

Evidence *in* Context

Issue: Point-of-Care Testing
Released: October 2014

Health research — synthesized and contextualized for use in Newfoundland & Labrador

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

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Cite as: Pant Pai, N., Grignon, M., Bornstein S., Navarro, P., Mackey, S. (2014) Troponin Point-of-Care Testing in Smaller Hospital and Health Centre Emergency Departments in Newfoundland and Labrador St. John's, NL: Newfoundland & Labrador Centre for Applied Health Research, Memorial University

ISBN 978-0-88901-462-6

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About This Report

About NLCAHR

The Newfoundland & Labrador Centre for Applied Health Research, established in 1999, contributes to the effectiveness of the health and community services system of the province and the physical, social, and psychological well-being of the population. NLCAHR accomplishes this mandate by building capacity in applied health research, supporting high quality research, and fostering more effective use of research evidence by decision makers and policy makers in the province's health system.

About the Contextualized Health Research Synthesis Program

In 2007, NLCAHR launched the Contextualized Health Research Synthesis Program (CHRSP) to provide research evidence that would help guide decision makers in the provincial health system on issues of pressing interest to Newfoundland and Labrador. Instead of conducting original research, CHRSP analyzes findings from high level research already conducted in the subject area, such as systematic reviews, meta-analyses and health technology assessments. Findings are then synthesized and subjected to a systematic process of contextualization: they are analyzed in terms of their applicability to the conditions and capacities of the unique context of Newfoundland and Labrador. Our contextual analysis includes assessing the specific forms an issue may take in this province as well as the applicability of any proposed solutions and methods to locally available resources, infrastructure, human resources, cultural conditions and financial capacities. CHRSP uses a combination of external experts and local networks to carry out and contextualize the research synthesis and to facilitate the uptake of the results by research users. CHRSP focuses on three types of projects: health services/ health policy projects, health technology assessment (HTA) projects, and projects that combine the two to examine processes for the organization or delivery of care involving a health technology.

About Our Partners

For this project, NLCAHR partnered with Eastern Health. Senior administrators from Eastern Health proposed the original CHRSP topic and participated on the CHRSP Project Team through the contextualization of the synthesis results to the drafting of the final report. Other members of the CHRSP Project Team included senior decision makers and local experts from the four provincial Regional Health Authorities and Emergency Department practitioners who provided additional contextualization analysis and contributions to the writing of the report.

Who Should Read This Report?

This report provides a synthesis of the relevant research-based evidence on the clinical effectiveness, feasibility and acceptability of cardiac troponin point-of-care testing for emergency departments in Newfoundland and Labrador in general, and for smaller hospitals and health centres in particular. In addition to the synthesis of research-based evidence, this report also provides an analysis of local contextual factors and the impact they may have on lab services in the province. This report is intended to inform and assist decision makers in the Department of Health and Community Services of Newfoundland and Labrador and the province's Regional Health Authorities who are involved in the planning, implementation and delivery of services. This CHRSP report is also meant to help guide decisions regarding lab services and the provision of point-of-care testing in emergency departments in the province. This report is also aimed at practitioners, researchers and other stakeholders involved in providing emergency health services in settings that do not have 24/7 central laboratory services. Decision makers from other jurisdictions, especially those with similar geography, resources and potential client populations, may also find the content helpful. The report includes explanations of research terms and technical language; accordingly, there is no need to have a specialized medical or health background in order to understand its content.

The Research Team

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

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Acronyms

ACS	Acute Coronary Syndrome
ALT	Alanine Aminotransferase
AMI	Acute Myocardial Infarction
AMSTAR	Assessment of Multiple Systematic Reviews
AUC	Area Under the Curve
CAD	Canadian Dollar
CBC	Complete Blood Count
CHRSP	Contextualized Health Research Synthesis Program
CI	Confidence Interval
cTnI	Cardiac Troponin I
cTnT	Cardiac Troponin T
CO₂	Carbon Dioxide
CV	Coefficient of Variation
DHCS	Department of Health and Community Services
DOOR	Diagnostic Odds Ratio
ED	Emergency Department
EUR	Euro
GBP	British Pound
INR	International Normalised Ratio
IQR	Inter-Quartile Range
MI	Myocardial Infarction
NSTEMI	Non- ST Elevation myocardial infarction
OR	Odds Ratio
PICO	Population, Intervention, Comparator, Outcome
POCT	Point-of-care test (or testing)
QALY	Quality-Adjusted Life Year
RCT	Randomized Controlled Trial
RHA	Regional Health Authority
ROC	Receiver Operating Characteristic
RN	Registered Nurse
RR	Relative Risk
STEMI	ST-Elevation Myocardial Infarction
TAIT	Time to Anti-Ischemic Therapy
TAT	Turnaround Time
UA	Unstable angina
USD	United States Dollar

Glossary

Acute Coronary Syndrome (ACS)	A term used to describe any condition that results in a sudden reduction in blood flow to the heart. ACS is the result of coronary arteries becoming narrowed or blocked. The three types of ACS are ST Elevated Myocardial Infarction (STEMI) or Non-ST Elevated Myocardial Infarction (NSTEMI) and Unstable Angina (UA).
AMSTAR	An 11-item instrument used to assess the methodological rigor of systematic reviews (1)
Blinding	Experimental design feature in which the research participants and/or researchers do not know if the participant is in the test group or control group. In ‘single blind’ experiments, participants are not aware of their group status. In ‘double blind’ experiments, researchers are also not aware of the participants’ group status.
Blood gas test	A type of test that measures the partial pressures of oxygen and carbon dioxide in the blood as well as the acidity (pH) of the blood. Results from this type of test can provide an indication of certain medical conditions or critical states.
Callback lab services	A service arrangement where medical laboratory staff can be ‘called back’ after hours to work. Newfoundland and Labrador medical laboratory staff are required to be paid for a minimum of three hours for a callback.
Cardiac troponin	Troponin is a type of protein complex made up of three individual proteins (troponin C, I and T). They interact to control striated muscle contraction, i.e., cardiac and skeletal muscle. Cardiac troponin I (cTnI) and T (cTnT) take a unique form in cardiac muscle. They are released into the blood when heart muscle cells have been damaged (2).
Cardiac troponin testing	Testing that measures the level of cTnI and cTnT in the blood stream in order to determine the severity of damage to the heart, in particular in cases of acute myocardial infarction (3).
Coefficient of Variation (CV)	Relative error expressed as a percentage and is the ratio of the standard deviation to the mean times 100. It indicates the extent of variability in relation to mean of the population.
Complete Blood Count (CBC)	A test that is ordered when a person exhibits signs and symptoms that may be related to disorders that affect the blood. CBC measures the concentrations of the cellular elements of the blood, including white blood cells, red blood cells, platelets as well as hemoglobin and hematocrit (% of a person’s blood that consists of red blood cells).

Confidence Interval (CI)	A measure of the reliability of an estimate. A CI specifies a range within which the true value of an estimated parameter is expected to lie. CIs for ratios that include the value of 1 and CIs for differences that include the value of 0 indicate that the test and control groups are not likely to be different.
Cost-effectiveness study	A study in which the monetary costs of an intervention are considered in terms of a single common health outcome that is measured in natural units, for example: the number of years with full mobility gained from a treatment or the number of placements in long-term care that are deferred.
Cost-minimization study	A study that analyzes alternative interventions that are assumed to produce equivalent outcomes in order to determine which of those interventions is least costly (4).
Cost-utility study	A study in which the monetary costs of an intervention are considered in terms of a single outcome, or considered in terms of multiple outcomes that are weighted or valued in relative terms. The combined outcome is measured in units that capture both the quantity and quality of the effects of the intervention, with the most common measure being the quality-adjusted life-year or QALY.
Clinical biochemistry test	A class of clinical pathology tests that relies on measuring various chemical constituents in serum and plasma, whole blood, urine and other body fluids. Clinical biochemistry tests may be used to confirm a diagnosis, screen for a disease, assist in the evaluation disease risk or prognosis.
Cytological tests	A class of clinical pathology tests that relies on testing at the cellular level in order to detect cell abnormalities.
Diagnostic odds ratio	A statistical measure of the effectiveness of a diagnostic test that expresses the strength of association between a test result and a disease. A large odds ratio generally indicates a high probability that the patient has the disease; conversely a low ratio is consistent with a low probability of disease. (See odds ratio).
Downs and Black Assessment Tool	A checklist that was developed to assess the methodological quality of both randomised controlled trials and non-randomised studies (5).
Effect size	A measure of the strength of a relationship between two variables, for example between a treatment for a health condition and recovery from that health condition. Effect sizes may be quantified by a range of different measures, including correlations, differences in means and relative risks.
Effectiveness	The ability of an intervention to produce the desired beneficial effect in actual usage.
Efficacy	The ability of an intervention to produce the desired beneficial effect in expert hands and under ideal circumstances.

Electrolyte testing	Measurement of the levels of different electrolytes in whole blood, serum plasma etc. (e.g. sodium, potassium, chloride and bicarbonate).
Grey literature	Research that is published non-commercially, which includes reports carried out by governments, health authorities and not-for-profit associations.
Health technology assessment	Research that studies the medical, social, ethical and economic implications of the development, diffusion, and use of health technology.
Incremental Cost-Effectiveness Ratio (ICER)	The ratio of the difference in costs between an intervention group and a control group to the difference in outcomes or effects between the two groups. Costs are most often measured in monetary units, while outcomes or effects are most often measured in terms of QALYs.
Inter-Quartile Range (IQR)	A measure of the statistical dispersion of a variable for a sample. The IQR is reported by the first and third quartile values for the variable in question, indicating the middle 50% of the sample.
Inter-Rater Reliability (IRR)	A statistical measure that quantifies the level of agreement between two or more raters.
International Normalised Ratio (INR)	A lab measurement that is used to determine how long it takes for blood to clot.
Length of Stay (LOS)	The time taken from patient registration or triage to the time the main service provider makes the decision to discharge the patient or to the time the patient is admitted (6).
Liver function tests	Blood tests used to assess the general state of the liver and biliary systems. These include tests for liver enzymes (e.g., alanine aminotransferase (ALT) and alkaline phosphatase), bile (e.g., bilirubin) and proteins (e.g., albumin), as well as tests that measure blood clotting (e.g., prothrombin time and INR).
Markov chain	A type of model that is based on random probability distribution that describes a sequence of possible events in which the probability of each event depends only on the present state and not on any past states.
Meta-analysis	A type of systematic review that uses statistical techniques to quantitatively combine the findings from primary research studies.
Micro-costing study	Micro-costing studies collect detailed data on resources utilized and the value of those resources. Such studies are useful for estimating the cost of new technologies or new community-based interventions, for producing estimates in studies that include non-market goods, and for studying within-procedure cost variation (7).
Micro-simulation study	A category of computer modeling that analyzes the interactions of individual units, e.g., patients or health professionals, in order to model the effectiveness of an intervention.

Myocardial Infarction (MI)	The clinical name for a heart attack. The syndrome that results from blood not flowing properly to the heart.
Negative likelihood ratio (NLR)	One of two types of likelihood ratios that help determine which diagnostic test will best help to rule-in or rule-out a disease in a patient. A NLR indicates how much trust to place in a negative reading indicating that a patient does not have the disease in question. n. The more the NLR exceeds 1, the greater the likelihood that the patient does not, in fact, have the disease. See Figure 3, p. 14 for summary of test performance measures.
Non-ST Elevation Myocardial Infarction (NSTEMI)	A type of ACS that is moderately severe, caused by the partial blockage of coronary arteries by a blockage or clot. The ECG shows no ST segment elevation as there is with a ST Elevation Myocardial Infarction.
Observer effect	Occurs when a subject under study modifies their behaviour as a result of being actively observed.
Odds ratio	The ratio of the likelihood of an outcome occurring in one group compared to the likelihood of it happening in another group. An odds ratio of 1 indicates that there is no difference between the likelihood of the outcome happening in one group and the likeliness of its happening in the other.
Positive likelihood ratio (PLR)	One of two types of likelihood ratios that help determine which diagnostic test will best help rule-in or rule-out a disease in a patient. A PLR indicates how much to increase the probability that a patient actually has a disease if the test is positive. The more the PLR is over 1, the greater the likelihood that the patient does, in fact, have the disease. See Figure 3, p. 14 for summary of test performance measures.
QALY	A measure that combines time and an assessment of quality of life. QALY stands for “quality adjusted life year.” A QALY unit is based on a scale that considers one year of life lived in perfect health worth 1 QALY. A year of life that is lived in a state of less than perfect health is worth less than 1 QALY. The quality of life is quantified as “the utility value,” a measure of the state of health of the person in question. A QALY value equals the utility value multiplied by the years lived in that state: UTILITY x TIME = QALY. QALYs are expressed in terms of “years lived in perfect health.” For example, half a year lived in perfect health is equivalent to 0.5 QALYs, the same as 1 year of life lived in a compromised state of health with utility 0.5 (6).
Randomized Controlled Trial (RCT)	A study in which a number of similar people are randomly assigned to two (or more) groups to test a specific drug/ treatment. The experimental group receives the treatment being studied; The comparison or <i>control group</i> receives an alternative treatment, a dummy treatment (<i>placebo</i>) or no treatment at all. The groups are followed up to see how effective the <i>experimental treatment</i> was. <i>Outcomes</i> are measured at specific times and any difference in response between the groups is assessed statistically. This method is used to reduce <i>bias</i> (8).

Receiver Operating Characteristic (ROC) curve	Used to measure the accuracy of a test, i.e., the test's ability to distinguish those with and without the condition under examination. The ROC curve plots the test's sensitivity against 1-specificity. If the area under the curve equals 1, the test perfectly predicts those with and without the condition. If the area under the curve equals 0.5, the test is random; its predictive value is equal to a coin toss and thus it cannot be trusted to predict those with and without the condition.
Renal function testing	A class of tests used to assess the state of renal functioning. Typical renal tests include measuring different blood components including creatinine, blood urea nitrogen, BUN (creatinine ratio), albumin, calcium, CO ₂ , chloride, glucose, phosphorus, potassium and sodium.
Relative Risk (RR)	A measure of the likelihood that an exposure will have a particular outcome. In the case of health services, RR is the ratio of the probability of an outcome occurring in a test group that received the health service compared to the probability of its occurring in a control group that did not receive it.
Sensitivity	In the context of screening or diagnostic testing, the proportion of persons <i>with</i> the disease/condition who are correctly identified as positive by a test. A test with a high sensitivity produces very few false negatives. This is particularly useful for screening tests to rule out a diagnosis for a condition, since negative test results are very likely to be true negatives. See Figure 3, p. 14 for summary of test performance measures.
Specificity	In the context of screening or diagnostic testing, the proportion of persons <i>without</i> the disease/condition who are correctly identified as negative by a test. A test with a high specificity produces very few false positives. This is particularly useful for diagnostic tests to rule in a diagnosis for a condition, since positive test results are very likely to be true positives.
ST-Elevation Myocardial Infarction (STEMI)	A severe type of heart attack in which blood to the heart is completely blocked. Characteristic changes in ST elevation show major damage to the heart muscle as measured by an electrocardiogram.
Systematic review	A literature review, focused on a specific and explicit research question that applies a systematic methodology to identify published and unpublished research evidence relevant to that question, and then select, appraise and synthesize the evidence.
Time to disposition	Time from patient registration or triage to the time the main service provider makes a decision about the patient's care needs, typically the decision to discharge or admit the patient (6).
Trapezoidal rule	In numerical analysis, the trapezoidal rule is a technique for approximating the definite integral. The trapezoidal rule works by approximating the region under the graph of the function as a trapezoid and calculating its area.

Turnaround time (TAT)	Generally speaking, this is the name for the interval between the time a test is administered to the time the test result is available. Studies may define this term slightly differently depending on the hospital protocols in place.
Usual care	Another term for 'standard care'.

The Research Question

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



Key Messages

The following key messages emerged from a synthesis of the evidence related to cardiac troponin point-of-care tests (POCT). Decision makers are also encouraged to review the Considerations for Decision Makers outlined at the end of this report, as these combine the evidence with local contextual factors that may have an impact in Newfoundland and Labrador (See Page 47).

1. In terms of test performance, the sensitivity and specificity of currently available cardiac troponin point-of-care tests are sufficient for their use as screening tests. Cardiac troponin POCT continues to improve at a significant rate and is becoming as accurate as central lab testing. (Effective Intervention)
2. In terms of clinical outcomes, cardiac troponin POCT does not appear to increase the risk of adverse cardiac-related events or readmission rates compared to central lab testing for patients seen in emergency departments. (Promising Intervention)
3. When compared to central lab testing, emergency department cardiac troponin point-of-care tests significantly and consistently reduce turnaround time for test results. (Effective Intervention)
4. Cardiac troponin POCT appears to have the capacity to reduce emergency department process time outcomes compared to central lab testing, but it cannot achieve those outcomes by itself. Other site-specific variables appear to have an equal or greater impact on those outcomes. Point-of-care testing must be considered in the full context of emergency department operations for improvements in patient throughput to be truly quantified.
5. Point-of-care testing has the greatest impact on emergency department process outcomes in facilities without a 24/7 central lab service.
6. The evidence for the overall cost benefits of emergency department cardiac troponin POCT is incomplete and inconsistent. The findings on the overall cost benefits are not conclusive.

Background

This point-of-care test (POCT) project was initiated through a topic submission from Eastern Health to the Contextualized Health Research Synthesis Program (CHRSP) asking us to address the use of POCT in smaller hospital and health clinic emergency departments (EDs) without 24/7 central lab facilities (i.e., Category B emergency departments, see below). These emergency departments are located in rural or remote parts of Newfoundland and Labrador, although some are within an hour's driving distance of a major hospital.

...the provincial health system plans on becoming accredited for POCT in emergency departments by 2015, and so the issue of which tests to have available has become particularly relevant.

Achieving adequate levels of medical testing in the emergency departments of smaller health centres requires the involvement of both medical laboratory services and departments of emergency medicine. From the perspective of lab services, providing high-quality and affordable testing in smaller health centres is a major challenge. Considerations include shortages in health human resources, challenges in maintaining quality testing, and being able to afford instruments and reagents at health centres with lower test volumes. From the emergency medicine perspective, the main issue is having a test available to expedite patient care decisions by the attending physician. As one of our project consultants told us:

The greatest value that can be provided by [point of care] testing is through the provision of timely test results in emergent cases for immediate patient management decisions. The timely availability of a small critical care testing menu can potentially offer the most significant impact on patient outcomes in rural health care centers.

As a result, the Regional Health Authorities (RHAs) and the Department of Health and Community Services (DHCS) are interested in point-of-care testing as a potential alternative to 24/7 lab services for emergency departments in smaller hospitals and health centres. Furthermore, the provincial health system plans on becoming accredited for POCT in emergency departments by 2015, and so the issue of which tests to have available has become particularly relevant.

The initial scope of the project included a broad range of clinical biochemical and hematologic tests that are commonly requested in emergency departments and are potential candidates for POCT. These include tests for: troponin, electrolytes, complete blood count (CBC), renal function, blood gas, liver function and blood clotting. In an effort to narrow the focus of this study to within manageable limits, the POCT CHRSP Project Team considered the following criteria:

1. The time course of the presenting conditions that would indicate the use of the POCT;
2. The effects of the POCT result on treatment decisions;
3. The potential impact on economic and process outcomes if the POCT were available;
4. The availability of research-based evidence about that POCT.

Weighing the merits of various tests for their potential impact in terms of the above criteria, the Project Team ultimately selected cardiac troponin point-of-care testing for suspected acute coronary syndrome (ACS)¹ as the focus of this study. The goal of this project was to investigate the research-based evidence concerning the effectiveness, feasibility and acceptability of cardiac troponin POCT in emergency departments in smaller hospitals and health centres. The topic was therefore refined and articulated as the following research question:

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

The POCT CHRSP Project Team then identified a set of priority outcomes for the final report:

- health service variables, including turnaround time and the overall time spent in the emergency department;
- costs of implementation and operation;
- the feasibility of accrediting staff to implement a troponin POCT standard;
- quality control and forward compatibility, e.g., the capacity for a POCT system to accept inputs from later versions of the equipment.

The Project Team had also hoped to develop a model for cardiac troponin POCT usage and costs/benefits based on emergency department and central lab administrative data sets. Such a model could be used to contextualize the evidence and to inform the report's list of considerations for decision makers. Ultimately, however, the Project Team had to abandon developing the model as the result of difficulties and delays with the data request.²

¹ See Online Companion Document, CHRSP Topic Refinement, for more details.

² See Online Companion Document, Data Request, for more details.

Emergency Department Lab Services in NL

Newfoundland and Labrador has three types of emergency medicine settings, termed *Category A*, *Category B*, and *Community Clinics in Labrador* (see Figures 1 and 2 below). These are characterized as follows:

- **Category A:** emergency departments in larger hospitals with a minimum of one physician dedicated to providing emergency services and onsite 24-hours a day. They are located in hospitals that have acute care beds and other specialty services. All Category A emergency departments have access to 24/7 medical lab services (9). Based on 2011 census data, Category A emergency departments are within a thirty-minute drive for approximately 70% of the respective populations on the island of Newfoundland (331,270/485,358) and in the Labrador territory (20,570/29,178);
- **Category B:** emergency departments in smaller hospitals and health clinics with a physician that is always available but may not be onsite. They are located in facilities that may or may not have acute care beds and other specialty services, are primarily in the more rural areas of the province, and have lower patient volumes. All Category B emergency departments have medical lab services during working hours (Monday to Friday, 8:00am-4:00pm). Most have callback medical lab services after hours but a minority do not (9). Based on 2011 census data, Category B emergency departments on the island of Newfoundland are within a thirty-minute drive for 22% of the island's population (103,697);
- **Community Clinics in Labrador:** fourteen clinics in Labrador, mostly located in remote coastal communities, focus on primary healthcare and are staffed by small numbers of nurses and support staff. In cases of medical emergency, Community Clinic nurses consult with emergency medicine physicians located in one of the three hospitals in Labrador Grenfell Health with Category A emergency departments. Airlift services can transfer emergency patients to the closest tertiary care centre if needed. Based on 2011 census data: Community Clinics in Labrador serve approximately one-fifth of the population (5,895).

Table 1 on page 20 of this report provides a detailed breakdown of driving time catchment population sizes. It is important to note that the population catchments for the different types of emergency department are not mutually exclusive—a household may be within a thirty-minute drive of both a Category A and a Category B facility.

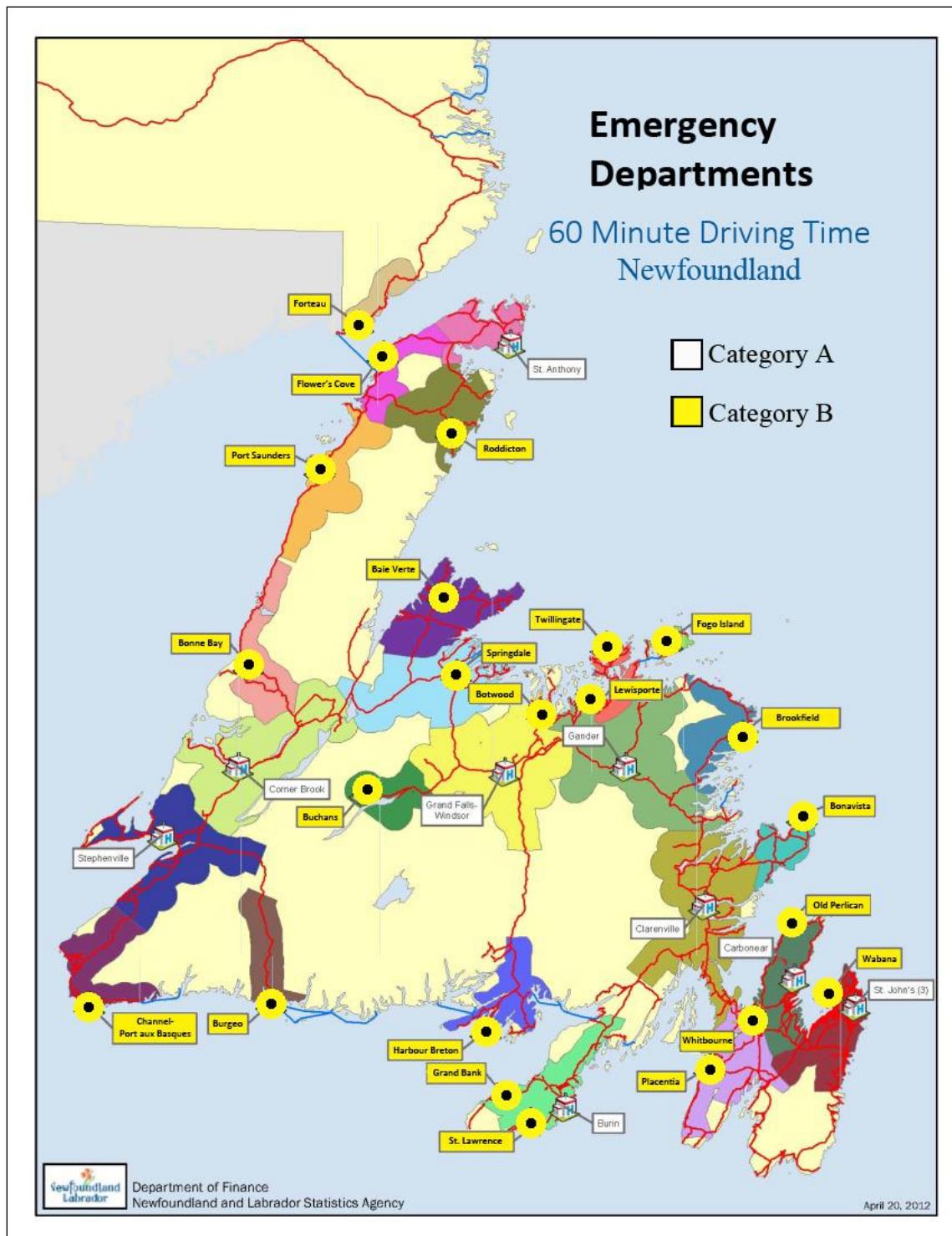


Figure 1: Emergency Departments in Newfoundland

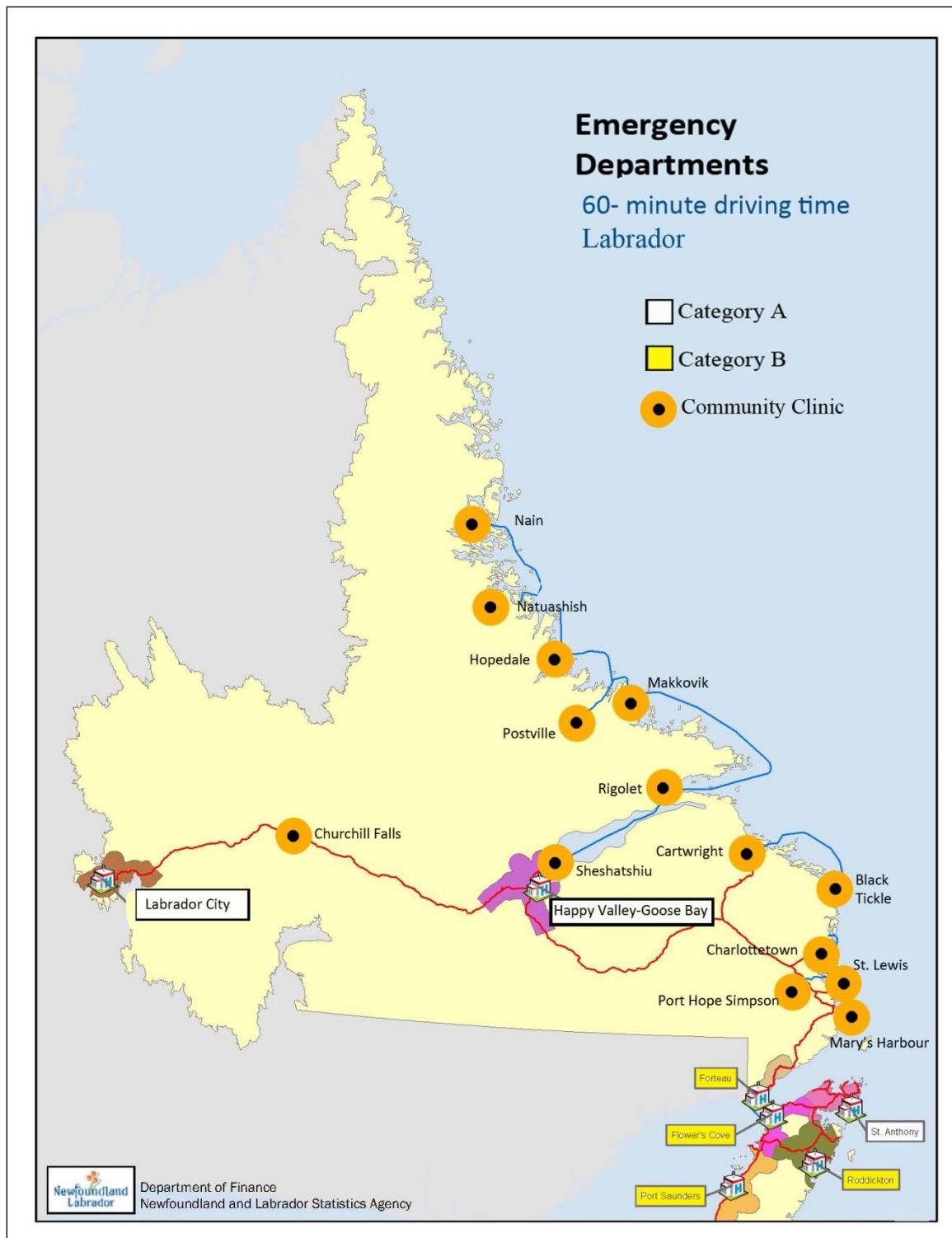


Figure 2: Emergency Departments and Emergency Care Facilities in Labrador

Table 1: Types of emergency care facilities and their population size based on select catchment areas

CATEGORY A EMERGENCY DEPARTMENTS		Population (2011)		
Regional Health Authority	Community (Facility Name)	30 Minute	60 Minute	Total
Eastern Health	St. John's (HSC / Janeway / St. Clare's)	197,081	7,519	204,600
	Carbonear (Carbonear General Hospital)	30,609	11,596	42,205
	Clarenville (Dr. G.B. Cross Memorial Hospital)	11,183	7,793	18,976
	Burin (Burin Peninsula Health Care Centre)	12,157	6,908	19,065
Central Health	Grand Falls-Windsor (Central Newfoundland RHA)	23,312	1,832	25,144
	Gander (James Paton Memorial Hospital)	12,638	15,694	28,332
Western Health	Corner Brook (Western Memorial Regional Hospital)	30,550	8,715	39,265
	Stephenville (Sir Thomas Roddick Hospital)	13,740	3,427	17,167
Labrador-Grenfell Health	Happy Valley-Goose Bay (Labrador Health Centre)	7,552	1,921	9,473
	Labrador City (Captain William Jackman Memorial Hospital)	9,228	0	9,228
	St. Anthony (The Charles S. Curtis Memorial Hospital)	3,790	1,079	4,869
CATEGORY B EMERGENCY DEPARTMENTS		Population (2011)		
Eastern Health	Wabana (Dr. Walter Templeman Health Centre)	10,046	162,290	172,336
	Whitbourne (Dr. William H. Newhook Community Health Centre)	10,107	63,089	73,196
	Placentia (Placentia Health Centre)	4,172	728	4,900
	Bonavista (Bonavista Community Health Centre)	6,198	2,101	8,299
	Old Perlican (Dr. A.A. Wilkinson Memorial Health Centre)	3,783	2,665	6,448
	Grand Bank (Grand Bank Community Health Centre)	4,322	6,978	11,300
	St. Lawrence (US Memorial Health Centre)	2,982	3,195	6,177
Central Health	New-Wes-Valley (Brookfield/Bonnews Health Care Centre)	3,107	4,378	7,485
	Botwood (Dr. Hugh Twomey Health Centre)	22,220	1,332	23,552
	Fogo Island (Fogo Island Health Centre)	2,380	257	2,637
	Lewisporte (North Haven Manor)	7,834	13,128	20,962
	Twillingate (Notre Dame Bay Memorial Health Centre)	5,105	2,391	7,496
	Springdale (Green Bay Health Centre)	4,629	2,969	7,598
	Baie Verte (Baie Verte Peninsula Health Centre)	2,620	3,029	5,649
	Buchans (A.M. Guy Memorial Health Centre)	775	99	874
Western Health	Harbour Breton (Connaigre Peninsula Health Centre)	1,711	1,250	2,961
	Norris Point (Bonne Bay Health Centre)	1,803	7,812	9,615
	Burgeo (Calder Health Centre)	1,464	0	1,464
	Channel-Port aux Basques (Dr. Charles L. LeGrow Health Centre)	6,288	2,092	8,380
Community Clinics in Labrador	Port Saunders (Rufus Guinchard Health Centre)	2,151	2,073	4,224
Community Clinics in Labrador		Population (2011)		
Nain	1,190	0	1,190	
Hopedale	555	0	555	
Natuashish	930	0	930	
Makkovik	360	0	360	
Postville	205	0	205	
Rigolet	305	0	305	
Black Tickle	170	0	170	
Cartwright	515	0	515	
St. Lewis	205	0	205	
Port Hope Simpson	440	0	440	
Mary's Harbour	385	0	385	
Labrador-Grenfell Health	Charlottetown	480*	0	480*
	Sheshatshui	1,276**	0	1,276**
	Churchill Falls	635	0	635

* 2006 Census Data; **2009 Indian Register Population for Atlantic First Nations

Health system administrators in Newfoundland and Labrador prioritize equitable access to health services but cannot afford the costs of maintaining around-the-clock labs for all emergency departments in the province. Attending physicians in Category B emergency departments are faced with a problematic situation when they see patients at night or on the weekends who present with conditions that require lab testing. If lab staff cannot be called back and a potential medical emergency is suspected, physicians must make patient management decisions with incomplete information. Physicians may wait until lab staff is available: they can admit patients overnight or send them back home. They may refer patients to the nearest hospital with an operating lab; however, referrals are often not convenient for patients living in rural areas, since it can mean driving more than an hour away and a significant number of these patients are older.

About Point-of-Care Tests

A point-of-care test (POCT), also known as a bedside test, is a type of portable technology that allows a medical test to be administered, analyzed, and read where the patient is located and without having to send a sample to a lab. These tests can be used in hospital departments, health clinics or ambulatory care settings. Administering POCT in Canada requires appropriate accreditation (10). The major appeal of point-of-care tests is that they can be administered and read by people who are not lab technicians to provide quick test results at the patient's bedside.

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POCTs typically analyze a specimen (e.g., blood or urine) for a specific component like a protein, metabolite or other small molecule (11). These components are referred to as biomarkers or analytes. POCT have been developed to detect a broad range of analytes. The POCT device may measure a single analyte, e.g., blood glucose meters, or it may be designed to measure multiple analytes from a single specimen using a single 'test panel,' e.g., a liver function panel that can measure seven or more biochemical constituents.

The interpretation of POCT results depends on the device. Qualitative POCT involve reading a test strip for a binary or ordinal outcome, e.g., positive/negative or strong/moderate/weak. Quantitative POCT produce a unit-based measurement that can be compared to other test results (12–14). Typically, the point-of-care test evolves to become quantitative as it develops higher sensitivity to detect low levels of the target analyte. POCT design is also advancing to the measurement of multiple analytes in one test panel, including cardiac, cancer and infectious disease panels (11).

All provinces in Canada now require accreditation of both central lab and point-of-care testing. Newfoundland and Labrador adopted an accreditation framework for medical testing based on the Ontario accreditation system in 2010. Prior to 2010, the province did not have an accreditation framework for biomedical testing. Many hospital emergency departments may have implemented a

range of POCTs, the most common being glucometers and urinalysis dipsticks. At present, all central labs in the province are accredited for a broad range of medical tests, while accreditation for POCT has been deferred until 2015. This means that, at time of writing, no POCTs except glucometers have been implemented in emergency departments in the province.

Regulatory agencies and professional bodies (e.g., the Medicines and Healthcare Products Regulatory Agency in the UK and the National Academy of Clinical Biochemistry in the US) have published guidelines and best practices to assist in the implementation of POCT. They identify the following potential advantages for POCT (13, 14):

- Turnaround time for test results is reduced;
- The need for clinical invasiveness is reduced due to smaller sample volumes;
- Access is increased to testing procedures in remote areas;
- Access to lab testing outside regular lab hours is increased, and that improves service accessibility to at-risk groups;
- Costs are reduced by triaging patients at points of clinical contact, reducing the length of stay, reducing the number of clinic visits and the number of admissions;
- Monitoring is facilitated for those conditions that need frequent testing.

At the same time, research on POCT in general has shown that there are also risks, since POCT can be unreliable, ineffective and/or cost ineffective if the following conditions are present (15):

- The clinical site has a history of poor compliance with quality control and quality assurance;
- The clinical site does not have the capability to perform the POCT and/or the ability to comply with regulatory guidelines;
- A central lab can provide adequate turnaround time compared to POCT;
- The POCT device has poor analytic or test performance;
- The POCT device is prone to instrument malfunction or operator error;
- The POCT is too expensive as compared to alternatives;
- The POCT is not medically necessary or will not improve operational efficiency of clinical services;
- The POCT is used for off-label applications, e.g., using glucose meters for the diagnosis of diabetes mellitus.

ACS and Troponin POCT

Acute coronary syndrome (ACS) refers to the clinical symptoms consistent with acute myocardial ischemia, the situation in which the heart muscle does not receive enough oxygenated blood. ACS includes three clinical conditions: unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI). Unstable angina and NSTEMI are closely related conditions: their pathophysiologic origins and clinical presentations are similar, but they differ in severity. A diagnosis of NSTEMI can be made when the ischemia is sufficiently severe to cause myocardial damage resulting in the release of cardiac troponin. In contrast, the patient is considered to have experienced UA if troponin cannot be detected in the bloodstream hours after the initial onset of

ischemic chest pain. White blood clots are found exclusively in patients with UA/NSTEMI, while STEMI patients have both red and white blood clots.

The differences in the underlying pathophysiology of UA/NSTEMI and STEMI call for different approaches and therapeutic goals. In UA/NSTEMI, the goal of antithrombotic therapy is to prevent further thrombosis and to allow endogenous fibrinolysis to dissolve the thrombus and reduce the degree of coronary stenosis; revascularization is frequently used to increase blood flow and prevent re-occlusion or recurrent ischemia. In contrast, in STEMI, the infarct-related artery is usually totally occluded, and immediate pharmacological or catheter-based reperfusion is the initial approach, with the goal of obtaining normal coronary blood flow.

Patients presenting with chest pain who are suspected of ACS represent the largest group of individuals who are admitted to hospital from emergency departments in the UK (17). An estimated 300,000 to

500,000 Canadians present to emergency departments with chest pain annually (19). Of these patients, an estimated 15%-25% receive a diagnosis of ACS while 2%-5% are misdiagnosed as having a less urgent condition and discharged (19,20). Patients presenting with ACS require rapid and accurate evaluation in the emergency room (21). For patients suspected of having ACS, faster assessment and correct classification of risk means a greater chance of limiting heart damage and maintaining cardiac function.

For patients suspected of having acute coronary syndrome, faster assessment and correct classification of risk means a greater chance of limiting heart damage and maintaining cardiac function.

Identifying ACS can be complex and time sensitive (22). Physicians face several significant challenges in assessing a patient with chest pain and suspected ACS. First, they must correctly identify those at high risk for a heart attack as distinct from those at low risk; and, second, they must ensure that patients at high risk are held at the hospital and treated appropriately while low risk patients are discharged. According to the National Academy of Clinical Biochemistry Lab

Medicine Practice Guideline (LMPG) for POCT, 2-5% of patients with acute myocardial ischemia are inappropriately discharged from the ED (14). Reportedly, this type of inappropriate discharge is the leading cause of malpractice lawsuits against ED physicians in the United States (14).

Assessing risk for ACS is based on patient history, clinical features, electrocardiogram (ECG) features and results from lab tests (16–18,23,24). Risk scores are used to predict the prognosis of the syndrome and to assist in determining the clinical course of action that will be taken. Most risk-stratification systems categorize patients into low, intermediate and high risk groups. Patients diagnosed with STEMI are always high risk, while those diagnosed with unstable angina are typically low risk. Patients diagnosed with NSTEMI can score anywhere within the range of risk scores, making them the most challenging of patients presenting with potential ACS.

Although several risk-scoring systems have been developed, all have been shown to have some limitations (17,25). In cases of suspected ACS, not all patients show the characteristic ECG changes required for a clinical diagnosis of acute myocardial ischemia. For example, patients without ECG abnormalities but with symptoms of restricted blood flow to the heart could be experiencing NSTEMI or

UA. This makes the use of biomarkers even more critical as an assessment measure for heart attack (3,23).

Cardiac troponins are considered the gold standard for diagnosing acute myocardial ischemia because they are a reliable indicator of heart damage.

To date, the most important cardiac biomarker for assessing risk in ACS is troponin. Troponin comprises a complex of three regulatory proteins (troponin C, troponin I and troponin T) that interact to control the calcium-mediated interaction of actin and myosin that causes the contraction of striated muscle (i.e., skeletal and cardiac muscle). Unlike troponin C, the other two proteins, troponin I and T, take a unique form in cardiac muscle and are known as cardiac troponin I (cTnI) and cardiac troponin T (cTnT). When heart muscle cells have been damaged, cTnI and cTnT are released into the blood. The levels of these two proteins are measured to indicate the severity of damage that has occurred. Elevated levels typically indicate more severe damage (2).

Cardiac troponins are considered the gold standard for diagnosing acute myocardial ischemia because they are a reliable indicator of heart damage (3,18). Troponin POCT has the potential to expedite the time to treatment in the ED by distinguishing low-risk patients from high-risk patients. Troponin POCT is administered at the patient's bedside, reducing the amount of time spent in the collection, transportation and processing involved in the more traditional central lab testing (21,26). Troponin POCT has become increasingly sensitive as the role of cardiac troponins in cardiac damage has become better understood and the technologies behind troponin POCT devices have improved³.

What we looked for

Searching for the Evidence

The CHRSP methodology synthesizes research-based evidence from the systematic review literature, which includes systematic reviews, health technology assessments (HTAs) and meta-analyses. Recent, high-quality primary research studies that have not yet been captured by the systematic review literature are also included in the synthesis. We identified evidence by searching periodical indexes of published articles as well as databases of grey literature (i.e., not commercially published reports).⁴ The selection criteria for inclusion in the synthesis are summarized in Table 2 below.

Article selection was carried out by two members of the CHRSP staff, with discrepancies resolved through discussion and, if needed, consultation with the Scientific Team Leader.

³ See Online Companion Document, Performance Measurement for Troponin POCT, for more details.

⁴ See Online Companion Document, Project Search Methods, for more details.

Table 2: PICOS and article eligibility criteria

Parameter	Eligibility	Criteria
Population	Include	Study population is presenting with potential ACS, adult, human
	Exclude	Study population has already been diagnosed with ACS or ACS has been previously ruled out
Intervention	Include	Troponin POCT for suspected ACS is one of the interventions, or the only one, that is studied in a real-world setting
	Exclude	Laboratory or real-world setting to determine diagnostic accuracy of troponin for ACS
Comparator	Include	All comparators are eligible for inclusion
Outcome	Include	All outcomes are eligible for inclusion
Setting	Include	Emergency departments, intensive care units, or any other health care facilities that see emergency cases or patients presenting with potential ACS
	Exclude	Emergency medical service settings involved in the transportation of patients, including ambulances and medevac services.
Article	Include	Any publication with a systematic review or recent randomized controlled trial not captured in the systematic review literature, or any health economic primary research article/report. Any article/report published between 2003 and 2013 in any language.
	Exclude	Any article/report that is a duplicate, based on a more detailed study that is already included in the synthesis.

We included five systematic reviews that synthesized evidence from a total of 150 individual primary research studies. The systematic review literature had virtually no overlap in terms of the primary research that was synthesized, since 99.9% of the primary research studies were cited by only one systematic review. We included eight primary research studies that were not captured by any of the included systematic reviews. In addition to these articles and reports, we included seven health economics research articles and reports that studied troponin POCT.⁵

Table 3: Summary of included studies

Systematic Review Literature		
Study	AMSTAR	Study Type
CADTH Optimal Use Report, 2012	73%	Health Technology Assessment
Lin, 2012	55%	Systematic Review
CADTH, 2012	45%	Review of Systematic Reviews
Storrow, 2009	45%	Systematic Review
Craig, 2004	36%	Health Technology Assessment
Primary Research Literature (health economic evidence not included)		
Study	Downs & Black	Study type
Collinson, 2013	89%	Point-of-care Arm of a Prospective Randomised Controlled Trial
Renaud, 2008	89%	Open-label, Randomized Single Center Trial
Goodacre, 2011	82%	Pragmatic Multicentre Randomised Controlled Trial
Bradburn, 2012	75%	Pragmatic Multicenter Randomised Controlled Trial
Loten, 2009	75%	Clustered Randomised Controlled Trial
Collinson, 2011	75%	Prospective Randomized Trial
Ryan, 2009	71%	Multicentre, Randomized Parallel Group Trial
Morgensen, 2011	54%	Randomised Clinical Trial

⁵ See Online Companion Document, Project Search Results, for more details.

Assessing the Evidence

For clinical outcomes and emergency department process outcomes, two CHRSP staff worked with the Project Team Scientific Leader to synthesize the evidence from:

- two systematic reviews, Lin et al., 2012 and Storrow et al., 2009 (27,28);
- two HTAs, CADTH, 2012-2013 and Craig et al., 2004 (29–32); and
- one review of systematic reviews, CADTH, 2012 (33).

For health economics outcomes, the CHRSP Project Team's Health Economist assessed the articles, extracted the data and synthesized the evidence.

Two CHRSP staff critically appraised the methodology of the included systematic review literature using the Assessment of Multiple Systematic Reviews (AMSTAR) which is an experimentally-validated instrument (1).⁶ It is important to point out that a low AMSTAR score does not necessarily mean that the review should be discarded; rather, a low score indicates that less confidence should be placed in the review's findings and that the review must be examined closely to identify its strengths and limitations.

Primary research literature was appraised using the Downs and Black tool (5). This appraisal tool provides a checklist to draw attention to a paper's methodological strengths and weaknesses and is appropriate for randomised controlled trials as well as non-randomised studies or observational studies.⁷ See Table 3 above for critical appraisal scores.

Discrepancies in scoring were resolved through discussion and, if required, through consultation with the Project Team Scientific Leader (NPP). The inter-rater reliability (IRR) was measured with Cohen's Kappa⁸: 0.87 (95 CI: 0.97, 0.77) for AMSTAR and 0.75 (95 CI: 0.89, 0.61) for the Downs and Black. Both these scores are considered to indicate "excellent inter-rater reliability" (34).

Data Extraction, Synthesis and Contextualization

For all but the health economic evidence, one CHRSP staff extracted the data from the included systematic reviews and primary research studies, while another CHRSP staff reviewed the work. Any disagreements identified upon review of the extracted data were discussed and resolved through discussion between the extractor and the reviewer. Any remaining discrepancies were resolved through consultation with the Project Scientific Leader. We extracted review findings from the systematic review literature, which we define as *a conclusion that is based on a combination of primary research evidence*. We extracted basic findings from the primary research literature that supplemented the review findings. The health economic evidence was sent to the Project Health Economist who extracted the data and conducted his own analysis.

⁶ See Online Companion Document, Critical Appraisal, for more details.

⁷ See Online Companion Document, Critical Appraisal, for more details.

⁸ Cohen's Kappa ranges from -1 to 1: 1 indicates complete agreement between raters; 0 is the level of agreement that would be expected if the ratings were selected at random; and -1 indicates complete inverse agreement between raters.

The results of the data extraction were grouped into different outcome categories, e.g., diagnostic accuracy and patient satisfaction, and formed the basis for the synthesis in this report.⁹ A draft of the report was prepared by the Project Scientific Lead, the Project Health Economist and two CHRSP staff. The draft was then reviewed by the Project Team which was consulted on the contextualization of the findings. External consultants were also contacted for additional contextualization.

What we found

Overview of the Evidence

Point-of-care testing, in general, has been available since the early 1990s and is, at present, a rapidly developing field of medical research. Research-based evidence for POCT, in general, reflects ongoing advances in instrumentation, especially with increasing abilities in the detection of target biomarkers (35). Significant improvements in POCT may not be captured by the most recent review literature as it takes years to publish high-quality systematic reviews and meta-analyses.

In the case of cardiac troponin POCT products in particular, there has been a rapid improvement in testing threshold sensitivity. New technologies are able to detect cardiac troponin with continually lower detection thresholds and more accurate detection capabilities resulting in a heterogeneous and changing state of POCT research protocols. Authors have noted the challenges in finding comparable studies for cardiac troponin POCT meta-analyses (27,28,32,33,36). As a result, there are fewer systematic reviews than would be expected, despite the availability of considerable primary research.

Table 4: Summary of design characteristics of included studies

Systematic Reviews	Population	Settings	Time Frame
CADTH Optimal Use Report, 2012	Average: 702.22 Range: 94-1452	EDs or Chest pain units Germany, New Zealand, United States, Canada, UK, France, Sweden.	Studies published between 2009-2012
Lin, 2012	Average/Range: Not available	Not available	Studies published between 2004-2010
CADTH, 2012 Apr	Average/Range: No studies on Troponin found	No studies on Troponin found	No studies on Troponin found
Storrow, 2009	Average: 540 Range: 33-2000	Single ED to Multicentre	Studies published between 2001-2008
Craig, 2004	Average/Range: No SR, MA or HTA found. Details of other studies reviewed not identified.	No SR, MA or HTA found. Details of other studies reviewed not identified.	No SR, MA or HTA found. Details of other studies reviewed not identified.

NB: Average and Range refer to the sample sizes of the included studies.

⁹ See Online Companion Document, Data Extraction Results of Included Studies, for more details.

RCTs	Population	Settings	Time Frame
Collinson, 2013	2263 (2243) POCT =1132 (1125) Non POCT= 1131(1118)	6 EDs	30 January 2007 and June 2008
Renaud, 2008	860 POCT= 428 CHLT=432	Single ED	November 2002 – April 2004
Goodacre, 2011	2243 POCT=1125 Standard Care=1118	6 EDs	January 30, 2007 – June 2, 2008
Bradburn, 2012	2243 Range= 327-469 per ED	6 EDs	January 30, 2007 – June 2, 2008
Loten, 2009	1194 POCT=467 Lab Test=445	2 EDs Eastern Australia John Hunter Hospital Belmont Hospital	November 2007 to January 2008
Collinson, 2011	2263 recruited POCT=1125 Non POCT=1131	6 EDs	30 January 2007 and 2 June 2008
Ryan, 2009	2134 recruited Range – 348-602 per site POCT =1000 Central Lab= 1000	4 EDs in the US	Between December 2004 and November 2006,
Morgensen, 2011	239 POCT= 109 Central Lab = 120	ED Kolding Sygehus, Denmark	October-November 2009 & February 2010 – April 2010

Several key issues have been highlighted in these reviews of troponin testing. The Canadian Agency for Drugs and Technologies (CADTH) in Canada has addressed the problem of a lack of review literature in several of its reports. CADTH has used a variety of reporting forms to investigate cardiac troponin POCT between 2007 and 2013. Report types range in comprehensiveness from Rapid Response Reports (these are essentially reference lists) to HTA-style Health Technology Inquiry Service reports. CADTH found the lack of review literature on this topic to result from: narrowly defined research questions; primary research protocols with diverse study designs, outcome measurements or endpoints; and limited timeframes when searching for evidence (27–32,36–38). CADTH’s Optimal Use Report also identified a general lack of economic evaluation of cardiac troponin testing, which was one of the main motivations for their report (29–31).

Some of our included studies had weaknesses in experimental design that could have introduced bias into the reported results. The study by Goodacre et al. (2011) was not sufficiently powered to detect potentially important differences in rates of adverse events (39), while the sample size in the study by Morgensen et al. (2011) lacked adequate power to detect anything but very large effect sizes (40). Lack of double blinding in the Bradburn et al. (2011) and Ryan et al. (2009) studies may have contributed to observer effects (41,42). Authors in both the Collinson et al. (2013) (p. 35, 64) and Renaud et al. (2008) (p. 222) indicated that there was the potential for selection bias in their studies (17,23). We did not identify any attrition bias, reporting bias or potential performance bias (affecting delivery intervention because of a lack of single blinding).

Test Performance

Test Performance refers to the ability of a test to differentiate between normal/healthy and abnormal/unhealthy states. It is the first and most important outcome category when considering the effectiveness of a medical test. In the context of this project, test performance refers to the ability of a cardiac troponin POCT to correctly distinguish patients who are positive for Acute Coronary Syndrome (ACS) from patients who present with similar clinical symptoms but who are negative for ACS. POCT results are compared against a “gold standard test,” which, in this case, would be cardiac troponin tested by a central laboratory.

Figure 3: Test performance matrix

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

* Sensitivity is more important than specificity when testing the performance of screening tests such as cardiac troponin POCT.

Test performance is measured by ratios that combine the different test outcome groups: true positives, false positives, true negatives and false negatives.

- **Sensitivity** is the ratio of true positives to all real positives.
- **Specificity** is the ratio of true negatives to all real negatives.¹⁰

Different medical tests make a trade-off between sensitivity and specificity, depending on their purpose:

- **Screening tests** determine whether a patient should be further studied or discharged. These tests prioritize sensitivity over specificity to increase the likelihood of detecting patients with the condition at the expense of false positives (patients without the condition that test positive);
- **Diagnostic tests** determine if a patient will receive a treatment. They prioritize specificity over sensitivity to rule out patients without the condition at the expense of false negatives.

Cardiac troponin POCT is considered a screening test: sensitivity is of greater importance than specificity.

¹⁰ See Online Companion Document, Performance Measurement for Troponin POCT, for more details.

Table 5: Sensitivity and specificity ranges for different cardiac troponin POCT products

Study	Analyzer	Setting	Sensitivity	Specificity	Notes
Collinson, 2013 (17)	Stratus CS	Admission, N=831	0.803 (0.687 to 0.891)	0.979 (0.966 to 0.988)	cTnI: detection limit 0.03 µg/l, analytical range 0.03–50 µg/l, interassay CV 4.0–8.2% (0.067–0.344 µg/l), the 99th percentile of the assay is 0.07 µg/l
	Stratus CS	Peak value, N=833	0.955 (0.875 to 0.991)	0.969 (0.954 to 0.980)	
CADTH Optimal Use Report, 2012 (16)	Roche Elecsys, Hs-cTnT	N=1,098	0.91 (0.87 to 0.94)	0.81 (0.80 to 0.82)	0.014 (99th percentile)
Collinson, 2011 (43)	Stratus CS cTnI	Admission N=1,074	0.845 (0.750 to 0.915)	0.976 (0.964 to 0.984)	cTnI detection limit 0.03 mg/l, analytical range 0.03e50 mg/l, inter-assay coefficient of variation (CV) 4.0e8.2% (0.067e0.344 mg/l).
	Stratus CS cTnI	90 min N=844	0.941 (0.713 to 0.999)	0.984 (0.973 to 0.992)	
	Stratus CS cTnI	Peak value plus change, N=1,078	0.976 (0.918 to 0.997)	0.963 (0.949 to 0.974)	The 99th percentile of the assay is 0.07 mg/l.
Takhshid, 2010 (44)	Vidas	Admission N = 123	42% (28%-55%)	100% (92%-100%)	Limit of detection <0.01 µg/l; 10% total imprecision concentration determined over 20 days using 2 kit lots and 2 calibrations per lot in 3 systems was 0.11 µg/l; and total imprecision (n=244) for quality control materials with concentrations at 0.58 µg/l were 3.3% and 3.4% respectively. A cTnI value ≥0.01 µg/l was suggestive of AMI <i>Findings not established by the authors, but by the manufacturer.</i>
Meek, 2012 (45)	Biosite	Admission N=248	92.6% (74.2-98.7)	98.7% (95.9-99.7)	For cTnI: limit of detection 0.05 ng/mL and 99th percentile 0.05 ng/mL
Stengaard 2013 (46)	Cobas h232	Admission (ambulance) N = 990	39 (32 -46)	95 (94-97)	Not reported
Wu, 2004 (47)	RAMP	Admission N = 365	90 (80 – 99)	86 (78 – 94)	The lower limit of detection was 0.03 ng/ml (10% coefficient of variance [CV] = 0.21 ng/ml) for cTnI The upper reference limit (normal range) was < 0.03 ng/ml for cTnI
Apple, 2004 (48)	I-Stat	Admission N = 186	Not reported	Not reported	Total imprecision (CV) of 10% and 20% were seen at 0.09 and 0.07 µg/l, respectively. The detection limit was 0.02 µg/l. The 99th percentile reference limit was 0.08 g/l.
Apple, 2009 (35)	PathFast	Not reported	Not reported	Not reported	99th percentile µg/L = 0.029 10% CV, µg/L = 0.014 <i>Based on manufacturer claims.</i>

The Health Technology Assessment by Craig et al. (2004) compared cardiac troponin POCT to traditional lab testing. This very comprehensive HTA is synthesized primary research from prior to 2002. At the time of writing, troponin POCT devices existed in both qualitative and quantitative designs. The Craig et al. HTA found that troponin POCT and central lab testing techniques differed significantly in terms of quality control. Most of the devices at that time, for either quantitative or qualitative design, did not meet the established criterion that has become the standard for POCT, i.e., detection of the biomarker with no greater than 10% coefficient of variation (CV) at the 99th percentile of the biomarker distribution for a reference population (see Online Companion Document for more details) (32). Unfortunately, as troponin assays became more sensitive and could measure at lower concentrations, many of these newer troponin assays could not achieve a 10% CV at the 99th percentile.

However, as described in the previous section, the development of cardiac troponin POCT technologies has been continuous and significant (see Table 5 above). Storrow et al. (2009) observe that POCT in general, and cardiac troponin POCT in particular, have “dramatically improved” in accuracy over the past decade (28). Recent primary research has demonstrated that, *as a screening test*, cardiac troponin POCT is a comparable and reliable alternative to lab testing:

- One primary study compared POCT for cardiac troponin and two additional cardiac analytes to a local lab protocol for cardiac troponin and found that POCT for “[cardiac] troponin alone is sufficient for early diagnosis and exclusion of AMI and can be reliably measured by point-of care testing within [two hours] if the method can define the 99th percentile” (43)
- Further analysis of the same POCT data by Collinson and colleagues published in 2013 found that measurements of cardiac troponin taken on admission and then again at 90 minutes enabled a low risk group of patients to be successfully discharged (17).

The main development in cardiac troponin POCT design is the ability to detect ever lower concentrations of the analyte in blood samples. A new class of cardiac troponin POCT is called the high sensitivity assay. There is some independent research-based evidence that high sensitivity POCT troponin testing can provide results more quickly (i.e. at lower troponin concentrations than ‘regular’ troponin POCT at comparable levels of accuracy to central lab testing).

In comparing the two tests, CADTH found that high-sensitivity cardiac troponin T (the hs-cTnT POCT) was more accurate than regular cardiac troponin I (cTnI POCT). Using a cut-off point of the 99th percentile values for a reference population, the sensitivity and specificity findings were as follows:

- Sensitivity for the hs-cTnT POCT for diagnosis of AMI were found to be 0.91 (95% CI, 0.87 to 0.94) and specificity was 0.81 (95% CI, 0.80 to 0.82);
- Sensitivity for cTnI POCT was found to be significantly lower (0.62, 95% CI, 0.58 to 0.66), while the specificity was slightly higher (0.96; 95% CI, 0.94 to 0.97) (29–31).

This indicates that hs-cTnT is a better screening test than cTnI.

Recently, Trinity Biotech of Ireland announced that it has received European approval for a high-sensitivity cardiac troponin I point-of-care diagnostic test. FDA approval in the US is pending (49).

Key Message:

In terms of test performance, the sensitivity and specificity of currently available cardiac troponin point-of-care tests are sufficient for their use as screening tests. Cardiac troponin POCT continues to improve at a significant rate and is becoming as accurate as central lab testing.

(Effective Intervention)



Clinical Health Outcomes

Clinical health outcomes are related to the patient's health after a cardiac troponin POCT in an emergency department setting. Such outcomes would include subsequent adverse cardiovascular-related events and readmission to hospital. Although the available evidence base is neither extensive nor highly-powered, the evidence does indicate that cardiac troponin point-of-care tests provide similar clinical health outcomes to those of central lab testing.

Goodacre et al. (2011) found a very low adverse cardiovascular-related event rate for patients who received troponin POCT (1/5) and no significant difference in adverse events between the POCT patients and control groups (39). Among patients who were discharged, only one out of the five adverse events under study occurred within one month of recruitment. In contrast, four out of five adverse events occurred among patients who were admitted to hospital (i.e., who were correctly identified as being at high risk.) As a note of caution, the authors indicated that the trial was not sufficiently powered to generalize these differences.

Collinson et al. (2011) reported that, compared to patients who were tested by the central lab, POCT did not increase major adverse coronary events including death, readmission or the need for revascularization within three months of the test. In 2013, Collinson et al. concluded that there was no difference in adverse events between patients tested with POCT and those tested via 'conventional management' (17,43).

CADTH's Optimal Use Report sought to find evidence on the effects of cTn tests on readmission rates; however, these were not reported in any of the included studies (29–31).

Key Message:

In terms of clinical outcomes, cardiac troponin POCT does not appear to increase the risk of adverse cardiac-related events or readmission rates compared to central lab testing for patients seen in emergency departments.

(Promising Intervention)



Emergency Department Process Outcomes

This category of outcomes measures the efficiency of POCT in an emergency department setting. To make these measurements, efficiency variables are grouped together to help ascertain the resources required to achieve a given outcome. For this project, the evidence on emergency department process outcomes, or efficiency, was mainly limited to studies that looked at the length of time taken for patients to achieve a particular endpoint. The range of possible endpoints, combined with the variability in definitions for each endpoint produces a great deal of heterogeneity among primary research study results. This, in turn, makes it challenging for systematic review studies to synthesize the available evidence.

Following are some of the emergency department process outcomes of concern to decision makers when considering cardiac troponin point-of-care testing.

Turnaround Time

Turnaround time (TAT) is the time elapsed between taking a blood sample from a patient and reporting the results of that sample. The most consistent and important synthesis finding in this project is that cardiac troponin POCT significantly reduces TAT compared to lab testing (28,42). Ryan et al. (2009) found that central lab testing for cardiac troponin took an average of 58 minutes (IQR 44 to 81 minutes) compared to 15 minutes (IQR 11 to 23 minutes) for POCT. Storrow and colleagues state unequivocally that “improvements in TAT are nearly universal” (28).

Key Message:

When compared to central lab testing, emergency department cardiac troponin point-of-care tests significantly and consistently reduce turnaround time for test results.

(Effective Intervention)



Time to Decision, Time to Disposition, Time to Treatment, Time to Transfer

These outcomes include measures of the time elapsed between the arrival of the patient at the care facility and a key decision being made or an action being taken. Beginning from various starting points (including the time the patient registered at the emergency department or the time the triage result was recorded), these outcomes include:

- **Time to Decision:** the elapsed time until a clinical decision is recorded about the treatment plan;
- **Time to Disposition:** the elapsed time until the decision to admit or discharge the patient is recorded;
- **Time to Treatment:** the elapsed time until a treatment is administered; and
- **Time to Transfer:** the elapsed time until a patient is transferred to another unit for care.

It is logical to assume that the consistent and significant improvement in turn-around time for the cardiac troponin POCT (as noted above) would have a subsequent effect on improving these time outcomes.

Some evidence does support this assumption. For example, Renaud found that the Time to Decision/clinical decision making process was shorter when POCT was used, as compared to using a central lab test. In a subset of patients suspected of being high-risk and having NSTEMI, POCT shortened the time to anti-ischemic therapy (TAIT) by nearly 40%. The median TAIT for POCT was 151 min (IQR =139-162 min) compared 198 min for central lab testing (IQR 187-210 min). An important corollary to this finding was that patients with vague symptoms were diagnosed sooner (23).

However, the available evidence on Time to Decision is not consistent. CADTH's Optimal Use Report could not find any eligible evidence to support a claim of improved Time to Decision: "No description related to ED times between the performance of cardiac troponin [POCT] tests and the diagnosis of MI or ACS was found in the included studies" p23 (29).

Furthermore, Storrow et al. (2009) could not confirm reduced Time to Treatment after a cardiac troponin POCT, but stated that the data suggested improvements in this area were possible (28).

These findings imply that factors other than test turnaround time influence the amount of time it takes to decide on the course of action for patients suspected of ACS and then to act on that decision. The effectiveness of POCT for improving these time outcomes appears to be mediated by those factors.

Length of Stay/Time to Discharge

Length of Stay (LOS) and Time to Discharge are outcomes that measure the overall elapsed time for a patient's visit to the emergency department. As with the time outcome measures described above, although the evidence consistently indicates that cardiac troponin POCT reduces turnaround time, this improvement does not necessarily result in consistent improvements in measures of the overall elapsed time spent in the emergency department:

- The systematic review by Storrow et al. could not find consistent improvements in LOS or Time to Discharge between POCT and central lab cardiac troponin testing (28).
- The RATPAC study found a reduction in the median, but not the mean LOS in the emergency department with troponin POCT compared to central lab testing (39,41).
- Renaud and colleagues found that troponin POCT did not demonstrate a significant difference in emergency department LOS compared to central lab methods (23).
- Loten and colleagues report an improvement of 48 minutes (approximately 10%), which they claim is an underestimate of the true improvement in patient emergency department LOS (50).

One explanation for these conflicting results is that, apart from affecting test turnaround time, cardiac troponin testing methods are not the determining factor for Emergency Department Process Outcomes (Bradburn, 2011; Storrow, 2009; Renaud, 2008, Ryan, 2009). Site-specific variables such as the individual facilities themselves, local protocols, existing and implemented guidelines for ACS and related symptoms, existing POCT and central lab cardiac troponin tests and staffing variables, appear to explain "the variation in outcomes and costs" (41). Renaud and colleagues cite the need for a whole-system approach to maximize timeliness of care (23). Ryan and colleagues (2009) also found the same, concluding:

Although our findings suggest that at some institutions point-of-care testing makes a difference, there is still a wide range of effects... 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.(42)

Key Message:

Cardiac troponin POCT appears to have the capacity to reduce emergency department process time outcomes compared to central lab testing, but it cannot achieve those outcomes by itself. Other site-specific variables appear to have an equal or greater impact on those outcomes. Point-of-care testing must be considered in the full context of emergency department operations for improvements in patient throughput to be truly quantified.



Cardiac Troponin POCT in Small Hospitals

The evidence reviewed so far compares testing with cardiac troponin POCT to testing carried out in open and operating central labs. In Newfoundland and Labrador, many facilities do not have access to 24/7 open and operating central lab services at the time when the troponin test is needed; therefore, a more meaningful comparison might be between the effects of POCT on test performance, clinical health outcomes and emergency department process outcomes when compared to call-back or no central lab testing whatsoever.

Little current research makes this direct comparison. However, we located one primary research study by Loten and colleagues that does include this assessment. In their multi-site RCT studying emergency department cardiac troponin POCT on length of stay, they included one facility that did not have a 24/7 central lab. Not surprisingly, they found that POCT had the greatest impact at that particular facility: “[a]s expected, the difference [LOS] 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***” (emphasis added). This study clearly indicates that those sites where central lab facilities are not available 24 hours a day could see the greatest improvements in terms of emergency department process outcomes such as length of stay (50).

Key Message:

Point-of-care testing has the greatest impact on emergency department process outcomes in facilities without a 24/7 central lab service.



Health Economic Evidence

Overview of the Health Economic Evidence

The health economic evidence for cardiac POCT in the emergency department is based on nine articles (see Table 7 below). Among those, six present the findings of economic analyses (cost minimization or cost-per-unit of outcome) comparing a bedside (POCT) strategy to a central (hospital or reference) lab strategy (32,41,51–54).

Three articles offer separate descriptive analyses of the costs and some of the benefits of POCT relative to standard assessment without making any attempt to calculate a cost-efficiency ratio (55–57). However, these documents do shed light on some of the issues discussed in the economic analyses (56,57) or provide point estimates of prices in one setting (32,55).¹¹

The following four studies describe a comparison between POCT and central lab testing within the same hospital:

- Craig et al. the HTA for the NHS in Scotland;
- Fitzgerald et al. for a study of the RATPAC trial in the UK
- Bradburn et al. for a study of the RATPAC trial in the UK
- Birkhahn et al. for a non-blinded RCT in one institution in the US) (32,41,51,53)

Craig et al. conducted a cost-minimization analysis asking whether, even though the average cost of one bedside test is higher, decreased costs from reduced turnaround times offset the difference in administration costs between the two strategies. Bradburn et al., Birkhahn et al. and Fitzgerald et al. run cost-utility analyses, with patient-hours saved (41,51) and QALY (53) as their outcome measures.

Table 6: Summary of included and excluded health economic evidence

Included Studies: Health Economic Evidence			
Citation	Source	Type	Measure
Birkhahn et al, 2011	CRD	POCT vs CL, cost-utility	Patient hours (time in ED)
Blattner et al, 2010	EMB	POCT vs no lab, cost-effectiveness	Cost benefits
Bradburn et al, 2012	CRD	POCT vs CL, cost-utility	Patient hours (discharge)
Craig et al, 2004	GLS	BS vs CL, cost-minimization	Multiple
Fitzgerald et al, 2011	CRD	POCT vs CL, cost-utility	QALY
Fitzgibbon et al, 2010	CIN	Survey of devices	Comparison of device price
Hortin, 2005	GS	Multiple cost perspectives of POCT	Costs per treatment
Lewandrowski, 2009	EMB	General comment	n/a
Van Dyck et al, 2012	CRD	Micro-simulation, cost-utility	QALY

¹¹ Craig et al., 2004 also provides a point estimate of prices in the Scottish NHS.

Table 6 continued...

Excluded Studies		
Citation	Source	Reason for Exclusion
Amsterdam et al, 2010	EMB	No economic evidence
Asassi et al., CADTH, 2013	GLS	Not POCT vs Central Lab
CADTH, 2012a	CRD	No studies measured cost
CADTH, 2012b	GLS	No economic evidence
CIMON/CADTH, 2007	GLS	No economic evidence
Collinson et al, 2013	GLS	Not POCT vs Central Lab
Goodacre et al, 2013	GS	Not POCT vs Central Lab
Goodacre, 2010	CIN	Same as Fitzgerald et al. 2011

Source abbreviations: CRD: Centre for Reviews Dissemination Database; EMB: Embase Biomedical Database; GLS: Grey Lit Search (see Online Companion Document); CIN: CINAHL Database; GS: Google Scholar.

The study by Blattner et al. was set in one hospital and one health district in New Zealand. It describes the effect of implementing bedside testing in a remote hospital with no lab facility. The choice prior to POCT availability in this hospital was between clinical assessment only and sending a sample to the nearest hospital, situated at a driving distance of two hours. POCT allowed emergency department physicians to enhance their diagnosis, disposition planning, and treatment decisions relative to clinical assessment alone and this has consequences on patient-care costs (i.e., fewer unnecessary admissions). POCT was more expensive than clinical assessment alone, but the aim of the cost-effectiveness study (cost-minimization) was to measure patient-care expenditures saved against the cost of implementing POCT in the remote hospital (52).

Lastly, Van Dyck et al. carried out a micro-simulation of the treatment chain of patients with chest pain. Patients could either go to the emergency department and receive standard care or visit a primary care physician equipped with POCT. The primary care physician could:

- diagnose the patient as having stable angina and prescribe appropriate medication;
- diagnose the patient as being free from ACS; or
- diagnose the patient as having unstable angina or AMI and refer them to an emergency department.

The study was run as a cost-utility analysis, with QALY as their outcome measure (54).

Overall Costs of ED Cardiac Troponin POCT

The main reason POCT is more expensive than central lab testing is the increased cost of the reagent slides or cartridges for POCT compared to the lower cost for central laboratory tests. This cost factor is compounded by the fact that each POCT quality control measurement will consume a new slide or cartridge (56,57). A central lab spreads its fixed costs for quality control over more tests, thereby reducing the average cost per test. However, the higher cost of POCT is highly conditional on its degree of connectivity and integration with central electronic management systems. As electronic quality controls (e-QC) are increasingly incorporated into POCT devices, bedside testing is predicted to cost less and eventually approach the same costs as central lab tests (57,58). A secondary reason why POCT has higher costs is that bedside clinicians are not trained to read test results and therefore require training,

whereas lab personnel do not.¹² Craig et al. found that point-of-care tests were 2.5 times more expensive per test than central lab testing in the Scottish NHS before 2004 (32).

A paper by Hortin raises the issue that an important (but unnoticed and unaccounted) source of cost for central lab testing of cardiac troponin is the time spent collecting, reading, and, in the case of central lab testing, sending samples to, waiting for and collecting back results.¹³ The author claims that nurses spend much more time interacting with the central lab than performing the tests themselves at the bedside (56).

Fitzgerald et al. carried out a micro-costing study of 246 patients (124 in the control group and 122 in the POCT group). They estimated an increased emergency department cost for POCT of USD 83 on average per patient compared to standard treatment (2007/08 prices). The increased cost came from greater staff cost (USD 18, 22%), cost for the POCT test itself to the emergency department¹⁴ (USD 60, 72%), and overhead costs to the emergency department (USD 5, 6%). Additional details of their work are included in a supplementary table from their publication, reproduced as Table 7 below. They accounted also for calibration costs of the device (around USD 2,200) and panel costs (USD 32 per panel) but not for the purchasing cost of the device or connectivity costs (53).

Table 7: Detailed unit costs for troponin POCT, Fitzgerald et al. (2011)

Data Supplement 3 Supplementary Table 3: Point-of-care testing unit costs	
Cost component	Cost, £(\$)
Panel costs (includes reagent, machine, and maintenance)	
Based on 1,500 full panels*	20.54 (32.06)
Based on 3,000 full panels*	15.70 (24.51)
Based on 3,000 troponin only panels*	5.70 (8.90)
Calibration and quality control for full panel (per annum)**	1,426 (2,225.78)
Calibration and quality control for troponin only panel (per annum)**	1,397 (2,180.52)

*Costs provided by Hilda Crockett, Marketing Manager Point of Care, Siemens Healthcare Diagnostics
**Based on 5 minute daily systems check, twice weekly 15 minutes quality control check and 5 min per reagent calibration check every 60 days, and Agenda for Change Grade 6 staff members (£29 per hour)

The study also found that, beyond the emergency department, patients in the POCT arm spent more days in intensive care and cardiac care units (difference in cost: USD 208) and had more expensive interventions (difference in cost: USD 90). Patients in the POCT arm were less costly on lab tests and some other items. Overall, patients in the POCT arm cost, on average, USD 320 more than patients in the standard treatment arm (53). This is the only micro-costing study available for ED cardiac troponin POCT.

¹² Although Hortin also seems to indicate that this is mainly the case for qualitative testing; this cost does not apply or apply as much to the cost of quantitative tests like the current forms of troponin POCT (56).

¹³ Rather, most studies assume that the elapsed time between collecting samples and receiving results is the same in the POCT and central lab testing arms, and therefore they do not bother to measure the time difference as a cost.

¹⁴ No cost to the central lab was factored in to the analysis.

Birkhahn et al. do not have any data on the cost of emergency department cardiac troponin POCT compared to standard care. They assume USD 20 per individual POCT (versus USD 7 per test in standard treatment). The paper does not calculate per-patient costs, but rather a cost-per-unit of outcome, in this case patient-hours in the emergency department. The cost per-patient can be inferred from the study as being approximately USD 46, which is less than the cost estimate reported by Fitzgerald et al. (201) from the RATPAC study above (51).

Van Dyck et al. carried out a micro-simulation and used a cost for cardiac troponin POCT of approximately USD 1,120, provided by a survey conducted by the Medicines and Healthcare Products Regulatory Agency in the UK (54). This is a much larger unit estimate than the USD46 used by Birkhahn et al. (51). Van Dyck and colleagues also calculates a net cost of POCT factoring in inpatient care; they estimate additional costs of EUR 480, a figure that is similar to the RATPAC estimate. However, based on the incremental ratios reported in the article (Incremental Net Monetary Cost and Incremental Health Benefit), the difference between POCT costs and standard care should be a savings of EUR 480 (54).

A paper by Blattner et al. reports that the total cost of implementing POCT for six months in a remote hospital in New Zealand is NZD 50,000. This includes a high proportion of fixed costs as well as the individual test materials themselves (52).

Economic Benefits of Cardiac Troponin POCT

The greatest measured benefit so far from cardiac troponin POCT has been in reduced turnaround time (TAT). This may save unnecessary admissions to a medical or cardiologic ward, thereby saving costs to the payer (insurer or patient) and/or better throughput, i.e., allowing the hospital to see more patients.

In the earliest study included in this health economic analysis, Craig et al. found that the main determinant of cost-savings via a reduction in TAT was not related to whether the test was performed at the bedside or in a central lab, but rather whether the central lab operated 24/7 and whether it worked continuously or by batch. A 24/7 continuously functioning central lab was as cost-effective as bedside testing, but a lab working only on weekdays and not after hours was more expensive, and more expensive still if working in batches (GBP 141 more per patient than POCT) (12).

The Craig et al. HTA also found that a two-test cardiac troponin POCT strategy, at presentation and at 10-12 hours, had the potential to reduce costs relative to central lab single-test methods. The two-test strategy reduced costs among patients who were appropriately given medications during the interim (12). However, the cardiac troponin POCT two-test strategy was shown to be more expensive than the lab two-test strategy (12).

Birkhahn et al. found that using cardiac troponin POCT allowed the ED to admit or send patients home more rapidly. As a result, the ED was able to process more patients in a given period of time. On average, using the POCT assay saved 6.5 hours in the ED per patient (two hours due to bedside use and four and a half hours due to the use of myoglobin) (51). Bradburn et al. (based on RATPAC) did not find any clear effect, and concluded that outcomes were highly setting-dependent (41). Blattner et al. found savings from implementing bedside testing in a remote hospital, but the comparator was a situation

where physicians used clinical assessment only (with no biomedical testing at all) and, therefore, hospitalized too often (52).

Two studies used quality-adjusted life years (QALYs) as an outcome measure. Van Dyck et al. and Fitzgerald et al. compared the gain in QALY resulting from receiving POCT to the gain in QALY from receiving standard treatment. The former study found a gain of 0.006 QALY from being in the POCT arm as compared to the standard arm (54). However, the POCT arm was in a primary care setting, and the link between the gain in QALYs and the use of POCT was not explained. Fitzgerald et al. further call these meagre results into question, finding the POCT arm resulted in a loss of 0.003 QALY compared to standard treatment (53).

Summary

The available health economics evidence is limited by the number of studies that have been published, as well as by a diversity of research methods that make comparisons difficult. These limitations add to the difficulties in drawing clear conclusions about the cost effectiveness of emergency department cardiac troponin POCT.

All six included studies did agree that using cardiac troponin POCT is more expensive per patient than standard central lab testing (32,41,51–54). The increase in costs is because of increased fixed-costs for quality control and training. The reported evidence on the difference in costs ranges greatly and appears to be unreliable.

The only situation in which there was evidence that the cost of POCT can be offset by monetary gains on post-testing treatment (i.e., inpatient cardiologic or intensive care) is the case of a remote hospital without any in-hospital testing alternative. In this case, the comparator was not central lab testing but clinical assessment with no quantitative testing (52). While this scenario is highly relevant to the current project, the different setting and jurisdiction, the single site and small sample size of the evidence compel a high level of caution in terms of generalizing the findings to Newfoundland and Labrador.

The evidence for cardiac troponin POCT cost per patient-hour saved in the ED suggests a moderate cost (51) but it must be kept in mind that this is an estimated cost and not a measured cost. Craig et al. 2004 have shown that a 24/7 central lab can save as many patient-hours as bedside testing (12).

The RATPAC study finds that using cardiac troponin POCT is heavily dependent on setting. Overall, that study found POCT to be costly and to not improve quality of life. However, they do not consider patient-hours saved in the ER as a possible benefit. Ultimately, the authors conclude that POCT is not a good strategy. Lastly, a micro-simulation of implementing POCT in family medicine practices is difficult to interpret, as it could generate a prohibitive cost per QALY or a societal benefit (41).

Key Message:

The evidence for the overall cost benefits of emergency department cardiac troponin POCT is incomplete and inconsistent. The findings on the overall cost benefits are not conclusive.



The Newfoundland and Labrador Context



The Contextualized Health Research Synthesis Program (CHRSP) interprets all project findings in consideration of the existing or expected circumstances of the province of Newfoundland and Labrador—a process known as contextualization. Most research evidence synthesized in a CHRSP report has been generated in places that are considerably different from our province in any number of ways. As a result, it may be the case that the research results cannot be directly applied here. We refer to ‘contextual factors’ as the local conditions, capacities and qualities that may have an impact on the reported effects of our included research evidence.

A contextual factor has the potential to enhance or to reduce the reported effectiveness, feasibility or acceptability of an intervention.¹⁵ We identify and assess contextual factors through the analysis of local data and research evidence¹⁶ as well as through interviews with local key informants that include local decision makers, administrators, front-line workers and stakeholder group representatives.

In some rare cases, we do find research that has studied the effects of one or more contextual factors. For the POCT CHRSP Project, the available research evidence indicated that contextual factors at the level of the organization of the emergency department and testing services did have a significant impact on measured outcomes (see below). However, most potential contextual factors were not adequately addressed in the available research evidence. As a result, we can only estimate the potential effects of those contextual factors.

Patient-Level Factors

Patient-level contextual factors include demographic trends in the province, geographic considerations (i.e., where people live) and cultural features of the population. Our consultants identified several patient-level contextual factors that merit consideration when making decisions about implementing emergency department cardiac troponin POCT.

Risk factors for ACS in rural and remote Newfoundland and Labrador: The first patient-level contextual factor is the existence of higher risk factor rates for ACS among people living in rural and remote parts of the province where hospitals and health centres would be most likely to use emergency department cardiac troponin POCT located (e.g., without 24/7 lab services and callback lab services or without callback services at all).

The root cause of ACS is arterial blockage and inflammation arising from atherosclerosis, which has the following risk factors: older age (45 for men, 55 for women), high blood pressure, high blood

¹⁵ See http://www.nlcahr.mun.ca/CHRSP/CHRSP_CONTEXT_IN_DETAIL.pdf for more detail on contextualization in CHRSP projects.

¹⁶ The project originally intended to include health informatics data on ED lab requests, but was not able to obtain all the data necessary for the analysis. See Online Companion Document, Data Request.

cholesterol, tobacco smoking, lack of physical activity and Type II Diabetes (59,60). All these risk factors tend to be over-represented in rural areas of North America in general, and in Newfoundland and Labrador in particular (61–65). Our consultants expected the increased rate of these risk factors to contribute to a higher incidence of patients presenting with potential ACS compared to national or even provincial rates. This factor would enhance the cost effectiveness of troponin POCT at the emergency department level as fewer lab technicians would be called back.



Patient transfers and monitoring: Our consultants reported that, in the past, emergency department patients presenting with ACS or angina symptoms would sometimes decline an ambulance transfer to another hospital with 24/7 lab services, opting instead to go home and return to the local hospital when lab services resumed the following morning. A POCT cardiac troponin screening test delivered on site would be able to differentiate NSTEMI ACS patients who require closer monitoring (and possible transfer) from those with angina who could potentially go home more safely for the night, thereby decreasing the chances of someone in the higher-risk NSTEMI ACS group being released inadvertently. The quicker turnaround time for POCT might also prevent delays in treatment and their resulting negative health consequences.

Patient acceptance: Our consultants also reported that patients and their caregivers are very likely to accept an emergency department troponin POCT as an alternative to central lab testing after hours. This high level of acceptance and low likelihood for rejection of a new testing system may enhance, or at the very least not detract from, the reported effectiveness of emergency department cardiac troponin POCT.

Design of Service Factors

Our consultants identified a number of contextual factors at the level of the design of service for emergency department troponin POCT. These factors mainly take into account the testing capacities of different types of Category B hospital emergency departments: those with 24/7 lab services (e.g., Carbonear General Hospital), those with lab callback services for after-hours testing (e.g., Old Perlican), and those without callback (e.g., Whitbourne).

Advantages of POCT for sites where no callback is available: Emergency department troponin POCT is expected to be the most advantageous in the health centres/hospitals that do not have any callback for lab services. Without emergency department troponin POCT, decisions about patients with possible ACS are made with incomplete information and a greater potential for error. Only one primary research study in our synthesis explicitly included a hospital without any callback services and found the clinical effectiveness, efficiency and cost effectiveness to be significantly improved (50).

Potential advantages for sites where callback is available: Our consultants also advised that even those sites that have callback lab services might be expected to have enhanced outcomes with emergency department troponin POCT. In some cases, attending physicians may not follow best practices in an effort to avoid lab technician callback because of the disruption, time commitment, and

associated costs of doing so. In these instances, the convenience of POCT availability might be expected to promote clinical effectiveness and efficiency in testing.

Potential risk of POCT misuse: Our consultants informed us that there are ways in which the effectiveness of emergency department cardiac troponin POCT could be undermined in hospitals in Newfoundland and Labrador.

- First, there is the potential risk that the cardiac troponin POCT device could be misused over time as a *diagnostic* test instead of a *screening* test. Staff at smaller hospitals working after-hours may start to consider an emergency department troponin POCT result as definitive, thereby increasing the likelihood of false positive results.
- Secondly, staff at any hospital may begin to substitute the more convenient and cheaper POCT for the more sensitive, costly and time-consuming lab test, again increasing the likelihood of false positive results.
- A third scenario that may present problems is the potential for confusion in distinguishing the results of a POCT *screening* test and those of a central lab *diagnostic* test.

These risks, while not specific to the province, are cause for legitimate concern. Our consultants did indicate, though, that the province's new system of accreditation (see below) and quality assurance measures, including protocols for use, are intended to prevent such misuse or misinterpretation.

Design of emergency department workspaces: A separate contextual factor concerning design of service is the physical layout of the emergency department workspace. Our consultants pointed out that many smaller hospitals and nursing stations have only one nurse present afterhours. As a result, the emergency department cardiac troponin POCT would need to be within close range of the nurse so that it can be accessed without leaving the patient unattended. Based on our consultations, it seems that most, if not all, facilities in the province have adequate and appropriate storage space to accommodate a troponin POCT in the emergency department. The POCT would also need to be designed in such a way that a single person could prep and administer the test relatively easily, since it is often the case that patients with ACS need physical assistance.



Health Human Resource Factors

In all emergency medicine settings in Newfoundland and Labrador, once the accreditation process has been completed, physicians will be responsible for ordering cardiac troponin POCT.¹⁷

Physician Confidence: Our consultants indicated that it would be critical for emergency department physicians to have confidence in the reliability and accuracy of troponin POCT testing in order to effectively implement the test. Without such acceptance, physicians will be less likely to request a cardiac troponin POCT in the emergency department. As a result, the cost-effectiveness of the test would be expected to decrease; the clinical effectiveness may decrease as well if the test is not used as

¹⁷ In remote Labrador Community Clinics, physicians order tests via a live telehealth link.

often as it should be to maintain skills and competency (50). The province's regional health authorities have a validation process in place for new biomedical tests that is intended and designed, in part, to



demonstrate the reliability and accuracy of new tests to physicians.

Nurse Training: While physicians will be responsible for ordering the test, emergency department nurses will be responsible for administering it. Nurses have traditionally administered bedside testing, (e.g., glucometers or urinalysis) and our consultants expected they would consider troponin testing professionally

acceptable. Nurses would be required to complete training, certification and re-certification on a regular schedule. Existing clinical educators would incorporate troponin POCT into existing curricula for ED nurses. These measures would be part of the accreditation process (described below) and would be expected to enhance the effectiveness of troponin POCT.

Potential Laboratory Technician Issues: Several consultants reported that there could be some "pushback" from lab technicians and their union about nurses being responsible for cardiac troponin POCT in the emergency department. This could affect the acceptability of emergency department troponin POCT at the inter-professional level and could also have a negative impact on its implementation and subsequent cost effectiveness if it is underused.

Laboratory Technician Turnover Rates: One final health human resource (HHR) contextual factor we identified relates to lab technician turnover rates in the province at this time. Our consultants told us that there is a wave of lab technician staff changes underway; government research corroborates this view (66). This is related, in part, to the province's decision to have all provincial labs become accredited. Our consultants suggested that seasoned lab technicians are taking early retirement or switching to new careers instead of going back to school and retraining in order to retain their jobs. Recruitment of lab staff in rural hospitals in this province has traditionally been challenging. Furthermore, the older generation of lab technicians was more likely to live in or near the community with the health centre where they worked and, once hired, would stay in the position for long periods of time. More recently-hired lab technicians are more likely to commute from larger population centres and to stay in their positions for shorter periods of time. Volatility in health human resources is perceived to be a risk for poorer performance in medical labs in terms of accuracy, efficiency and cost effectiveness (67,68). An unstable lab technician workforce is expected to contribute to less clinical and cost-effective lab testing in general, and since lab technician staff are responsible for POCT quality assurance measures, an unstable workforce could affect POCT clinical and cost effectiveness as well.

Organization of Health Services Factors

The organization of health services supporting any point-of-care testing program is one area where research-based evidence is available.

Site-specific organizational factors: As mentioned previously, site-specific variables had significant impacts on turnaround time and time to discharge (42). Ryan and colleagues found that the individual

test sites, with their own unique combination of organizational features, had a significant effect in mediating the clinical effectiveness, efficiency and cost effectiveness of emergency department troponin POCT.¹⁸ Although the authors could not definitively identify which features were responsible, they concluded that the overall effectiveness of emergency department POCT in general is critically influenced by the successful implementation of ancillary services and system protocols.

Accreditation: A major contextual factor regarding the organization of health services in Newfoundland and Labrador is the recently-adopted accreditation requirements for lab testing. Accreditation for point-of-care testing will go into effect in 2015 and requirements will include designing a certification program for lab staff, designating a resource person in each lab responsible for overseeing lab testing and quality assurance, implementing a data collection and analysis system, and establishing a range of other quality assurance measures including quality control protocols. Lab staff will be responsible for POCT quality control measures, while the clinical staff (i.e., nurses) will administer the point-of-care tests. Our consultations indicate that having these standards, policies and practices in place is expected to enhance the clinical and cost effectiveness of troponin POCT compared to conditions without a standardized accreditation system (as was the case in the province until recently).

Newer protocols vs. older standards: There has been confusion among healthcare workers about new accreditation requirements. In particular, workers have questioned why previously administered POCT, like blood glucose glucometers, were stopped and why their re-implementation will include more stringent quality control and quality assurance measures. Our consultations indicated that some clinical staff view the new version of the tests as added work (instead of seeing it as the same work with different standards of practice). Some lab technicians are concerned that the clinical staff will not be sufficiently rigorous with the testing equipment, and as a result, they do not want to be responsible for, or accountable for, POCT devices. Our consultants believe that these issues will need to be addressed and clarified in order for cardiac troponin POCT to be implemented effectively and efficiently.

Need for Effective Monitoring: A second issue related to accreditation is effective monitoring of POCT performance to detect anomalies and errors. This requires the collection, tracking, compilation and analysis of data from individual POCT devices. Local lab technicians will be responsible for much, if not all, of the data collection at the hospital level, while the compilation of hospital level data will occur at the sub-regional and regional levels. Our consultations indicate that there have been some major challenges in integrating data from multiple hospitals and/or sub-regions, and these challenges could pose problems for effective monitoring of POCT devices across RHAs. Our consultants also told us that the collection, review and analysis of such potentially large pools of data will require additional human resources. These factors could potentially reduce the clinical and cost effectiveness of troponin POCT testing at the regional or provincial level, as well as other types of point-of-care testing (e.g., blood clotting POCT or liver function POCT) that may be considered in the future.

¹⁸ The authors did not test individual organization features as independent variables, but rather identified the mediating effects of the organizational features through *post hoc* tests.

Economic Factors

Economic contextual factors that will have an impact on the cost effectiveness of troponin POCT testing in Newfoundland and Labrador must be considered when implementing the tests in smaller hospitals and health clinic emergency departments.

Offsetting the cost of patient transfers: One major economic contextual factor when considering the use of cardiac troponin point-of-care tests is the cost of transferring a patient from one institution to another via ambulance to be tested. An emergency department cardiac troponin POCT program would reduce the need for such transfers by screening out patients who are negative for ACS, while confirming the need for transfers in those patients requiring care in a larger healthcare centre.

Reduced demand for callback: An emergency department cardiac troponin POCT may also reduce the need for lab staff callback, which requires a minimum pay period of three hours.

As a result of an anticipated reduced demand for patient transfers and lab technician callbacks, the cost effectiveness of emergency department cardiac troponin POCT may be higher in NL compared to that reported in the research literature.

Factors with the potential to increase costs: Two economic contextual factors could decrease the local cost effectiveness of emergency department cardiac troponin POCT. The first involves the increased time for developing, implementing and maintaining the quality control and other quality assurance measures required for accreditation that were not previously standardized across hospitals in Newfoundland and Labrador. The second is the cost of designing, implementing and maintaining a comprehensive data collection and monitoring system to evaluate POCT in general and emergency department troponin POCT specifically. The available evidence does not appear to include these costs for practices and infrastructure that may already exist in other jurisdictions. Accordingly, the actual cost effectiveness of ED cardiac POCT for troponin, and other POCT tests, may be lower in Newfoundland and Labrador than what is reported in the literature we have reviewed.

Political Factors

Two main types of political factors were identified by our consultants as being unique to the Newfoundland and Labrador context.

Public perception of biomedical testing in the province: The healthcare system of Newfoundland and Labrador has had, over the past ten years, numerous episodes where lab testing results have been found to be in error. As a result, the public has a certain lack of trust in the capacity of the provincial health care system to provide adequate testing, quality control and/or monitoring. While our consultants agreed that patients and their caregivers are still likely to accept a new technology like emergency department troponin POCT, any problems with the new technology, especially in its early stages, could significantly lower its acceptability by the public and possibly its use by clinical staff.

Possible conflict within the healthcare system: The second political factor identified by our consultants relates to the potential for conflict from within the healthcare system. Conflicts may arise from either the laboratory technicians and/or the emergency department clinical staff. Laboratory

technicians have voiced resistance to being held responsible for quality assurance when clinical staff are administering POCT tests. They have also protested the recently-announced regional centralization of central lab testing. In terms of the clinical staff, our consultants told us that there are some complaints about the recent restrictions on POCTs, and in the case of some tests like glucometers, reintroduction with additional quality control measures. Clinical staff may perceive the new accreditation-related measures as additional and unwanted work.

In order for any POCT to be implemented successfully in the province, both laboratory and clinical healthcare workers will need to accept and support the new tests and the required quality assurance measures required by accreditation.

Considerations for Decision Makers

We list below considerations that health system decision makers may wish to take into account when considering emergency department cardiac troponin point-of-care testing for smaller hospital and health centres. These suggestions are based on the synthesis findings as refracted through the professional perspectives of the clinicians, administrators, and decision makers on the project team, most of whom currently work within the provincial health system.

1. Cardiac troponin point-of-care testing technology is sufficiently accurate and reliable to be used as a screening test for acute coronary syndrome in emergency departments in Newfoundland and Labrador.
2. Hospital and regional level supports for POCT in the emergency department will strongly influence the effectiveness, efficiency and cost-effectiveness of cardiac troponin POCT. In particular, adherence to quality control measures and clinical protocols is required for POCT to realize its potential benefits. Emergency department physicians and nurses, and central lab technicians, will need to accept any proposed POCT to sustain quality control measures and protocols.
3. The requirement for accreditation for POCT in the province will help ensure that the appropriate quality control measures and protocols are implemented and sustained. However, health human resource challenges are potentially significant, particularly for smaller hospitals in Newfoundland and Labrador; these challenges could have an impact on sustaining those measures and protocols.
4. Tracking and monitoring are crucial requirements of POCT quality control. In order to properly implement POCT, the RHAs will need to be able to compile and analyze data from multiple sites in a timely and effective manner.

5. When implemented properly and used appropriately, cardiac troponin POCT, used as a screening test, does not increase the risk of adverse events or readmission rates compared to central lab testing; furthermore this POCT significantly reduces the Turnaround Time for test results, and has the potential to reduce other emergency department time outcomes and to improve patient throughput.
6. When implemented properly, cardiac troponin POCT, used as a screening test, can reduce time to anti-ischemic therapy for high-risk patients and time to a negative diagnosis among low-risk patients, especially in hospitals and health centres without an operating central lab.
7. The evidence does not provide a clear indication of the economic impacts of ED cardiac troponin POCT in Newfoundland and Labrador, though it does suggest that POCT will be the most cost-effective in hospitals without 24/7 central lab services.

In addition to the foregoing considerations, which are based on the available research-based evidence and the Newfoundland and Labrador context, decision makers may wish to consider the continuing advances in technology for point-of-care testing. Advances in miniaturization, bioassays, biosensors and health informatics are happening at a rapid pace, while the costs of these technologies continue to decrease. As a result of this technological context, the number and variety of point-of-care testing devices can be expected to proliferate and to extend into emergency departments and other healthcare settings including acute care, primary care, long-term care and, increasingly, into the patient's home.

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