • An attempt was made to blind those measuring the main outcomes of the intervention. • Statistical tests used to assess the main outcomes were appropriate. • Compliance with the intervention was reliable. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population.	• No attempt was made to blind study subjects to the intervention they received. • It is unclear if the time period between the intervention and outcome was the same for cases and controls. • Study subjects were not randomized to intervention group. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.

First Author, Publication Date	Strengths	Limitations
	• The cases and controls were recruited over the same time. • There was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were taken into account.	
Storrow, 2006[36]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The characteristics of the patients included in the study were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • Actual probability values were reported (except where $P < 0.001$). • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population. • The cases and controls were recruited over the same time. • Losses of patients to follow-up were taken into account. • The study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.	• Adverse events that may have been a consequence of the intervention were not reported. • The characteristics of patients lost to follow-up were described. • The characteristics of patients lost to follow-up were not described. • It is unclear if the subjects asked to participate in the study were representative of the entire population from which they were recruited. • No attempt was made to blind those measuring the main outcomes of the intervention. • It is unclear if compliance with the intervention was reliable. • Study subjects were not randomized to intervention groups. • There was no adjustment for confounding in the analyses from which the main findings were drawn.
Venge, 2013[43]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • Actual probability values were reported.	• The characteristics of the patients included in the study were not clearly described. • The distributions of principal confounders in each group of subjects to be compared were not clearly described. • The characteristics of patients lost to follow-up were not described. • It could not be determined if compliance with the intervention was reliable. • It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention group.

First Author, Publication Date	Strengths	Limitations
	• The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The time period between the intervention and outcome was the same for cases and controls. • The cases and controls were recruited from the same population.	• It could not be determined if there was adequate adjustment for confounding in the analyses from which the main findings were drawn. • Losses of patients to follow-up were not taken into account. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.
Venge, 2010[46]	• The hypothesis/aim/objective of the study was clearly described. • The main outcomes to be measured were clearly described. • The interventions of interest were clearly described. • The main findings of the study were clearly described. • The study provided estimates of the random variability in the data for the main outcomes. • All important adverse events that may have been a consequence of the intervention were reported. • Actual probability values were reported. • The staff, places, and facilities where the patients were treated were representative of the treatment the majority of patients receive. • It was made clear if any of the results of the study were based on data dredging. • The time period between the intervention and outcome was the same for cases and controls. • Statistical tests used to assess the main outcomes were appropriate. • The main outcome measures used were accurate (valid and reliable). • The cases and controls were recruited from the same population.	• The characteristics of the patients included in the study were not described. • The distributions of principal confounders in each group of subjects to be compared were not described. • The characteristics of patients lost to follow-up were not described. • It could not be determined if compliance with the intervention was reliable. • It is unclear if there was adequate adjustment for confounding in the analyses from which the main findings were drawn. • It is unclear if losses of patients to follow-up were taken into account. • It could not be determined whether an attempt was made to blind those measuring the main outcomes of the intervention. • Study subjects were not randomized to intervention group. • It could not be determined whether the subjects asked to participate in the study were representative of the entire population from which they were recruited. • It could not be determined whether the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance < 5%.

Table 18: Critical Appraisal of Evidence-Based Guidelines (AGREE II)[15]

Guideline Producer, Publication Year	Strengths	Limitations
European Society of Cardiology guidelines, 2011[59]	• Scope and purpose of the guidelines are clear • Recommendations are specific and unambiguous • The method for searching for and selecting the evidence are clear • Methods used for formulating the recommendations are clearly described • Health benefits, side effects, and risks were stated in the recommendations • Target users of the guideline are clearly defined • Level of evidence was graded	• Unclear whether patients' views and preferences were sought • Unclear whether the guidelines were piloted among target users • Procedure for updating the guidelines not provided • Potential cost implications of applying the recommendations was not considered
National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines, 2007[60]	• Scope and purpose of the guidelines are clear • Recommendations are specific and unambiguous • The method for searching for and selecting the evidence are clear • Methods used for formulating the recommendations are clearly described • Health benefits, side effects, and risks were stated in the recommendations • Target users of the guideline are clearly defined • Level of evidence was graded	• Unclear whether patients' views and preferences were sought • Unclear whether the guidelines were piloted among target users • Procedure for updating the guidelines not provided • Potential cost implications of applying the recommendations was not considered

Appendix 9: Diagnostic Accuracy

Table 19: Diagnostic Accuracy — Sensitivity and Specificity at Admission for POC Devices Measuring cTn, Considering Relevant Patient Characteristics

Study and Sample Size	% Diagnosed with MI	99th Percentile[a] mcg/L (% CV)	Patient Characteristics	Sensitivity % (95% CI)				Specificity % (95% CI)			
cTnI Device				**i-STAT**	**ATQ90**	**Cardio3**	**Stratus**	**i-STAT**	**ATQ90**	**Cardio3**	**Stratus**
Lee- Lewandrowski[20] N = 204	10.8	0.080 (16.5)	NR	63.0				94.0			
Palamalai[18] N = 169	11.2	i-STAT: 0.080 (16.5) ATQ90: 0.023 (12.3)	NR	32.0 (13.0 to 57.0)	26.0 (9.0 to 51.0)			92.0 (86.0 to 96.0)	93.0 (87.0 to 96.0)		
Ivandic[17] N = 119	NR	0.020 (12.3)	Excluded STEMI		76.1 (64.1 to 85.7)				95.0 (87.7 to 98.6)		
Hjortshoj[21] N = 458	23.0	0.039 (10)	• Excluded STEMI • 11% prior MI • 2.2 h after onset of symptoms		58.0 (47.0 to 69.0)				94.0 (91.0 to 96.0)		
Aldous[16] N = 962	22.9	0.050 (17)	29% prior MI			87.7 (83.6 to 91.1)				93.1 (91.9 to 94.1)	
Diercks[19] N = 858	9.6	0.050 (10)[b]	• Excluded low pre-test probability of cardiac disease • 25% prior MI • 3.9 h after onset of symptoms			66.7 (55.2 to 76.5)				95.9 (94.0 to 97.2)	
Amodio[25]; (Di Serio[24]) N = 516	21.3	0.070 (10)	23% prior MI				63.6 (53.9 to 72.6)				93.1 (90.2 to 95.4)
Di Serio[23] N = 41	NR	0.070 (10)	NR				92.0				
cTnT Device				**AQT90 cTnT**		**Cobas**		**AQT90 cTnT**		**Cobas**	
Ter Avest[22]				68.0 (49.0 to 82.0)				87.0 (82.0 to 91.0)			
Andersson;[1] Nilsson[61]						67.0				98.0	
Stengaard[62]	NR	0.014 (NR)	Patients in ambulance			39.0 (32.0 to 46.0)					

CI = confidence interval; cTn = cardiac troponin; cTnI = cardiac troponin I; cTnT = cardiac troponin T; CV = coefficient of variation; h = hours; MI = myocardial infarction; NR = not reported; POC = point of care; STEMI = ST segment elevation myocardial infarction.
[a] Manufacturer 99th percentile and corresponding CV, or the 99th percentile at 10% CV.[87]
[b] Study used 0.050 mcg/L threshold, as researchers developed their own reference.

Table 20: Diagnostic Accuracy — Positive and Negative Predictive Values at Admission for POC Devices Measuring cTnI, Considering Relevant Patient Characteristics and 99th Percentiles

Study and Sample Size	% Diagnosed With MI	99th Percentile[a] mcg/L (% CV)	Patient Characteristics	Positive Predictive Value % (95% CI)				Negative Predictive Value % (95% CI)			
cTnI Device				**i-STAT**	**ATQ90**	**Cardio3**	**Stratus**	**i-STAT**	**ATQ90**	**Cardio3**	**Stratus**
Lee-Lewandrowski[20] N = 204	10.8	0.080 (16.5)	NR	58.0				95.0			
Palamalai[18] N = 169	11.2	i-STAT: 0.080 (16.5) ATQ90: 0.023 (12.3)	NR	33.0 (13.0 to 59.0)	31.0 (11.0 to 59.0)			91.0 (86.0 to 95.0)	91.0 (85.0 to 95.0)		
Ivandic[17] N = 119	NR	0.020 (12.3)	Excluded STEMI		84.9				91.5		
Hjortshoj[21] N = 458	23.0	0.039 (10)	• Excluded STEMI • 11% prior MI • 2.2 h after onset of symptoms		71.0 (58.0 to 81.0)				90.0 (86.0 to 93.0)		
Aldous[16] N = 962	22.9	0.050 (17)	29% prior MI			79.1 (75.3 to 82.1)				96.2 (95.0 to 97.3	
Diercks[19] N = 858	9.6	0.050 (10)[b]	• Excluded low pre-test probability of cardiac disease • 3.9 h after onset of symptoms			65.8 (54.3 to 75.6)				96.0 (94.2 to 97.3)	
Amodio[25] N = 516	21.3	0.070 (10)	23% prior MI				56.7				93.2
cTnT Device				**AQT90 cTnT**		**Cobas**		**AQT90 cTnT**		**Cobas**	
Ter Avest[22]				NR				NR			
Andersson;[1] Nilsson[61]						NR				NR	
Stengaard[62]	NR	0.014 (NR)	Patients in ambulance			68.0 (59.0 to 77.0)				86.0 (84.0 to 88.0)	

CI = confidence interval; cTnI = cardiac troponin I; cTnT = cardiac troponin T; CV = coefficient of variation; h = hours; MI = myocardial infarction; NR = not reported; POC = point of care; STEMI = ST segment elevation myocardial infarction.
[a] Manufacturer 99th percentile and corresponding CV, or the 99th percentile at 10% CV.[87]
[b] Study used 0.050 mcg/L threshold (although literature states the threshold is 0.020 mcg/L) and stated the 10% CV was used.

Table 21: Diagnostic Accuracy of the POC Devices and Central Laboratory Relative to Time of Blood Sample in the Various Studies

Time of Blood Draw	i-STAT	AQT90 FLEX	Cardio3 Panel	Cobas h232	Stratus	Central Laboratory
Sensitivity						
Admission	32%[18] 63%[20]	26%[18] 76%[17]	67%[19] 88%[16]	67%[1]	77%[25]	68%[18] 88%[20] 90%[16] 91%[17] 100%[1]
3 h	68%[18]	NR	NR	NR	NR	95%[18]
6 h	68%[18]	NR	NR	NR	NR	100[18]
6 to 9 h	NR	85%[21]	NR	NR	NR	98%[21]
Specificity						
Admission	92%[18] 94%[20]	87%[22] 95%[17]	93%[16] 96%[19]	98%[1]	84%[25]	75%[1,22] 81%[18] 84%[17] 87%[20] 94%[16]
3 h	90%[18]	NR	NR	NR	NR	81%[18]
6 h	91%[18]	NR	NR	NR	NR	84%[18]
6 to 9 h	NR	91%[21]	NR	NR	NR	78%[21]
Positive Predictive Value						
Admission	33%[18] 58%[20]	31%[18] 85%[17]	66%[19] 79%[16]	50%[1]	57%[25]	10%[1] 31%[18] 48%[20] 60%[17] 82%[19]
3 h	46%[18]	NR	NR	NR	NR	38%[18]
6 h	50%[18]	NR	NR	NR	NR	44%[18]
6 to 9 h	NR	71%[21]	NR	NR	NR	53%[21]
Negative Predictive Value						
Admission	91%[18] 95%[20]	90%[21] 95%[22]	94% to 97%[19] (range from 1 study)	99%[1]	93%[25]	95%[18,21] 97%[19] 98%[20,22] 100%[1]
3 h	96%[18]	NR	NR	NR	NR	99%[18]
6 h	96%[18]	NR	NR	NR	NR	100%[18]
6 to 9 h	NR	96%[21]	NR	NR	NR	99%[21]
Positive-Likelihood Ratio						
Admission		5.37[22]	16.2[19]	NR	4.83[25]	3.63[22]
3 h			12.9[19]	NR	NR	NR
6 h			11.8[19]	NR	NR	NR
Negative-Likelihood Ratio						
Admission		0.26[17] 0.37[22]	0.35[19]	NR	0.27[25]	0.12[22]
3 h		0.12[17]	0.16[19]	NR	NR	NR
6 h		0.08[17]	0.14[19]	NR	NR	NR

h = hours; NR = not reported; POC = point of care.

Appendix 10: Clinical Utility

Table 22: Turnaround Time

Author Study Design Number of Patients (N)	Type of cTn	Point of Care	Central Laboratory	Time Saved (Minutes)
Setting: Emergency Department				
Definition of Turnaround Time: Time From Blood Draw to Result				
Ryan[26] RCT N = 2,134	cTnI	Median 15 min (range 11 to 23 min)	Median 58 min (range 44 to 81 min)	43 min
Altinier[33] Prospective N = 100	cTnI	Median 17 min	Median 83 min	66 min (*P* = 0.0001)
Cramer[34] Prospective N = 358	cTnT	Median, 20 min (range 15 to 25 min)	Median 92 min (range 75 to 124 min)	72 min
Mozina[35] Prospective N = 31	cTnI	Mean, 20 min ± 5 min (SD)	(Core laboratory): Mean 104 min ± 33 min (SD)	84 min (*P* < 0.001)
Storrow[36] Prospective N = 253	cTnT	Mean 126 min ± 84 (SD) or 126 min	Mean 144 min ± 108 (SD)	18 min (*P* = 0.001)
Caraghe;[32] Prospective N = 205	cTnI	Mean 39 min ± 12.1 min (SD)	Mean 87 min ± 27.5 min (SD)	48 min
Lee-Lewandrowski[37] Pre/post N = NR	cTnI	Mean 17 min	Mean 110 min	93 min
Singer[38] Pre/post N = 2,386	cTnI	Median 45 min (range 34 to 69 min)	Median 70 min (range 55 to 101 min)	25 min
Other Definitions of Turnaround Time				
Singer[30] Pre/post N = 366	cTnI	Mean 15 min (95% CI, 14 to 15)	Mean 83 min (95% CI, 77–89)	From blood in analyzer to result: • time saved: 68 min
Koehler[27] Pre/post N = 201	cTnT	Mean 51 min	Mean 105 min	From door to result: • time saved: 54 min (*P* < 0.000)
Meek[28] Pre/post N = 671	cTnI	Median 18 min (range 16 to 20 min)	Median 77 min (range 60 to 108 min)	Time from loading to printed results: • time saved: 59 min
Renaud[29] RCT N = 833	cTnI	Time from collection to physician notification: • Median 38 min (range 35 to 42 min); Time from presentation to anti-ischemic therapy: • Median 151 min (range 139 to 162 min)	Time from collection to physician notification: • Median 109 min (range 104 to 115 min) Time from presentation to anti-ischemic therapy: • Median 198 min (range 187 to 210 min)	Time from collection to physician notification: • Time saved: 71 min (*P* < 0.001) Time from presentation to anti-ischemic therapy: • Time saved: 147 min (*P* < 0.001)
Di Serio[31] Retrospective N = NR	cTnI	Median 26 min	Median 83 min	"Arm to report" time: • Time saved: 57 min (*P* = 0.0001)

Author Study Design Number of Patients (N)	Type of cTn	Point of Care	Central Laboratory	Time Saved (Minutes)
Setting: Cardiology Services and Coronary Care Units				
Definition of Turnaround Time: Time From Blood Draw to Result				
Apple[49] Pre/post N = 555	cTnI	Mean, 19 min (95% CI, 17 to 20)	Mean 76 min (95% CI, 68 to 84)	57 min ($P < 0.001$)
Collinson[50] RCT N = 263	cTnT	Median, 20 min (range, 20 to 38 min)	Median 79 min (range 25 to 1,018 min)	59 min ($P < 0.0001$)

CI = confidence interval; cTn = cardiac troponin; cTnI = cardiac troponin I; cTnT = cardiac troponin T; min = minutes; NR = not reported; POC = point of care; RCT = randomized controlled trial; SD = standard deviation.
Note: *P* values are not available when not indicated.

Table 23: Length of Stay

First Author Type of cTn, Study Design Number of Patients	Point of Care	Central Laboratory	Time Saved
Length of Emergency Room Stay			
Meek[28] cTnI, Pre/post n = 671	For discharged patients: median 4.9 h (range 3.8 to 7.3 h) For admitted patients: median 10.2 h (range 7.7 to 14.3 h)	For discharged patients: median 9.1 h (range 7.6 to 11.3 h) ($P < 0.0001$) For admitted patients: median 12.2 h 733.5 (range 8.9 to 17.8 h) ($P = 0.007$)	For discharged patients: 2.7 h (162 min) For admitted patients: 2.0 h (120 min)
Loten[40] cTnI, RCT n = 912	Median 6.4 h	Median 7.2 h ($P = 0.063$)	0.8 h (48 min)
Renaud[29] cTnI, RCT n = 833	Median 5.2 h (range 3.4 to 6.8 h)	Median 5.1 h (range 3.8 to 6.7 h) ($P = 0.99$)	–0.1 h (–6 min)
Singer[30] cTnI, Pre/post n = 366	Mean 5.2 h (95% CI, 4.6 to 5.8)	Mean 7.1 h (95% CI, 6.6 to 7.7)	1.9 h (114 min)
Asha[41,57] cTnT, RCT n = 487	Mean 4.3 h	Mean 4.5 h ($P = 0.21$)	0.2 h (12 min)
Length of Hospital Stay			
First Author Setting Type of cTn, Study Design Number of Patients	**Point of Care**	**Central Laboratory**	**Time Saved**
Apple[49] Cardiology services cTnI, pre/post n = 555	Mean 52.6 h	Mean 56.6 h ($P = 0.05$)	4.0 h (240 min)
Collinson[50] CCU cTnT, RCT n = 263	Median, 202.3 h (95% CI, 166.9 to 240.8)	Median 218.0 h (95% CI, 192.6 to 258.8) (*P* not statistically significant)	15.7 h (942 min)
Goodacre[39] ED cTnI, RCT n = 2,243	Mean 29.6 h	Mean 31.8 h (95% CI, 3.7 to 8.0 hours) ($P = 0.462$)	2.2 h (132 min)

CI = confidence interval; CCU = coronary care unit; cTn = cardiac troponin; cTnI = cardiac troponin I; cTnT = cardiac troponin T; ED = emergency department; h = hours; RCT = randomized controlled trial.
Note: *P* values are not available when not indicated.

Table 24:Time to Clinical Decision in the Emergency Department

First Author Type of cTn Study Design (Number of Patients)	Point of Care	Central Laboratory	Time Saved
Ryan[26] cTnI RCT (n = 2,134)	Median: 321 min (range 245 to 440 min)	Median: 330 min (range 250 to 451 min)	9 min
Deledda[42] Multiple markers Pre/post (n = 4,886)	Mean: 195 min (SD 129)	Mean: 221 min (SD 149)	26 min

cTn = cardiac troponin; cTnI = cardiac troponin I; min = minutes; RCT = randomized controlled trial; SD = standard deviation.
Note: *P* values are not available when not indicated.

Table 25: Time to Discharge in the Emergency Department

Study Setting, Type of cTn Study Design Number of Patients	Point of Care	Central Laboratory	Time Saved
Ryan[26] ED, cTnI RCT n = 2,134	Median: 270 min (range 208 to 364 min)	Median: 277 min (range 209 to 365 min)	7 min
Asha[41,57] ED, cTnT RCT n = 487	Mean: 205 min	Mean: 210 min	5 min (P = 0.04)
Deledda[42] ED, multiple markers Pre/post n = 4,886	Mean: 195 min (SD 129)	Mean: 221 min (SD 149)	26 min

Ctn = cardiac troponin; ctni = cardiac troponin I; ctnt = cardiac troponin T; ED = emergency department; min = minutes; RCT = randomized controlled trial; SD = standard deviation.
Note: *P* values are not available when not indicated.

Table 26: Mortality and Major Adverse Events Outcomes

First Author; Setting Type of cTn; Study Design Number of Patients	Outcome	Point of Care	Central Laboratory
Mortality			
Asha;[41,57] ED cTnT; RCT n = 487	Death	0.5%	0%
Collinson;[50] CCU cTnT; RCT n = 263	6 month mortality	12.2% (16/131)	9.8% (13/132) P = NS
Goodacre;[39] ED cTnI; RCT n = 2,243	Death	1% (6/1, 125)	0.2% (2/1, 118) (P = 0.142)
Ordonez-Llanos;[47] ED cTnT; prospective n = 1,410	Non-cardiac death after 1 year follow-up (OR)	1.4% (95% CI, 0.4 to 5.7)	2.4% (95% CI, 0.6 to 9.0)

First Author; Setting Type of cTn; Study Design Number of Patients	Outcome	Point of Care	Central Laboratory
Venge;[43] ED cTnI; prospective n = 508	Prediction of death during 31-month follow-up period	i-STAT: • sensitivity: 36% (95% CI, 24 to 49) • specificity: 89% (95% CI, 96 to 92) • PPV: 33% (95% CI, 22 to 46) • NPV: 91% (95% CI, 87 to 93) Stratus CS: • sensitivity: 40% (95% CI, 28 to 54) • specificity: 84% (95% CI, 81 to 88) • PPV: 27% (95% CI, 18 to 37) • NPV: 91% (95% CI, 87 to 93)	Access (CL): • sensitivity: 77% (95% CI, 65 to 87) • specificity: 76% (95% CI, 72 to 80) • PPV: 32% (95% CI, 25 to 40) • NPV: 96% (95% CI, 93 to 98) Architect (CL): • sensitivity: 72% (95% CI 59 to 83) • specificity: 82% (95% CI, 78 to 85) • PPV: 36% (95% CI, 28 to 45) • NPV: 95% (95% CI, 93 to 97)
Venge;[46] ED cTnI; prospective n = 1,069	Prediction of death (median follow-up: 3.3 months)	i-STAT: 50% Stratus: 54%	Access: 88% Architect: 81%
Cardiac Events			
Cullen;[44] ED cTnI; prospective n = 704	30-day cardiac event rate in low-risk patients	0% (95% CI, 0 to 25.9)	0% (95% CI, 0 to 21.5)
	30-day cardiac event rate in high-risk patients	24.8% (95% CI, 20.2 to 30.1)	28.6% (95% CI, 23.4 to 34.4)
Ordonez-Llanos;[47] ED cTnT; prospective n = 1,410	Cardiac events after 1 year follow-up (OR)	2.1 (95% CI, 1.5 to 3.0)	2.2 (95% CI, 1.6 to 3.1)
Other Adverse Events and Composite End Points			
Goodacre;[39] ED cTnI; RCT n = 2,243	Major AE after 3 month follow-up	3% (36/1,125)	2% (26/1,118) (*P* = 0.313)
Collinson;[50] CCU cTnT; RCT n = 263	CEP (death, MI, unstable angina, readmission with UA or need for urgent revascularization) at 6 months	67% (88/131)	66% (87/132) *P* = NS
Asha;[41,57] ED cTnT; RCT n = 487	CEP events (AMI, coronary revascularization, cardiac arrest, or mortality) in patient with a negative first cTn test at 3 months follow-up	10.4%	5.4%

AE = adverse event; AMI = acute myocardial infarction; CCU = coronary care unit; CEP = composite end points; CI = confidence interval; CL = central laboratory; cTn = cardiac troponin; cTnI = cardiac troponin I; cTnT = cardiac troponin T; CVD = cardiovascular disease; ED = emergency department; h = hours; MI = myocardial infarction; NPV = negative predictive value; NR = not reported; NS = not significant; OR = odds ratio; PPV = positive predictive value; RCT = randomized controlled trial; UA = unstable angina.
Note: *P* values are not available when not indicated.

Table 27: Patients' Quality of Life (EQ-5D) in the Emergency Department

Author, cTn Type, Study Design, Number of Patients	Time Point	Point of Care	Central Laboratory
Goodacre;[39] ED; cTnI RCT; n = 2,243	1 month	0.742	0.759, *P* = 0.614
	3 months	0.752	0.759, *P* = 0.638

cTn = cardiac troponin; cTnI = cardiac troponin I; ED = emergency department; EQ-5D = EuroQoL 5-Dimensions Questionnaire; RCT = randomized controlled trial.

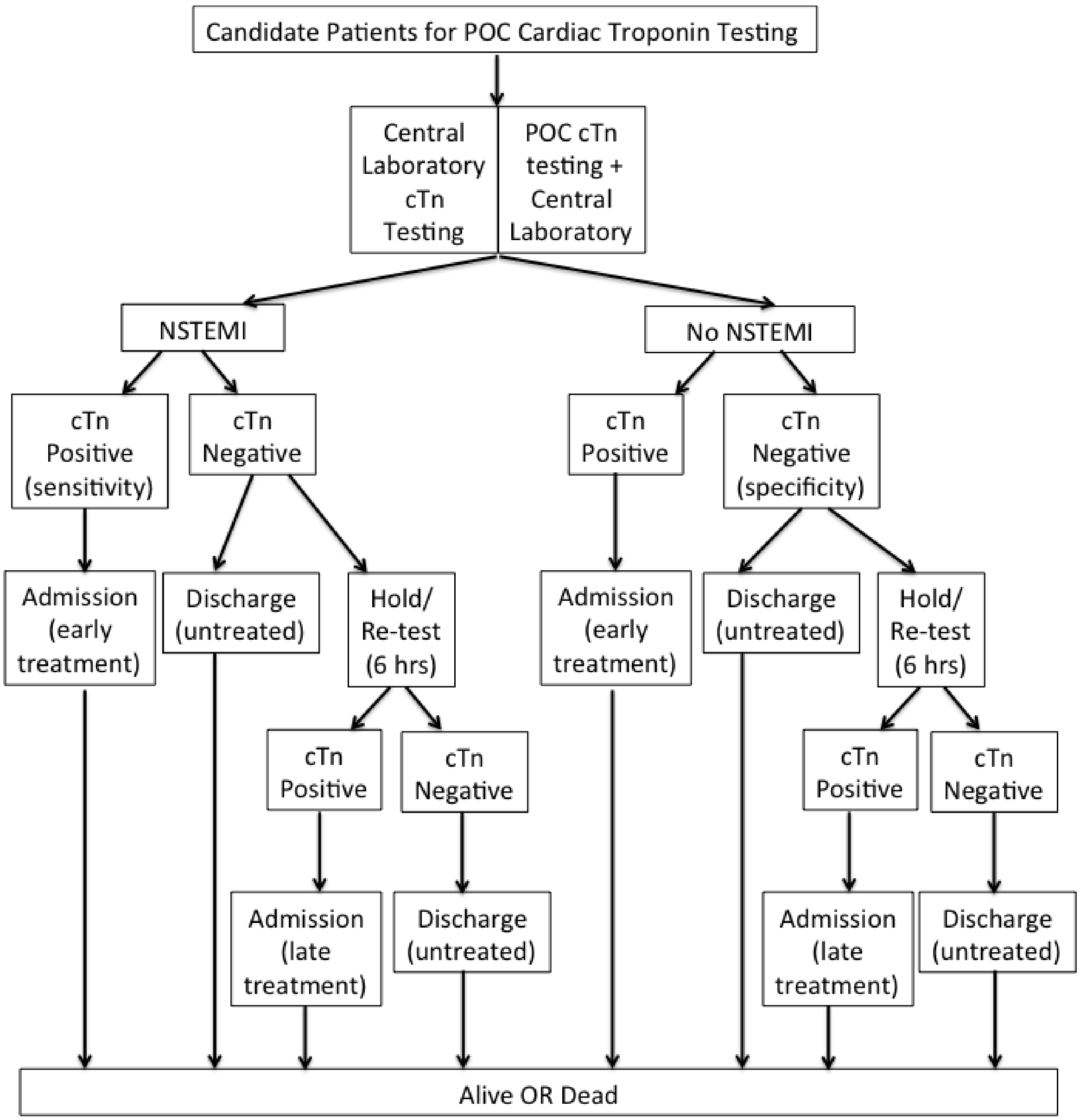
Table 28: Staff Satisfaction in the Various Settings

Author; cTn Type Study Design; Number of Patients	
Emergency Department Setting (Settings With a Central Laboratory)	
Koehler;[27] cTnT Pre/post; n =, 201	82% of staff rated satisfaction as excellent with POC testing
Altinier;[33] cTnI Prospective; n = 100	• POC easy to use: 100% • Safety for operator 91% • Essential in the ED: 64% • Better management: 82%
Lee-Lewandrowski;[37] POC cTnI compared with ED satellite laboratory cTnT Pre/post; n = NR	Staff satisfaction with accuracy: • **POC:** 3.68/5 • **CL:** 4.33/5 Staff satisfaction with TAT: • **POC:** 4.00/5 • **CL:** 2.06/5
Singer;[38] cTnI Pre/post; n = 2,386	• 92% of staff found POC testing had great overall value • 88% of physicians agreed that POC testing improved patient flow
Remote Health Care Centres (No Central Laboratory)	
Shephard;[52,56] remote centres Survey; n = 33 health centres	• 95% of device-operator respondents stated that POC testing was more convenient than transporting patients for CL services. • Staff satisfaction with cTn testing: 96% with POC; 31% with no POC (*P* < 0.001)
Unspecified Health Care Setting (Unclear if Central Laboratory Available)	
FitzGibbon;[53,58] unspecified setting and type of cTn Survey; n = 100 health professionals	• cTnI is the most commonly used cardiac marker (75%) • 47% of staff strongly agree POC usage increased patient convenience (13% disagree) • 40% strongly agree POC reduced TAT (0% disagree) • 33% strongly agree POC enables earlier treatment (0% disagree) • 0% strongly agree POC reduced reoperation and readmission (13% disagree)
Liikanen;[54] unspecified setting or type of cTn Survey; n = 406 health care units	Reasons for staff using POC: • shortening of TAT: 96% • laboratory test not available: 71%

CL = central laboratory; cTn = cardiac troponin; cTnI = cardiac troponin I; cTnT = cardiac troponin T; ED = emergency department; NR = not reported; POC = point of care; TAT = turnaround time.
Note: *P* values are not available when not indicated.

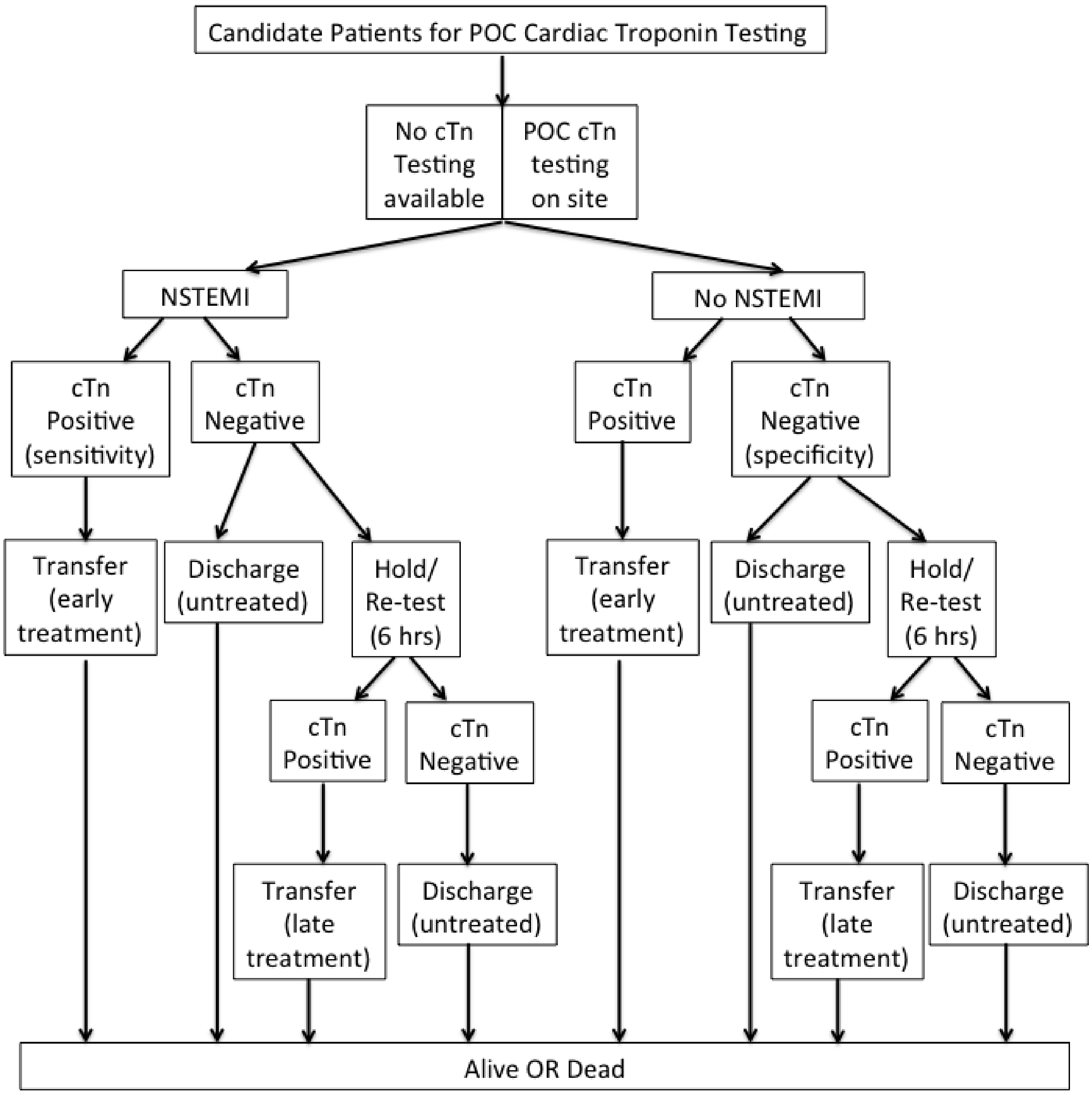
Appendix 11: Schematics for the Economic Models

Figure 7: Schematic of the Economic Model for Context 1: POC Cardiac Troponin Testing Versus Central Laboratory Testing



cTn = cardiac troponin; hrs = hours; NSTEMI = non-ST segment elevation myocardial infarction; POC = point of care.

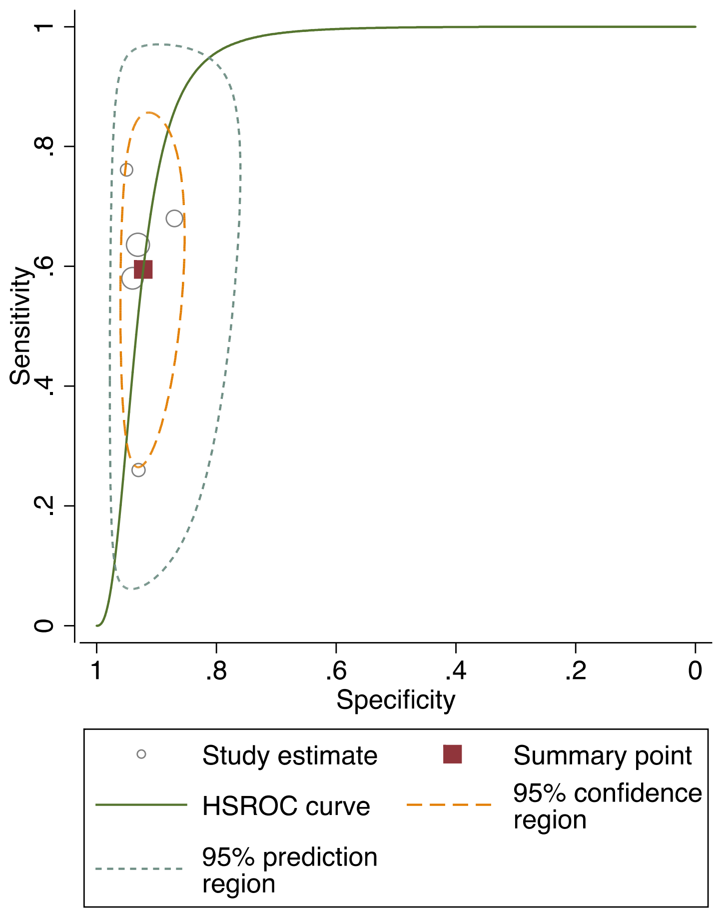
Figure 8: Schematic of the Economic Model for Context 2: POC Cardiac Troponin Testing Versus No cTn Testing



cTn = cardiac troponin; hrs = hours; NSTEMI = non-ST segment elevation myocardial infarction; POC = point of care.

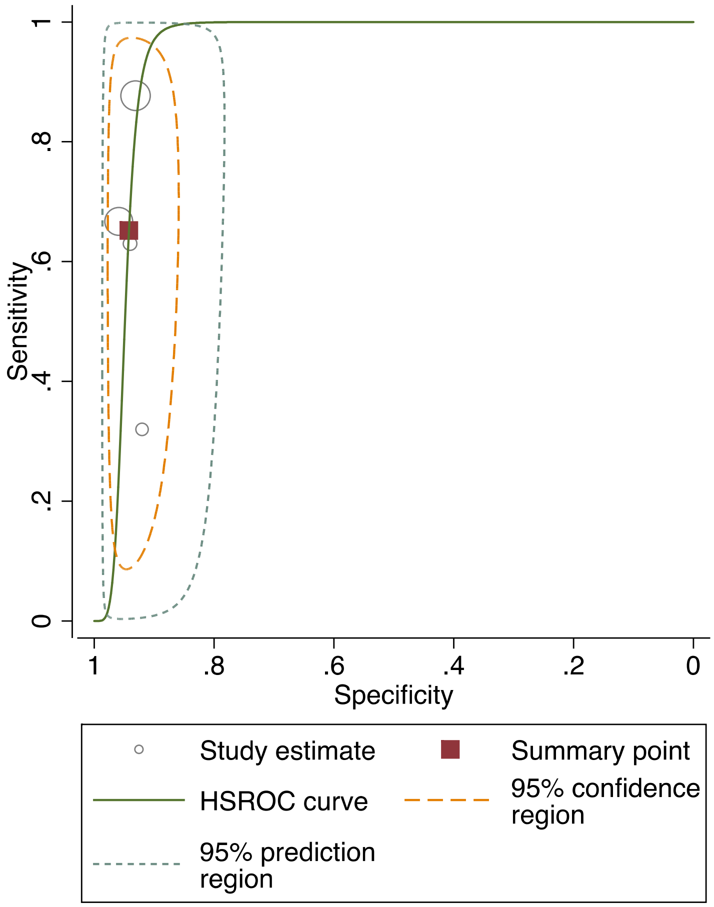
Appendix 12: Summary Receiver Operating Characteristic Curve for the Pooled Diagnostic Accuracy of POC cTn Devices

Figure 9: Desktop POC cTn Device



cTn = cardiac troponin; hierarchical summary receiver operating characteristic; POC = point of care.

Figure 10: Summary Receiver Operating Characteristic Curve for the Pooled Diagnostic Accuracy of the Hand-held POC cTn Device



cTn = cardiac troponin; hierarchical summary receiver operating characteristic; POC = point of care.