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CHRSP

Health research - synthesized and contextualized for use in Newfoundland and Labrador

CHRSP is a flagship program of the
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ONLINE COMPANION DOCUMENT

Troponin Point-of-Care Testing in Smaller Hospital and Health Centre Emergency Departments

in Newfoundland and Labrador

Nitika Pant Pai, Michel Grignon, Stephen Bornstein, Pablo Navarro, Sarah Mackey

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Preface

This Online Companion Document complements the final 'Evidence in Context' report on *Troponin Point-of-care Testing in Emergency Departments of Smaller Hospitals and Health Centres in Newfoundland and Labrador*, an evidence synthesis conducted through the Contextualized Health Research Synthesis Program (CHRSP) at the NL Centre for Applied health Research. This Online Companion Document contains a range of background information on the development of the project, point-of-care testing in general, details on the methodology used in the CHRSP project, details of the results of our analyses, and tables summarizing the contextualization factors for the project. The purpose of the Online Companion Document is to provide the supporting details and data needed for a critical reading of the 'Evidence in Context' report, while keeping the final report as succinct and focused on results as possible.

References to this document in the online version of our 'Evidence in Context' report will link directly to the relevant section(s). The reader will also find bookmarks in the navigation pane.

CHRSP Topic Refinement

Selection of Point-of-Care Test

Table 1: Top 10 lab requests by rank for smaller hospitals in Eastern Health

ER Category:	A	A	A	B	B	B	B	B	B	
Hospital Name:	General Hospital	Dr. G.B. Cross Memorial Hospital	Burin Peninsula Health Care Centre	Dr. A.A. Wilkinson Memorial Health Centre	Dr. William Newhook Community Health Centre	Placentia Health Centre	Bonavista Community Health Centre	Grand Bank Community Health Centre	U.S. Memorial Health Centre	
Town:	Carbonear	Clarenville	Burin	Old Perlican	Whitbourne	Placentia	Bonavista	Grand Bank	St. Lawrence	
Analyte										Rank Sum
Potassium	3	1	1	2	2	4	1	1	1	1.8
Complete Blood Count	1	4	2	1	1	2	2	2	3	2.0
Sodium	3	1	1	2	5	5	1	1	1	2.2
Est GFR by MORD	3	2	3	2	3	3	5	3	2	2.9
Urea Nitrogen	3	3	4	2	5	6	5	3	2	3.7
Chloride	3	5	6	2	5	5	5	3	2	4.0
Creatinine	3	5	6	2	5	6	5	3	2	4.1
C02	3	5	6	2	5	7	5	3	2	4.2
Random Glucose	2	5	8	2	4	1	6	7	6	4.6
Routine Urinalysis/Micro	4	6	5	3	2	9	3	4	5	4.6
AST (SGOT)	5	7	7	4	N/A	5	4	5	4	5.1
Akaline Phosphatase	8	7	7	7	N/A	8	4	5	4	6.3
Albumin	8	7	7	7	N/A	8	4	5	4	6.3
Total Bilirubin	8	7	7	7	N/A	8	4	5	4	6.3
ALT (SGPT)	8	7	7	7	N/A	8	4	5	4	6.3
C-Reactive Protein	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	7	7.0
Troponin	6	8	9	5	6	10	9	6	8	7.4
INR	7	9	9	6	N/A	N/A	8	8	10	8.1
Creatine Kinase	9	10	N/A	8	N/A	N/A	7	N/A	9	8.6
Lactate Dehygrogenase	10	N/A	N/A	9	N/A	N/A	N/A	N/A	N/A	9.5

Table 2: CHRSP Team Member ranking of potential diagnoses/tests for project focus

Rank	Potential Diagnosis	Analyte
1	ACS	Troponin
1	Multiple	Electrolytes
2	Multiple	CBC
3	Renal function	Urea Nitrogen (BUN)
4	Diabetes et al	Glucose
4	Pregnancy/Pre-term	Fetal fibronectin and other
5	Gas exchange	Blood Gas
5	CV conditions	INR
5	Liver function	ALT and others
5	Renal function et al	Creatinine
6	CV conditions	D-Dimer

Research Question:

"What does the scientific literature and local knowledge tell us about the clinical effectiveness, feasibility and acceptability of [troponin] point-of-care testing for emergency departments of smaller hospitals and health centres in Newfoundland and Labrador?"

Data Request

The project submitted a request to the Health Information Services & Informatics Branch of Eastern Health for de-identified administrative data from the emergency departments and central labs of hospitals in Eastern Health. The request was approved by the provincial Health Research Ethics Board. The scope of the request was for one year of data (2012) for the following variables:

- The test that was requested
- The protocol used for the requested test (i.e., which method of testing was used on the sample to give the result)
- De-identified code for the physician who made the request
- Date/time the request was made
- Date/time for collection of sample for the test
- Date/time the test results were reported
- Address or emergency room affiliation of the physician who made the request
- The facility where the lab test was actually carried out
- Age of patient
- Presenting conditions/symptoms
- Preliminary diagnosis

- Quality indicators, e.g., if test had to be done over again, an ambiguous result was obtained, etc.
- Discharge disposition of the patient - home or admitted (outcome)
- CTAS level (complexity of the patient on arrival)
- LOS in ED
- Patient Postal code (population based)
- Clinical action, e.g., a change in preliminary diagnosis, an order of a confirmatory or staging test, initiation or flagging for medication, counselling or an improvement in the patients presenting condition/symptoms that resulted post-test

The intent had been to develop a model of emergency department cardiac troponin testing that could be used to assess the impacts of the implementation of an ED cardiac troponin point-of-care test. However, several challenges delayed the delivery of the data and the development of the model was abandoned.

Performance Measurement for Troponin POCT

Test Outcome ↓	**Condition** (determined by gold standard) ↓ **Condition Positive**	↓ **Condition Negative**	**Test performance measures↓**
Test Positive	**True Positive**	**False Positive**	**Precision** = True Positive / Test Positive
Test Negative	**False Negative**	**True Negative**	**Negative Prediction Value** = True Negative / Test Negative
Test performance measures→	**Sensitivity*** = True Positive / Condition Positive	**Specificity** = True Negative / Condition Negative	**Accuracy** = (True Positive + True Negative) / Total Population

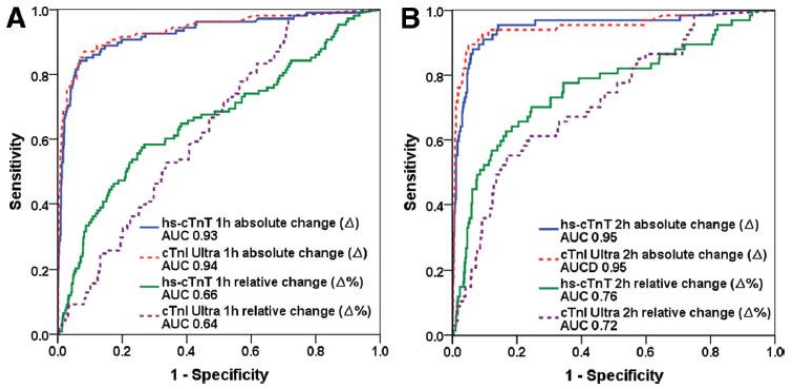

Figure 5. Receiver operating characteristic curves of 1-hour and 2-hour changes. Receiver operating characteristic curves showing the diagnostic performance for the diagnosis of acute myocardial infarction provided by absolute (Δ) and relative (Δ%) changes in high-sensitive cardiac troponin T (hs-cTnT) and cardiac troponin I ultra (cTnI-ultra) within the first hour (**A**) and within the first 2 hours (**B**) are shown. AUC indicates area under the curve.

From:	Reichlin, Tobias, Affan Irfan, Raphael Twerenbold, Miriam Reiter, Willibald Hochholzer, Hanna Burkhalter, Stefano Bassetti et al. "Utility of absolute and relative changes in cardiac troponin concentrations in the early diagnosis of acute myocardial infarction." *Circulation* 124, no. 2 (2011): 136-145. (1)

Diagnostic test performance is measured by outcomes that include:

- Sensitivity: the proportion of the number of correctly diagnosed positive cases to the actual number of positive cases (see above)
- Specificity: the proportion of the number of correctly diagnosed negative cases to the actual number of negative cases (see above)
- Receiver Operating Characteristic (ROC): the proportion of the number of correctly diagnosed positive cases to the number of incorrectly diagnosed negative cases (see above)

Cut-off Points:	The values of any diagnostic test performance outcomes are profoundly affected by the cut-off value at which the test considers an individual case as positive for the condition in question. For troponin POC testing, the cut-off is defined as the concentration of cardiac troponin (cTn) at the 99th percentile with a coefficient of variation (CV) of less than 10%:

- The concentration of cTn at the 99th percentile is the concentration found in the top 1 percentile of a normal, healthy population which is determined with a minimum sample size of 120 males and 120 females (to account for gender differences).
- The CV is a measure of precision and indicates the random error of a measurement. The CV of any test will increase as the concentration of analyte departs from an optimal testing level. In practice this means that the CV increases (i.e., the precision decreases) at very low levels of the analyte.
- In the case of troponin testing, a 10% CV means that the test is reliably measuring the concentration of cTn accurately. From 1996 to 2002, troponin cTn tests were, in general,

insufficiently precise, and as a result it was advocated that only results from tests with low CV be used in establishing benchmarks.

- "Detection of a rise and/or fall of the measurements is essential to the diagnosis of acute MI. An increased cTn concentration is defined as a value exceeding the 99th percentile of a normal reference population [upper reference limit (URL)]. This discriminatory 99th percentile is designated as the decision level for the diagnosis of MI and must be determined for each specific assay with appropriate quality control in each laboratory. The values for the 99th percentile URL defined by manufacturers, including those for many of the high-sensitivity assays in development, can be found in the package inserts for the assays or in recent publications.

Values should be presented as nanograms per liter (ng/L) or picograms per milliliter (pg/mL) to make whole numbers. Criteria for the rise of cTn values are assay-dependent but can be defined from the precision profile of each individual assay, including high-sensitivity assays. Optimal precision, as described by coefficient of variation (CV) at the 99th percentile URL for each assay, should be defined as _10%. Better precision (CV _10%) allows for more sensitive assays and facilitates the detection of changing values. The use of assays that do not have optimal precision (CV _10% at the 99th percentile URL) makes determination of a significant change more difficult but does not cause false positive results. Assays with CV _20% at the99th percentile URL should not be used. It is acknowledged that pre-analytic and analytic problems can induce elevated and reduced values of cTn. Blood samples for the measurement of cTn should be drawn on first assessment and repeated 3-6 h later. Later samples are required if further ischemic episodes occur, or when the timing of the initial symptoms is unclear. To establish the diagnosis of MI, a rise and/or fall in values with at least one value above the decision level is required, coupled with a strong pre-test likelihood. The demonstration of a rising and/or falling pattern is needed to distinguish acute- from chronic elevations in cTn concentrations that are associated with structural heart disease."

From:	Thygesen, Kristian, Joseph S. Alpert, Allan S. Jaffe, Harvey D. White, Maarten L. Simoons, Bernard R. Chaitman, Hugo A. Katus et al. "Third universal definition of myocardial infarction." Journal of the American College of Cardiology 60, no. 16 (2012): 1581-1598. (2)

Project Search Methods

Screening Criteria (Title & Abstract)

Population

- ✓ Include if the population is presenting with potential ACS
- ✓ Include if the population is human
- ✗ Exclude if the population has already been diagnosed with ACS or ACS has been ruled out already

Intervention

- ✓ Include if the intervention that is studied, or one of the interventions that is studied, is a troponin POC
- × Exclude if the article is an assessment of whether or not troponin is a valid indicator of POC

Comparator

- ✓ All comparators are eligible for inclusion

Outcome

- ✓ All outcomes are eligible for inclusion

Setting

- ✓ Include if setting is: Emergency Departments, Intensive Care Units, or any other facilities like nursing stations or health centres, that will see emergency cases.
- ✓ Include if setting is primary care and the patient is presenting with potential ACS and a troponin POC is used.

Exclude

- × Ambulances.

Eligibility Criteria (Full Text Review)

Population	How is the ~~disease~~/condition defined? • Any emergent patient with symptoms that could include Acute Coronary Syndrome (Myocardial Infarction, Angina) What are the most important characteristics that describe the participants relevant to your review? • Patients presenting to the ER with chest pain, thoracic pain Are there any relevant demographic factors? (e.g. age, sex ethinicity) • Special attention to those patients in rural settings What is the setting • Emergency departments • Intensive Care Units • Other settings in facilities for the treatment of emergency cases, e.g., nursing station or a health centre Who should make the diagnosis • Practitioners in the ER that do not have formal lab training Are there any co-morbidities to be excluded? • No

	Are there any other types of people who should be excluded or considered in the review (because they are likely to react to the intervention in a different way? • ~~People presenting to primary care physicians~~ How will studies involving only a subset of relevant participants be handled? Included
Intervention	Does the intervention have variations (e.g. dosage, components, mode of delivery, personnel, frequency, duration, and timing)? • POC for troponin in acute care setting delivered by someone other than a lab technician, any form of POC test, e.g., i-STAT, single analyte test, etc. Are all variations to be included (e.g. is there a minimum dose or components without which the intervention may not be expected to work in the same way)? How will trials including the intervention of interest combined with another intervention (co-intervention) be handled? • YES Is the intervention provided or accessed differently in different contexts? No
Comparison	What are you interested in comparing the intervention to (e.g. an active intervention, no intervention or placebo, any available comparison)? This depends on the primary question of the review • POC vs lab test, POC troponin vs other POC troponin What is the usual alternative to your intervention of interest in practice? • Blood testing for troponin via lab If comparing to a specific intervention, describe in detail as above.
Outcome	What are the important outcomes that you plan to measure in your review • Clinical effectiveness of POC troponin testing versus laboratory testing (sensitivity, specificity, accuracy, reliability) • Length of stay in ER • Impact on admissions • Turnaround time for results • Patient/practitioner satisfaction • Economic costs (direct, indirect and subsequent) • Implementation costs • Training requirements and standards • Institutional acceptance Will the outcomes form part of the selection criteria? • NO Which will be your primary outcomes? • Clinical effectiveness

	• Turnaround time for results • Economic costs Which will be your secondary outcomes? • Length of stay in ER • Impact on admissions • Patient/practitioner satisfaction • Implementation costs • Training requirements and standards • Institutional acceptance Which primary and secondary outcomes will be your main outcomes (max of 7) to be included in summaries of the completed review such as your Abstract, Plain Language summary of Findings Table? These outcomes should be essential for decision making, and have an emphasis on patient-unimportant outcomes. • Primary + LOS + Satisfaction + Training Have you included possible adverse effects? • Yes How should the outcomes be measured (e.g. validated tools)? • Not applicable Are there important time points at which outcomes should be measured (e.g. long enough to expect an observable effect)? • No Have you included outcomes relevant to all potential decision-makers? Hope so
Setting/Study Design	Which designs will you include, and what is your rationale? • Systematic Reviews (including meta-analyses and meta-reviews) • HTAs Randomized Controlled Trials

Search Strings (Clinical Health Outcomes)

Focus put on the potential diagnostic outcomes as the primary concept, and then cross-reference them against the "testing" concept, which should be the same for all sub-topic searches.

Search Concept	PubMed	CINAHL	Embase
Populations of interest (potential diagnosis)	"Acute Coronary Syndrome "[Mesh] OR ("acute coronary syndrome"[tiab] NOT medline[sb]) OR "Myocardial Infarction"[Mesh] OR (("myocardial infarction"[tiab] OR "heart attack"[tiab]) NOT medline[sb]) OR "Angina, Stable"[Mesh] OR "Angina, Unstable"[Mesh] OR ("angina"[tiab] NOT medline[sb])	(MH "Acute Coronary Syndrome") OR "acute coronary syndrome" OR (MH "Myocardial Infarction") OR "myocardial infarction" OR "heart attack" OR (MH "Angina, Stable") OR "angina" OR (MH "Angina, Unstable") OR (MH "Chest Pain") OR "chest pain" OR "thoracic pain"	'acute coronary syndrome'/exp OR 'heart infarction'/exp OR 'angina pectoris'/exp OR 'thorax pain'/exp OR 'heart attack' OR 'myocardial infarction' (you can do these if you uncheck Extensive Search)
Intervention (Analyte)	"Troponin"[Mesh] OR ("troponin"[tiab] NOT medline[sb]) OR	(MH "Troponin") OR "troponin" OR	'troponin'/exp 'troponin I ELISA kit'/exp OR
Intervention (Class of test)	"Point-of-Care Systems"[Mesh] OR ("point of care"[tiab] OR "POC"[tiab] NOT medline[sb]) OR "Biological Markers/blood"[Mesh] OR ("biological markers"[tiab] NOT medline[sb]) OR "Clinical Laboratory Techniques"[Mesh] OR "Diagnosis"[Mesh] OR "Medical Laboratory Science"[Mesh] OR "Clinical Chemistry Tests"[Mesh] OR "i-STAT"[tiab]	(MH "Point-of-Care Testing") OR "point-of-care testing" OR "point-of-care testing" OR (MH "Diagnostic Tests, Routine") OR "diagnostic tests" OR (MH "Laboratory Test Panels") OR "laboratory test panels" OR (MH "Diagnosis, Laboratory") OR "Diagnosis, Laboratory" OR (MH "Biological Markers") OR "biomarker" (MH "Chemistry, Analytical") OR "analyte" OR "i-STAT"	'point-of-care testing'/exp OR 'biological marker'/exp OR 'laboratory device'/exp OR 'laboratory diagnosis'/exp
Setting	"Emergency Service, Hospital"[Mesh] OR (("emergency department"[tiab] OR "emergency room"[tiab])NOT medline[sb]) OR "Intensive Care"[Mesh] OR "Intensive Care Units"[Mesh] OR ("intensive care"[tiab] NOT medline[sb]) OR "Emergency Medical Services"[Mesh] OR ("emergency medical services"[tiab] NOT medline[sb])	(MH "Emergency Service") OR "emergency department" OR "emergency room" OR (MH "Emergency Medicine") OR "emergency medicine" OR (MH "Intensive Care Units") OR "intensive care unit" OR "intensive care units"	'emergency ward'/exp OR 'intensive care unit'/exp
Hedges & limits	10 Years All languages Human only studies	10 Years All languages Human only studies Exclude Medline results	10 Years All languages Human only studies

Project Search Results

PubMed Search Results

May 14, 2013

Query	Items found
Search #1 AND #2 AND #3 Filters: Systematic Reviews; Review; Randomized Controlled Trial; Meta-Analysis; published in the last 10 years	350
Search #1 AND #2 AND #3 Filters: Systematic Reviews; Review; Randomized Controlled Trial; Meta-Analysis; Government Publications; published in the last 10 years	350
Search #1 AND #2 AND #3 Filters: Systematic Reviews; Review; Randomized Controlled Trial; published in the last 10 years	350
Search "Emergency Service, Hospital"[Mesh] OR (("emergency department"[tiab] OR "emergency room"[tiab])NOT medline[sb]) OR "Intensive Care"[Mesh] OR "Intensive Care Units"[Mesh] OR ("intensive care"[tiab] NOT medline[sb]) OR "Emergency Medical Services"[Mesh] OR ("emergency medical services"[tiab] NOT medline[sb])	163385
Search "Troponin"[Mesh] OR ("troponin"[tiab] NOT medline[sb]) OR "Point-of-Care Systems"[Mesh] OR ("point of care"[tiab] OR "POC"[tiab] NOT medline[sb]) OR "Biological Markers/blood"[Mesh] OR ("biological markers"[tiab] NOT medline[sb]) OR "Clinical Laboratory Techniques"[Mesh] OR "Diagnosis"[Mesh] OR "Medical Laboratory Science"[Mesh] OR "Clinical Chemistry Tests"[Mesh] OR "i-STAT"[tiab]	6175442
Search "Acute Coronary Syndrome "[Mesh] OR ("acute coronary syndrome"[tiab] NOT medline[sb]) OR "Myocardial Infarction"[Mesh] OR (("myocardial infarction"[tiab] OR "heart attack"[tiab]) NOT medline[sb]) OR "Angina, Stable"[Mesh] OR "Angina, Unstable"[Mesh] OR ("angina"[tiab] NOT medline[sb])	159391

CINAHL Search Results

May 14, 2013

Query	**Results**
(S2 OR S3) AND (S1 AND S4 AND S5) Limiters - Published Date from: 20030501-20131231; Exclude MEDLINE records	74
(S2 OR S3) AND (S1 AND S4 AND S5)	469
S2 OR S3	44,410
(MH "Emergency Service") OR "emergency department" OR "emergency room" OR (MH "Emergency Medicine") OR "emergency medicine" OR (MH "Intensive Care Units") OR "intensive care unit" OR "intensive care units"	77,305
(MH "Biological Markers") OR "biomarker" OR (MH "Chemistry, Analytical") OR "analyte" OR "i-STAT"	28,272
(MH "Troponin") OR "troponin" OR (MH "Point-of-Care Testing") OR "point-of-care testing" OR "point-of-care testing" OR (MH "Diagnostic Tests, Routine") OR "diagnostic tests" OR (MH "Laboratory Test Panels") OR "laboratory test panels" OR (MH "Diagnosis, Laboratory") OR "Diagnosis, Laboratory"	17,699
(MH "Acute Coronary Syndrome") OR "acute coronary syndrome" OR (MH "Myocardial Infarction") OR "myocardial infarction" OR "heart attack" OR (MH "Angina, Stable") OR "angina" OR (MH "Angina, Unstable") OR (MH "Chest Pain") OR "chest pain" OR "thoracic pain"	41,004

Embase Search Results

May 14, 2013, 1:52:32 PM

#1 AND #2 AND #3 AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [meta analysis]/lim OR [randomized controlled trial]/lim OR [systematic review]/lim) AND ([article]/lim OR [article in press]/lim OR [review]/lim) AND [embase]/lim	94
#1 AND #2 AND #3	1,770
'emergency ward'/exp OR 'intensive care unit'/exp AND [embase]/lim	108,771
'troponin'/exp OR 'troponin i elisa kit'/exp OR 'point-of-care testing'/exp OR 'biological marker'/exp OR 'laboratory device'/exp OR 'laboratory diagnosis'/exp AND [embase]/lim	371,974
'acute coronary syndrome'/exp OR 'heart infarction'/exp OR 'angina pectoris'/exp OR 'thorax pain'/exp OR 'heart attack'/exp OR 'myocardial infarction'/exp AND [embase]/lim	275,449

Grey Lit Search Results (Summary)

Using "Grey Matters: A Practical Search Tool for Evidence-Based Medicine"

Searched the following sections:

- Health Technology Assessment Agencies
- Health Economics
- Retrieved a total of 27 items for Full Text Review
- See below for details

Grey Lit Search Results (Details)

Health Technology Assessment (HTA) Agencies Canada

- Alberta College of Family Physicians: http://www.acfp.ca/WhatWeDo/ToolsforPractice.aspx
  - Nothing found
  - Searched troponin and point-of-care testing and tried the category search under cardiology
- Alberta Health and Wellness. Alberta Health Technologies Decision: http://www.health.alberta.ca/initiatives/AHTDP-completed-reviews.html
  - Nothing relevant found
  - Do have one on Point-of-Care Testing with Portable Prothrombin Time Systems (2010) STE report
- CADTH: http://www.cadth.ca/en/search
  - CADTH - 2007 - Clinical and Cost-Effectiveness of Point-of-Care Troponin Testing Devices in a Remote Health Care Settings (3)
  - CADTH - 2008 -POC Troponin T Testing in Remote Nursing Stations Guidelines for Use (4)
  - CADTH- 2010 - Point-of-care Troponin I and Myoglobin Testing in a Pre-hospital Setting: Clinical Effectiveness and Guidelines (5)
  - CADTH - 2012 - Optimal Use Report, Nov Vol2, Issue 1, High-Sensitivity Cardiac Troponin for the rapid diagnosis of ACS in ER, Clinical and Cost (6)
  - CADTH - 2012 - Rapid Response Report, October, POC vs Central Lab Testing ACS Acute Care (7)
  - CADTH - 2012 - Rapid Response Report, POCT A Review of Systematic Reviews on Testing Accurary and Cost-Effectiveness (8)

    - CADTH - 2013 - Optimal Use Report, March, Vol 2, Issue 1A Troponin Science Report Optimal Use Report (9)
    - CADTH- 2012 - Environmental Scan, Dec, Cardiac Troponin Assays Diagnosis ACS (10)
    - CADTH- 2012 -Rapid Response Report, Feb, Assessment Troponin ACS and AMI in ER, Clinical, Economic
    - CADTH- 2013 - Optimal Use Report, Mar, Vol2,Issue 1b, Recommendations Troponin Assays ER (11)
    - CADTH- 2013 - Rapid Response Report, Jan, Troponin ER Review of Guidelines (12)
- Health Quality Council of Alberta: http://www.hqca.ca/index.php?id=115
    - Nothing found
- Health Quality Council. Saskatchewan. **(**HQC**)** : http://www.hqc.sk.ca/
    - Nothing found
- Health Quality Ontario
    - INR point-of-care but no troponin
- The Institut national d'excellence en santé et en services sociaux **(**INESSS**).** INESSS le savoir prend forme [formerly AETMIS]
    - Nothing that i could find
- Institute for Clinical Evaluative Sciences **(**ICES**).** ICES: Canada's leading health services research institute: http://www.ices.on.ca/webpage.cfm?site_id=1&org_id=31
    - Kavsak P, Wang X, Ko D, MacRae A, Jaffe A. Short- and long-term risk stratification using a next-generation, high-sensitivity research cardiac troponin I (hs-cTnI) assay in an emergency department chest pain population. Clin Chem. 2009; 55 (10): 1809-1815. (13)
    - Other info on troponin as diagnostic but not POC
- Institute of Health Economics **(**IHE**).** Publications Library : : http://www.ihe.ca/publications/library/
    - Nothing found
- Manitoba Centre for Health Policy (MCHP). Deliverables : http://mchp-appserv.cpe.umanitoba.ca/deliverablesList.html
    - Nothing found
- McGill University Health Centre (MUHC). Technology Assessment Unit: http://www.mcgill.ca/tau/publications/
    - Material on poc but not involving troponin
- Ottawa research hospital: http://www.ohri.ca/ksgroup/publications.asp
    - Nothing troponin related
- Program for Assessment of Technology in Health (Canada) PATH
    - Nothing found
- University of British Columbia. Therapeutics Initiative: Evidenced-Based Drug Therapy : http://www.ti.ubc.ca/DrugAssessments
    - Nothing found

HTA United States:

- Agency for Healthcare Research and Quality (AHRQ).
    - Technology Assessments: http://www.ahrq.gov/clinic/techix.htm
    - Evidence-based Practice Centers' evidence reports and technology assessments: http://www.ahrq.gov/clinic/epcquick.htm
    - EPC Topics in Process: http://www.ahrq.gov/clinic/epc/epcprogress.htm
    - Effective Health Care Reports: http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/

        - Searched but nothing found
- Blue Cross and Blue Shield Association. Technology Evaluation Center (TEC): http://www.bcbs.com/blueresources/tec/tec-assessments.html
    - Nothing found
- California Technology Assessment Forum. Assessments (CTAF) : http://www.ctaf.org/assessments
    - Nothing found, other things on cardiac just no sign of point of care
- Centers for Medicare & Medicaid Services (CMS). Technology Assessments: http://www.cms.gov/medicare-coverage-database/indexes/technology-assessments-index.aspx?TAId=85&bc=AAAQAAAAAAAA&
    - POC for H1a1c, none for cardiac
- Institute for Clinical and Economic Review(ICER)
    - http://www.icer-review.org/index.php/Table/Appraisals/
    - None for POC
- U.S. Department of Veterans Affairs Research & Development. VA Technology Assessment Program. Health Technology Assessment Reports and Summaries (VATAP): http://www.va.gov/VATAP/Phase2pubspage.asp
    - Nothing Found
- University HealthSystem Consortium (UHC): https://www.uhc.edu/
    - Need membership login
- Washington State Health Care Authority. Health Technology Assessment Findings (HCA): http://www.hta.hca.wa.gov/assessments.html
    - Nothing on POC

HTA International:

- Departemento de Sanidad. Basque Office for Health Technology Assessment (OSTEBA): http://www.osasun.ejgv.euskadi.net/r52-2536/es/
    - Does not contain English reports or summaries
- Swedish Council on Technology Assessment in Health Care (SBU): http://www.sbu.se/en/
    - Nothing on POC, biomarkers mentioned but in the context of diagnosis
- Swiss Federal Office of Public Health. Swiss Network for Health Technology Assessment (SNHTA): http://www.snhta.ch/resources/overview.html
    - No reports or scientific publications at this time
- Healthcare Improvement Scotland : http://www.healthcareimprovementscotland.org
    - Troponin consultation report
        - Issues for Remote and Rural Areas: NL mentioned in this report!
        - Point-of-care testing with troponin also in this report
- National Health Service for Wales. ATTRACT : http://www.attract.wales.nhs.uk/
    - Nothing found
- National Institute for Health and Clinical Excellence (NICE). NHS National Institute for Health and Clinical Excellence : http://www.nice.org.uk/
    - A report to be finished September 2014 on Acute Heart Failure (can't tell if it will include POC)
    - Nothing on POC
- National Institute for Health and Clinical Excellence (NICE). Published evidence summaries: new medicines: http://www.nice.org.uk/mpc/evidencesummariesnewmedicines/PublishedESNM.jsp
    - Nothing Found
- National Institute of Health Research. Horizon Scanning Centre (NHSC). Outputs by Specialty: http://www.nhsc-healthhorizons.org.uk/outputs/specialties/

    - Point-of-care for hemoglobin but not troponin
- NETSCC, HTA [formerly NCCHTA]. NIHR Health Technology Assessment Programme: http://www.hta.ac.uk/research/index.shtml
    - Goodacre report is here under the NHS reports: "Systematic review, meta-analysis and economic modelling of diagnostic strategies for suspected acute coronary syndrome" 2013 (we have this one) (14)
    - Collinson, 2013. Randomised Assessment of Treatment using Panel Assay of Cardiac markers – Contemporary Biomarker Evaluation (RAT PAC CBE). HTA (this one is new) (15)
- NHS Purchasing and Supply Agency. Centre for Evidence-based Purchasing (CEP): http://nhscep.useconnect.co.uk/CEPProducts/Catalogue.aspx
    - Purchasing and Supply Agency, 2006. Report 06020 Three point-of-care devices for troponin measurement. (new)

Health Economics International

- Agency for Healthcare Research and Quality. National Quality Measures Clearinghouse: http://www.qualitymeasures.ahrq.gov/index.aspx
    - Nothing found
- Australian Government Department of Health and Ageing. Pharmaceuticals Benefits Scheme - Browse by Medicine Listing (PBS) : http://www.pbs.gov.au/browse/medicine-listing
    - This is mostly to do with drugs
- European Network of Health Economic Evaluation Databases
    - Goodacre, 2004. Randomised controlled trial and economic evaluation of a chest pain observation unit compared with routine care (16)
    - Point-of-care testing in blood gas and electrolyte analysis 2003
- Federal Reserve Bank of St. Louis. Economic Research Division. Ideas database (IDEAS): http://ideas.repec.org/
    - Blattner, 2010. Changes in clinical practice and patient disposition following the introduction of point-of-care testing in a rural hospital [76.750%] (17)
    - Peacock, 2003. New Biochemical Tools for Diagnosing Acute Coronary Syndromes: Impact on Patient Outcomes and Resource Utilization in Hospitals [17.795%] (18)
- International Society for Pharmacoeconomics and Outcomes Research. Value in Health: Journal of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR): http://www.valueinhealthjournal.com/issues
    - Point-of-care for INR, coagulation, nothing on troponin and POC
- John Wiley & Sons, Inc. Health Economic Evaluations Database (HEED): http://onlinelibrary.wiley.com/book/10.1002/9780470510933
    - Hafner, 2003. Patientennahe Bestimmung der Troponine zur Diagnostik akuter Koronarsyndrome (19)
    - Hallani , 2005. Use of a quantitative point-of-care test for the detection of serum cardiac troponin T in patients with suspected acute coronary syndromes (20)
    - Takakuwa, 2009.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 (21)
    - Meek, 2012. Effect on emergency department efficiency of an accelerated diagnostic pathway for the evaluation of chest pain (22)
    - Liikanen, 2013. Training of nurses in point-of-care testing: a systematic review of the literature (23)

- National Centre for Pharmacoeconomics [Ireland]. Pharmacoeconomic Evaluations (NCPE): http://www.ncpe.ie/pharmacoeconomic-evaluations/
    - Nothing found
- NHS EED, economic evaluations of health care interventions
    - Van Dyck, RATPAC, Birkhahn, Comite d'Evaluation et de Diffusion des Innovations Technologiques (we have these already) (24)
    - Mundy L, Merlin T, Parrella A. I-STAT ® cardiac Troponin I (cTnl) test for the assessment of biomarkers for acute myocardial infarction in patients presenting to emergency departments. Horizon Scanning Prioritising Summary - Volume 5 Adelaide: Adelaide Health Technology Assessment (AHTA). 2004 (25)
- University of Aberdeen. Health Economics Research Unit (HERU): http://www.abdn.ac.uk/heru
    - Nothing found

Health Economics: Canada

- Hospital for Sick Children [Toronto]. Paediatric Economic Database Evaluation (PEDE): http://pede.ccb.sickkids.ca/pede/search.jsp
    - Childhood database – not relevant
- McMaster University. Centre for Health Economics and Policy Analysis. Publications database (CHEPA) : http://www.chepa.org/research-products
    - Nothing on POC from the working papers section
- Ontario Ministry of Health and Long-Term Care. Ontario Case Costing Initiative (OCCI): http://www.occp.com/mainPage.htm
    - Nothing found. They have a costing analysis tool but it doesn't look useful for our purposes.
- Public Health Agency of Canada: http://www.phac-aspc.gc.ca/ebic-femc/ebic-femc98/index-eng.php
    - Not useful for our purposes
- Toronto Health Economics and Technology Assessment Collaborative. Toronto Health Economics and Technology Assessment (THETA): http://theta.utoronto.ca/
    - Nothing found

Other Search Methods

We employed supplementary search methods to identify relevant literature that may have been missed when searching periodical indexes or the research evidence databases. This included:

1. Contacting authors of systematic review articles to inquire about any possible updates to existing systematic reviews or other systematic review literature we may have missed.
2. Checking reference lists of included review articles.
3. Checking the reverse citation results of all review and primary research articles.

Suggestions from Authors of Included Articles

May be Included

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. 2013;17:v-122. – HTA [Report Link] (15)

Excluded

Goodacre S, Thokala P, Carroll C, Stevens J, Leaviss J, et al. Systematic review, meta-analysis and economic modelling of diagnostic strategies for suspected acute coronary syndrome. Health Technol Assess 2013;17(1). –HTA [Report Link] (14)

Carroll C, Al Khalaf M, Stevens JW, Leaviss J, Goodacre SW, Collinson P, Wang J. Heart-type fatty acid binding protein as an early marker for myocardial infarction: Systematic review and meta-analysis. Emerg Med J 2013;30:280-286. DOI: 10.1136/emermed-2012-201174. (26)

Flow of Articles

Databases were searched. The results (# Returned Articles) were then screened by Title and Abstract. The eligible, screened articles were then retrieved for a full text review. The articles and publication type that were eligible for inclusion are listed below.

Legend: PR = Primary Research (RCTs); SR = Systematic Review; HTA = Health Technology Assessment

Database Queried	# Returned Articles	Full Text Review	Included Articles
Pubmed (27–31)	350	36	1. Lin, 2012 (SR) 2. Bradburn, 2012 (PR) 3. Goodacre, 2011 (PR) 4. Mogensen, 2011(PR) 5. Ryan, 2009 (PR)
CINAHL	74	27	0(SR) 0(PR)
Embase (32,33)	94	17	0(SR) 6. Loten, 2010 (PR) 7. Renaud, 2008 (PR)
Grey Lit (12,34–37)	X	27	8. CADTH, 2012 (Other) 9. CADTH, 2013 (Other) 10. Craig, 2004 (HTA) 11. Collinson, 2011 (PR) 12. Storrow, 2009 (SR)
Other (Author suggestions, reference lists) (15)	3	2	13. Collinson, 2013
Total	521	109	13

Full Text Review Aggregate Categories

Literature Type	Excluded	Included
Primary Literature	45 Excluded if: Non-randomized Design, Articles More than 5 years old	8 Included if: Randomized, Articles published within last 5 years 1. Bradburn, 2012 (28) 2. Collinson, 2013 (15) 3. Collinson, 2011 (36) 4. Goodacre, 2011 (29) 5. Loten, 2010 (32) 6. Mogensen, 2011 (31) 7. Renaud, 2008 (33) 8. Ryan, 2009 (30)
Narrative Reviews	Excluded if: Narrative Review 15	0
Other	Excluded if: Other design 27	0
Systematic Literature (Including HTAs)	1. Michell, 2005 (I)* 2. Liikanen, 2013 (P)&(I) 3. Mant, 2004 (I) & (S) 4. Cimon, 2007(NI) 5. Cimon, 2008 (NI) 6. CADTH HTA, 2010 (NI)	1.CADTH, 2012 (7) 2.CADTH, 2013 (6) 3.Craig,2004 (35) 4.Lin, 2012 (27) 5.Storrow, 2009 (37)

*SR literature was excluded if it didn't meet the pre-set criteria for one or more of the following I = intervention, P= population, S= setting, D = Dates or NI = No Information

Critical Appraisal

AMSTAR

The AMSTAR instrument is detailed below. Items #3, 5, 6, 7 and 8 are considered 'key methodological criteria' by CHRSP. (38)

#	Item	Description	Notes	Criteria
1	Was an 'a priori' design provided?	The research question and inclusion criteria should be established before the conduct of the review.	*"Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."*	A. Research question, or statement of either research objectives or purpose of the paper
				B. Inclusion criteria

			“	C. Protocol or ethics approval or pre-determined/a priori published research objectives
2	Was there duplicate study selection and data extraction?	There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.	*“2 people do study selection, 2 people do data extraction, consensus process or one person checks the other’s work.”*	A. Duplicate study selection or one person checks the other’s work
				B. Duplicate data extraction or one person checks the other’s work
				C. Consensus process
3	Was a comprehensive literature search performed?	At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by [a grey lit search], consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	*“*If *at least 2 sources + one supplementary strategy used, select “yes” (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).”*	A. At least two electronic sources
				B. Years
				C. Names of databases
				D. Key words/MeSH terms
				E. One supplementary strategy
4	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	*“If review indicates that there was a search for “grey literature” or “unpublished literature,” indicate “yes.” SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.”*	A. No language search restrictions
				B. No publication type search restrictions, grey lit search = YES

5	Was a list of studies (included and excluded) provided?	A list of included and excluded studies should be provided.	*"Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no.""*	A. Both included AND excluded studies must be available for review. Excluded studies are those that passed title/abstract filtering and went on to full-text review. Information on the included and excluded studies can be presented as: lists within the body of the text, referenced at the end of the publication, linked to an online document or actually available from the author/publisher.
6	Were the characteristics of the included studies provided?	In an aggregated form such as a table, data from the original "=studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.	*"Acceptable if not in table format as long as they are described as above"*	A. Aggregate description of characteristics of included studies, e.g. participant age, gender, health status, etc.
7	Was the scientific quality of the included studies assessed and documented?	'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.	*"Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable)."*	A. Quality score provided for EACH included study (quality scoring tool or checklist must be described) B. Some description of quality items, with a separate result for each included study
8	Was the scientific quality of the included studies	The results of the methodological rigor and scientific quality should be	*"Might say something such as "the results should be interpreted with caution*	A. Must score YES on #7

	used appropriately in formulating conclusions?	considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	*due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7"*	B. Must show some recognition of impact of quality and methodological rigour

Downs & Black Checklist

The Downs & Black Checklist assesses the study quality of both randomised and non-randomised studies, provides an overall score for study quality, a profile of scores for the quality of reporting, internal validity (bias and confounding) and power, and also for external validity. The instrument is detailed below. (39)

ALL CRITERIA	DESCRIPTION OF CRITERIA (with additional explanation as required, determined by consensus of raters)	POSSIBLE ANSWERS
1	Is the hypothesis/aim/objective of the study clearly described? Must be explicit	Yes/No
2	Are the main outcomes to be measured clearly described in the Introduction or Methods section? If the main outcomes are first mentioned in the Results section, the question should be answered no. ALL primary outcomes should be described for YES	Yes/No
3	Are the characteristics of the patients included in the study clearly described? In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given. Single case studies must state source of patient	Yes/No
4	Are the interventions of interest clearly described? Treatments and placebo (where relevant) that are to be compared should be clearly described.	Yes/No
5	Are the distributions of principal confounders in each group of subjects to be compared clearly described? A list of principal confounders is provided. YES = age, severity	Yes/No
6	Are the main findings of the study clearly described? Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions.	Yes/No
7	Does the study provide estimates of the random variability in the data for the main outcomes? In non-normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported.	Yes/No
8	Have all important adverse events that may be a consequence of the intervention been reported? This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverse events (COMPLICATIONS BUT NOT AN INCREASE IN PAIN).	Yes/No
9	Have the characteristics of patients lost to follow-up been described? If not explicit, NO. RETROSPECTIVE if not described = UTD; if not explicit re: numbers agreeing to participate = NO. Needs to be >85%	Yes/No/UTD
10	Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes/No
11	Were the subjects asked to participate in the study representative of the entire population from which they were recruited? The study must identify the source population for patients and describe how the patients were	Yes/No/UTD

	selected.	
12	Were those subjects who were prepared to participate representative of the entire population from which they were recruited? The proportion of those asked who agreed should be stated.	Yes/No/UTD
13	Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive? For the question to be answered yes the study should demonstrate that the intervention was representative of that in use in the source population. Must state type of hospital and country for YES.	Yes/No/UTD
14	Was an attempt made to blind study subjects to the intervention they have received? For studies where the patients would have no way of knowing which intervention they received, this should be answered yes. Retrospective, single group = NO; UTD if > 1 group and blinding not explicitly stated	Yes/No/UTD
15	Was an attempt made to blind those measuring the main outcomes of the intervention? Must be explicit	Yes/No/UTD
16	If any of the results of the study were based on “data dredging”, was this made clear? Any analyses that had not been planned at the outset of the study should be clearly indicated. Retrospective = NO. Prospective = YES	Yes/No/UTD
17	In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? Where follow-up was the same for all study patients the answer should yes. Studies where differences in follow-up are ignored should be answered no. Acceptable range 1 yr follow up = 1 month each way; 2 years follow up = 2 months; 3 years follow up = 3months.....10years follow up = 10 months	Yes/No/UTD
18	Were the statistical tests used to assess the main outcomes appropriate? The statistical techniques used must be appropriate to the data. If no tests done, but would have been appropriate to do = NO	Yes/No/UTD
19	Was compliance with the intervention/s reliable? Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. Surgical studies will be YES unless procedure not completed.	Yes/No/UTD
20	Were the main outcome measures used accurate (valid and reliable)? Where outcome measures are clearly described, which refer to other work or that demonstrates the outcome measures are accurate = YES. ALL primary outcomes valid and reliable for YES	Yes/No/UTD
21	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population? Patients for all comparison groups should be selected from the same hospital. The question should be answered UTD for cohort and case control studies where there is no information concerning the source of patients	Yes/No/UTD
22	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time? For a study which does not specify the time period over which patients were recruited, the question should be answered as UTD. Surgical studies must be <10 years for YES, if >10 years then NO	Yes/No/UTD
23	Were study subjects randomised to intervention groups? Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation.	Yes/No/UTD
24	Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.	Yes/No/UTD
25	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? In nonrandomised studies if the effect of the main confounders was not investigated or no adjustment was made in	Yes/No/UTD

	the final analyses the question should be answered as no. If no significant difference between groups shown then YES	
26	Were losses of patients to follow-up taken into account? If the numbers of patients lost to follow-up are not reported = unable to determine.	Yes/No/UTD
27	Did the study have sufficient power to detect a clinically important effect where the probability value for a 1-5 difference being due to chance <5% Sample sizes have been calculated to detect a difference of x% and y%.	.

Data Extraction Results of Included Studies

This section describes the data extraction results from the included literature for the Point-of-care CHRSP Project. The synthesis findings from the systematic review literature and the research findings from the primary research literature are categorized by outcome and described in two separate tables below. Following these tables are more detailed summaries of each included article, including critical appraisal scores, PICO descriptions, the reported findings and the authors assessment of the article.

Synthesis Findings Summary: Categorized by Outcome

Diagnostic Test Performance: Diagnostic Accuracy, Risk Stratification		
Reference	Synthesis Findings	Pro/Con
CADTH, 2012-2013	"Aldous et al. (2011)20 focused their analysis on NSTEMI patient (n = 1,000), hs-cTnT was compared with point-of-care cTnI (POC-cTnI).The sensitivity and specificity of hs-cTnT for diagnosis of AMI at a cut-off point of 99th percentile were found to be 0.91 (95% CI, 0.87 to 0.94) and 0.81 (95% CI, 0.80 to 0.82) respectively. POC-cTnI showed significantly lower sensitivity (0.62, 95% CI, 0.58 to 0.66), and higher specificity (0.96; 95% CI, 0.94 to 0.97) values."p19	Con: POC less accurate than High Sensitivity cTnT testing, the standard test may be obsolete within a short period of time
Craig, 2004	"Among the quantitative point-of-care analysers, only the TROPT Quantitative® (troponin T) and the Stratus® CS (troponin 1) appear able to meet the important criterion of preserving comparability with central laboratory analysers (but currently this comparability has only been demonstrated for the Dimension® 'X' family of analysers in the latter case) and of acceptable low end precision. The TROPT Quantitative® is not clearly superior to laboratory based troponin T analysers but the Stratus® CS, on the other hand, is superior to many currently available troponin I laboratory analysers and appears comparable with the remainder. Other point-of-care analysers may be useful in selecting high-risk patients for early therapy but since negative results would need to be confirmed by more sensitive laboratory based tests, their use would be unlikely to result in major cost reductions from early discharge."p79 "…it should be noted that few, if any, of the currently available	Pro: Some but not all POC analysers are equal to laboratory testing Con: specific devices differ in terms of accuracy and would have to be evaluated prior to selection

	laboratory troponin assays meet the ESC criterion of 10% CV at the 99% point of the troponin distribution in the normal population (Apple et al., 2002a; Bertrand et al., 2002) and that the relative merits of different approaches to providing a troponin testing service may change as the technology improves. The TROPT Quantitative® has lower precision than the corresponding laboratory-based troponin T systems and has false-positive and false-negative rates relative to those analysers of between 3 and 4%. As, such, it would not in its current form be suitable for risk stratification at the low troponin T levels (0.01 µg/L) suggested by, for example James el al. (2003), but would be suitable if a cut-off of 0.05µg/L is used. It is therefore important to supplement the troponin T point-of-care test with a cardiac stress test. The stress test identifies patients who, although classified as low risk by a point-of-care test, may have an elevated risk of adverse cardiac outcomes. A more accurate laboratory analyser may also identify these patients. The results also suggest the most accurate laboratory analyser should be used whenever there is less time pressure. The Stratus® CS, although providing acceptable or nearly acceptable precision, (Christenson et al., 2002; Altinier el al., 1999) is different from other point-of-care analysers such as the TROPT QuantitativeV or devices such as point-of-care glucose testers. It can be interfaced to laboratory or hospital systems."p79 (Craig, 2004) "Both the Stratus® CS and TROPT Quantitative® suffer from the problem that, unlike laboratory analysers, once the machine has been 'committed' there is an unavoidable delay of ≤ 20 minutes before the next sample can be analysed."p80 (Craig, 2004)	We believe that these advances have in fact happened with high sensitivity testing, but we are unsure At this point in time early POC testing was shown to benefit from supplemental tests Con: This is an intriguing problem
Clinical Outcomes: Cardiovascular Events, Quality of life, Readmission Rate		
Reference	Synthesis Findings	Pro/Con
Craig, 2004	"For point-of-care testing to be clinically effective, either as a replacement for or in addition to central laboratory testing in this situation, the following two conditions must be met. Firstly, there must be evidence that treatment delay is associated with poorer clinical outcomes." & "Secondly, the necessary decision making and treatment systems must be in place to benefit from timely access to troponin results without needing to wait, for example, until the next consultant ward round."p69	Interesting, but not our situation where there is no available central laboratory testing at the moment Also very interesting, and will have to be addressed in the contextualization
Craig, 2004	"The qualitative point-of-care testing readers are unlikely to have sufficient clinical effectiveness, for the reasons described in Section 4.3.3.3.4.1. Specifically, they rely on experienced readers to avoid variability, particularly near the detection limit and they remove the possibility of adopting a different,	Con: Qualitative POC is not sufficient

	possibly more appropriate, threshold than that chosen by the manufacturer (James et al., 2001b; Azzazy & Christenson, 2002).”p79	
CADTH, 2012-2013	“The review found no evidence reporting on the effects of cTN tests on quality of life outcomes”p23	N/A
CADTH, 2012-2013	“Readmission rates were not reported in any of the included studies”p23	N/A
Lin, 2012	“In patients presenting to the emergency department with chest pain or symptoms suggestive of cardiac ischemia, there is inadequate evidence to suggest the routine use of novel biomarkers in isolation in the diagnosis of ACS. However, there is some evidence for the potential use of several novel biomarkers when combined with cardiac-specific troponin. Further studies are required to evaluate the diagnostic utility of novel biomarkers, particularly when used as part of a multi-marker approach.”p689	Pro: cardiac troponin remains the most reliable biomarker to use; they are looking for a novel biomarker that could replace it, but they do not have it yet
ED Efficiency Measures: Length of Stay, Turnaround Time, Time to Therapy, Throughput, Time to Discharge		
Reference	Synthesis Findings	Pro/Con
CADTH, 2012-2013	“No description related to ED times between the performance of cTn tests and the diagnosis of MI or ACS was found in the included studies”p23	N/A
Craig, 2004	“…there is no published evidence that the introduction of point-of-care troponin testing alone is associated with reduced overall length of stay when compared with laboratory-based troponin testing.”p70	N/A
Storrow,2009	“More importantly, improvement in other ED efficiency measures (e.g., time to therapy and total ED length of stay), although more variable and site specific, suggests that significant improvements in ED throughput can be attained.”p123 “Improvements in other ED efficiency measures, such as throughput, are more variable but can be attained.” p124	Pro: time improvements are possible, but influenced as much or more by site than treatment method
Storrow, 2009	“Our findings demonstrate that improvements in TAT are nearly universal”p123 (Storrow, 2009) “Our review suggests that laboratory TAT can be significantly reduced by the use of ED point-of-care cardiac biomarkers.”p124	Pro: consistently faster TAT
Organizational Factors		
Reference	Synthesis Findings	Pro/Con
Craig, 2004	“The issue of whether a central laboratory service which is only available during a restricted period such as between 09:00 and 17:00 hours Monday to Friday, should be supplemented by an ‘out-of-hours’ point-of-care testing service will be examined in the Economic Evaluation Chapter of this HTA (see Chapter 5). Any such combined service (i.e. Point-of-care and central laboratory) must adopt the same cut-off values to avoid clinical confusion.”p79 –	KEY for our project, see Chapter 5 (More for MG, but of interest nonetheless)

	"The economic model concludes that: • Hospitals assessing patients with non-ST elevation ACS should use point-of-care tests if their laboratories cannot offer a service consistent with clinical decision-making timescales … If laboratories cannot provide seven days per week service with turnaround times of within two hours, then hospitals would reduce the cost per patient by using point-of-care tests"	Unclear on the implications of these findings, will require input from MG.
Generally		
Reference	Synthesis Findings	Pro/Con
Craig, 2004	"No compelling evidence has been found to suggest that central laboratory testing for troponin must be replaced by point-of-care testing in general."p79	Neither pro or con for our purposes
Reported Lack of Evidence		
Reference	Synthesis Findings	Pro/Con
Lin, 2012	"The included studies were heterogeneous in their diagnostic endpoints. There were some studies that used ACS as an endpoint, which includes AMI as well as unstable angina, while others used only AMI. In addition, there was heterogeneity in the reference standards used to define their respective diagnostic endpoints (e.g. final diagnosis by a cardiologist, emergency department discharge diagnosis or positive troponin assay). Of the included studies, there were 49 studies that evaluated central lab assays and the remaining 9 studies evaluated bedside point-of-care (POC) testing.15–23"p685	N/A
Storrow, 2009	"Furthermore, point-of-care assays have dramatically improved in accuracy over the past decade; thus, newer trials may have included physician decision making influenced by these changes, resulting in the potential for additional biases. Owing to the heterogeneity of the trials and planned inclusion of studies with diverse designs, it was not our intent to combine results statistically."p123	N/A
CADTH, 2012	"Given its broad scope, this review was limited to evidence from health technology assessments and systematic reviews…. No studies were retrieved for the use of POCT in electrolytes, blood gases, troponin, complete blood count and liver function. This does not necessarily reflect a lack of research in these areas, but rather a lack of reviewing of the collective evidence."p6	N/A
Craig, 2004	"No published HTAs relating to point-of-care troponin testing have been found."p69	N/A

Craig, 2004	In terms of POC meta-analyses: "Unfortunately for the majority of variables considered here, the studies available are sufficiently dissimilar that formal meta-analyses are impractical. "p77	N/A
CADTH, 2012-2013	Study using POC was not included in the pooled analysis p17	N/A

Primary Research Findings: Categorized by Outcome

Diagnostic Test Performance: Diagnostic Accuracy, Risk Stratification		
Reference	Synthesis Findings	Pro/Con
Collinson, 2011	"…POCT allows safe accurate diagnosis in this population."p317 "….troponin measurement performed by POCT alone is sufficient and that the measurement of additional markers does not significantly improve diagnostic efficiency beyond the measurement of troponin alone."p316 "Troponin alone is sufficient for early diagnosis and exclusion of AMI and can be reliably measured by point-of-care testing within 2 h if the method can define the 99th percentile."p317	Pro: reliable alternative
Collinson, 2013	"The findings of RATPAC-CBE support the widespread implementation of high-sensitivity troponin assays. They also support the use of troponin alone as the gold standard diagnostic test and suggest that additional measurement of myoglobin and CK-MB is not required.."p65	Pro: reliable alternative
Clinical Outcomes: Adverse Event Rate, Decision Making, Time to Anti-Ischemic Therapy		
Reference	Synthesis Findings	Pro/Con
Collinson, 2013	"The measurement of cardiac troponin as cTnT or cTnI over a short time frame offers the best strategy for early confirmation or exclusion of an AMI. In this study, a low-risk group was successfully discharged on the basis of admission and 90-minute measurements. Questions remain as to what is the optimal timing for troponin measurement. In addition, troponin measurement needs to be incorporated within a clinical decision-making strategy that utilises clinical and ECG findings. Of all markers studied, only H-FABP appears to offer some improvement in diagnostic efficiency that might also be cost-effective. However, as yet, measurement of H-FABP is not carried out on routine clinical laboratory equipment suitable for a 24-hour diagnostic service."p66	Pro: efficient Con: Optimal timing for troponin still questionable
Goodacre, 2011	"The overall adverse event rate was very low and most events occurred in patients admitted after initial assessment. Only one of the five adverse events in patients who were initially discharged home occurred within 1 month of recruitment, so there is little evidence of significant missed pathology"p195	Pro: reliable alternative
Renaud,	"…we found that POCT was associated with a faster decision-	Pro: more efficient

2008	making process than CHLT was. POCT was associated with a shorter [time to anti-ischemic therapy] TAIT (median 151 min, IQR = 139–162 min) compared to CHLT (median 198 min, IQR 187–210 min). Therefore, the diagnosis of myocardial infarction could be made slightly earlier in the subset of patients with vague symptoms (Figure 2).”p221 “Point-of-care testing resulted in shortening the [time to anti-ischemic therapy] TAIT, particularly for 38.9% of high-risk patients with a low suspicion of ACS. For non-troponin testing, previous studies have not always shown a significant benefit of implementing POCT in the ED.21,39–42 By studying only patients with suspicion of NSTE-ACS, for whom treatment decision or bed request may be delayed until the cTnI result is known, we were able to show a difference in TAIT.23,43” p222	
ED Efficiency Measures: Time to Discharge, Length of Stay, Test Turnaround Times		
Reference	Synthesis Findings	Pro/Con
Bradburn, 2012	“The heterogeneity in outcomes was highly statistically significant (c2¼75.5, degrees of freedom¼5, p<0.001), indicating that the effect of point-of-care testing varied significantly between the participating hospitals.”p235 “This study has shown that the effect of point-of-care panel assessment varied markedly between hospitals, suggesting that the effect of point-of-care panel assessment may depend on the setting and that the general findings of the RATPAC trial may not apply at all hospitals. It is likely that differences in the facilities available, local protocols, existing guidelines for chest pain, existing troponin assays or staff using the point-of-care tests explain the variation in outcomes and costs. However, caution should be taken about attempting to identify explanations for outlying results in specific characteristics of the hospital concerned. The estimates of proportion of patients successfully discharged or mean costs per patient are subject to substantial random error when analysed at individual hospital level. For example, the reversed trend observed in the proportion successfully discharged at Leeds was based on eight cases in the control group versus one in the intervention group being successfully discharged within 4 h after assessment. Furthermore, a statistically significant result for a specific hospital (such as the comparison of mean costs per patient at Edinburgh) is one of many hypothesis tests and thus carries a risk of being a spurious false-positive finding.”p236 “…some evidence of the effect of local practice on outcome seems to be apparent in figure 1, which shows the differences between the hospitals in terms of the proportion of patients in hospital as a function of time from initial attendance.”p236 (Bradburn, 2012)	Con: this indicates that the greatest source of test performance variability is at the hospital level, meaning that we cannot ensure reproducing the same results.

Goodacre, 2011	"The use of the point-of-care cardiac marker panel resulted in a greater proportion of patients being successfully discharged after emergency department assessment and a reduction in the median, but not the mean length of initial hospital stay. It was associated with more patients avoiding any inpatient stay over the 3-month follow-up but did not lead to any difference in the total or mean number of inpatient hospital days. This was because patients in the point-of-care arm who were admitted to hospital tended to accrue more inpatient days. Point-of-care assessment was also associated with a small increase in coronary care admission and chest pain-related outpatient follow-up. These findings suggest that point-of-care assessment changes the emergency department disposition of patients with undiagnosed chest pain and may reduce inpatient bed turnover, but does not reduce inpatient bed occupancy). Interpretation of these findings depends upon one's perspective. For the patient, emergency physician or admitting physician point-of-care testing has the potentially beneficial effect of reducing the need for hospital admission. For the health service manager point-of-care testing may offer some benefit by reducing inpatient bed turnover but does not appear to reduce bed occupancy."p193	Pro: more efficient
Loten, 2010	"We demonstrated time savings of approximately 48 minutes, out of an average LOS of almost 7 h, although this was not significant after adjusting for clustering. Using the Health Department target of discharge within 8 h, we found a statistically significant absolute increase of 10% meeting this outcome in the POC group. This may be a small increase but represents 6e12 h in ED monitored beds each day with attendant effects on safety and efficiency of patient treatment.23 As expected, the difference was more marked at the site where pathology was not available around the clock; it is in these situations when the most potential gains could be made. It is important to note that the difference seen between the two groups in our study probably represents an underestimate of the potential gains. This is evidenced by the fact that the majority of patients during the POC allocated weeks (53%) continued to receive only the laboratory troponin measure. The potential reasons for this are: < Mistrust of the POC machine. Nursing staff anecdotally noted that doctors were often not acting upon the results of the POC system, but rather waiting for a confirmatory result from the laboratory. < Unfamiliarity. Physicians perhaps needed more training than was given as part of the validation study and more time to effect behaviour change than the 4 months that had elapsed. <	Pro: more efficient

	Time pressure on staff. Although the POC machine is faster, providing results in 10 minutes, this was time required of the medical or nursing staff who could have otherwise continued with their other work."p197	
Renaud, 2008	"Nonetheless, our findings underscore the limited impact of POCT for shortening ED LOS."p222 "Nevertheless, despite hastening decision-making, we did not demonstrate a significant difference in the study group average LOS in the ED. This suggests that POCT is only part of the whole-system approach that is required to improve timeliness of care.21–23 Indeed, many other factors determine the duration of ED visits, such as the absence of centralized bed assignment in our hospital. Apart from chance variation, we could not explain the unexpected trend toward a longer LOS for the POCT group."p222	Con: indicates inter-hospital variability
Ryan, 2009	"we show that point-of-care testing decreased test turnaround time compared with central laboratory testing and greatly increased the proportion of test results available to the physician within a 30- or 60-minute period.13 However, this did not translate to a time savings in discharging patients across all study sites. At site 2, point-of-care testing increased time to ED departure among discharged patients, whereas at other sites the effect was a mean time savings, which range from about 22 minutes to about 44 minutes."p324 "Our results demonstrate variable direct benefits of point-of-care testing, and when benefits are evident these are not as extensive as might be assumed from the common conception that rapid results translate into rapid decision making. Although our findings suggest that at some institutions point-of-care testing makes a difference, there is still a wide range of effects. Delays in the preanalytic and postanalytic aspects of testing must be optimized to improve brain-to-brain times. In conclusion, the effect of point-of-care testing on length of stay in the ED varies between settings. At one site, point-of-care testing decreased time to admission, whereas at another, point-of- care testing increased time to discharge. Potential effects of point-of-care testing on patient throughput should be considered in the full context of ED operations."p327	Mixed: POC may be more efficient in terms of TAT, but other factors are more important in terms of patient benefits. Still though, this suggests that POC troponin is a viable alternative to central lab testing in smaller hospitals.
Organizational Factors		
Reference	Synthesis Findings	Pro/Con
Bradburn, 2012	"Overall, the present analysis suggests that the intervention would be more likely to have an impact at hospitals where it is more distinct from standard care, where it helps to address specific service targets and where it is used by decision making clinicians. However, these observations are difficult to generalise between settings." p236	These aren't really pieces of evidence but help point to organizational issues that may affect effective POC uptake.
Loten, 2009	"We suggest that successful introduction of POC testing for	To address in contextualization

	troponin requires not just a comprehensive training and maintenance programme but also an effective initiative to change the clinical culture surrounding its use."p197	
Mogensen, 2011	"In this study a study assistant without other assignments handled the POCT analysis. In real life a staff member might have other assignments in addition to the POCT analysis, which will prolong the time to the POCT answer. Furthermore the central laboratory was placed around 300 meters away. If transport time to the central laboratory is reduced this will reduce the difference in turnaround time between POCT and central laboratory."p6	To address in contextualization

Notes on data extraction results by outcome category

Evidence of Diagnostic Test Performance

Diagnostic Accuracy Systematic Review Literature	**CADTH OUR** • For POC only Sensitivity and Specificity reported • Others not available for POC: Positive likelihood ratio, Negative likelihood ratio, Diagnostic Odds ratio, Area under the curve of the Reciever operating characteristic curve, Intended to measure: changes in continuous measures (e.g., quality of life) as weighted mean difference and for changes in binary measures (such as thromboembolic events, acute and chronic cardiovascular events, revascularization procedures, heart failure, recurrence, readmission and death), as relative risks but there was a scarcity of studies reporting those outcomes **CADTH 2012 Apr** • Sought diagnostic accuracy as an outcome but didn't find any systematic review literature for troponin **Storrow, 2009** • Diagnostic test characteristics were not sufficient for inclusion **Lin, 2012** • "there was heterogeneity in the reference standards used to define their respective diagnostic endpoints (e.g. final diagnosis by cardiologish, emergency department discharge diagnosis or positive troponin assay)." • Sensitivity/Specificity **Craig, 2004** • Sensitivity, false positive, false negative • Misclassification rates pooled analysis o 5 studies for TROPT Sensitive relative to laboratory analysers found "pooled false-negative and false-positive rates were 4% (95% CI 0.04, 0.06) and 5%(95% CI 0.04,0.06) respectively" o 2 studies for TROPT Quantitative reported "pooled false-negative and false-positive rates were 3% (95% CI 0.01,0.05) and 4% (95%CI 0.02, 0.07) respectively • Follow up rates were sought but either no studies reported follow-up event rates and the two that did had different follow up periods and therefore couldn't be pooled.
Diagnostic Accuracy Primary Research Literature	**Bradburn, 2012** • Not an outcome **Collinson, 2011** • Reciever Operator Characteristic curve analysis • Comparison of Area under the curve • Individual maker values change (delta) and combination of presentation or 90 min value plus delta • Sensitivity, Specificity, • Positive Predictive Value, Negative Predictive Value • MI definition **Collinson, 2013** • Not an outcome

	Goodacre, 2011 • Not an outcome **Loten, 2009** • Not an outcome **Morgensen, 2011** • Not an outcome **Renaud, 2008** • Not an outcome **Ryan, 2009** • Not an outcome

Length of Stay

SR ED Length of stay	**CADTH OUR** • Not an outcome **CADTH, 2012 Apr** • Not an outcome **Storrow, 2009** Included studies in defined as: • ED presentation to ED departure • ED Presentation to bed assignment • ED triage to ED departure **Lin, 2012** • "there was heterogeneity in the reference standards used to define their respective diagnostic endpoints (e.g. final diagnosis by cardiologish, emergency department discharge diagnosis or positive troponin assay)." **Craig, 2004 calls it early discharge and early therapy** • No systematic literature reviewed for this but for primary studies "No studies have compared the use of point-of care testing with central laboratory testing for decision rules based on cardiac troponin as a single marker"
PR Length of Stay	**Bradburn, 2012** • Proportion in hospital 12- 36 hours later **Collinson, 2011** • Not an outcome **Collinson, 2013** • Not an outcome **Goodacre, 2011** • Length of stay **Loten, 2009** • LOS defined as from patient arrival to physical departure from the ED either to an inpatient bed or discharge **Morgensen, 2011** • Not an outcome **Renaud, 2008** • ED length of stay defined by the time from presentation to inpatient

	bed assignment **Ryan, 2009** • Length of stay defined as from presentation to the time of departure from the ED, either to an inpatient setting or to home.

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