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Point-of-Care Cardiac Troponin Testing in Patients With Symptoms Suggestive of Acute Coronary Syndrome – Project Protocol

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INTRODUCTION

Chest pain can result in broad, differential diagnoses including acute coronary syndrome (ACS) such as a heart attack (i.e., acute myocardial infarction [MI]), as well as non-cardiac conditions, including gastro-esophageal reflux, anxiety, or muscular pain.^{1,2} Individuals who present with chest pain or other symptoms suggestive of ACS undergo investigations such as clinical assessment or electrocardiogram (ECG) to rule out a potential acute MI.³ However, clinical assessment and ECG findings are often inconclusive and further investigation may be required.

ACS refers to a group of conditions that result from a decrease of blood flow in the coronary arteries, leading to reduced blood supply to the heart muscle (myocardial ischemia), and if severe and prolonged, leading to heart muscle necrosis (myocardial infarction). The most common symptom of ACS is pressure-like chest pain radiating to the left arm or jaw, associated with shortness of breath, nausea, and sweating. ACS includes ST segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI), and unstable angina (UA).¹

STEMI results from complete and prolonged occlusion of a coronary artery and is defined as an ACS with an ST segment elevation on ECG, and an increase in cardiac biomarkers such as creatine kinase isoenzymes MB, cardiac troponin I (cTnI), or cardiac troponin T (cTnT). NSTEMI results from partial and transient occlusion of a coronary artery and is defined as ACS without an ST elevation but with an elevation of cardiac biomarkers. UA results from myocardial ischemia that, unlike in STEMI and NSTEMI, is not severe enough to cause myocardial damage and release detectable quantities of cardiac biomarkers, and is defined as ACS without an ST elevation and without an elevation of cardiac biomarkers.¹

A 2013 CADTH report cited that in Canada there were an estimated 818,847 emergency room visits for suspected ACS, and an estimated 109,109 hospitalizations for ACS in 2009.^{4,5} In Canada, acute MI requiring in-patient acute care has been listed as one of the top 15 most expensive medical conditions.⁶ Given the broad range of differential diagnoses, between 2000 and 2008 approximately 75% to 85% of patients who presented to emergency departments with chest pain were not diagnosed with ACS.⁷

Because of the similarity of the symptoms of MI with other conditions, and the transient or non-specific ECG findings,² in 2012 several leading international cardiac associations published a universal definition of acute MI, using cardiac troponin (cTn) as a diagnostic determinant. This definition states that for a diagnosis of acute MI to be made, there must be a “*detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin) with at least one value above the 99th percentile upper reference limit,*” along with at least one other criterion, such as pathological Q waves in the ECG or symptoms of ischemia.¹

The conventional method of assessing cTn concentrations is through central laboratory tests, with recent emergence of high-sensitivity cTn tests. Central laboratory cTn testing can provide evidence of acute MI⁸ with a one-hour recommended turnaround time.⁹ Due to the development of higher-sensitivity cTn assays, thresholds of positive cTn values have decreased from 1.5 mcg/L in 1995 to 0.04 mcg/L since 2007.¹⁰ The heightened sensitivity of cardiac biomarker tests may result in an increase in false diagnoses of NSTEMI and a corresponding decrease in diagnoses of UA. Further, blood cTn concentrations can be increased in non-cardiac conditions such as renal failure or neuromuscular diseases, which can also lead to an increased potential for false-positives.¹¹

Central laboratories are not always on-site or available for use 24 hours a day, seven days a week. Point-of-care (POC) testing is a care model that moves the assay to the patient and is now available to measure cTn levels. POC cTn tests offer significantly shorter turnaround times for biomarker detection, typically providing results within 10 to 20 minutes.³ POC cTn testing has been used to expedite patient care in hospital emergency departments and various settings where central laboratory testing is not available, such as with paramedics in land or air ambulance, and in rural or remote medical clinics. This can potentially accelerate decisions regarding patient therapy, transfers, hospital admissions, and discharge for individuals presenting with ACS. The result could theoretically be less congested emergency departments and fewer patient transfers to larger hospitals for further assessment. Improved patient flow may result in cost reductions from fewer unnecessary hospital admissions and decreased laboratory costs.⁸

How POC cTn testing is, or could be, integrated into the ACS management pathway depends primarily on the setting of care. For example, most emergency departments in large urban centres have access to central laboratories 24 hours a day, seven days a week. In these settings, POC cTn testing may have a role in shortening test result turnaround time, which could help decrease time to discharge if MI is not diagnosed. In settings where central laboratories are open only for defined working hours, POC cTn may help to avoid unnecessary patient transfers to a percutaneous coronary intervention (PCI) facility for those with a negative first test awaiting serial testing when a central lab reopens. In settings with no access to a central laboratory, the role of POC cTn is most likely to avoid patient transfers to PCI facilities for people ultimately diagnosed with UA. These scenarios are examples only, and are meant to highlight the variety in treatment pathways among different settings and demonstrate the range of POC cTn applications.

POC tests are available in Canada for assessing both cTnI and cTnT in various health care settings (Table 1). To date, no high-sensitivity POC tests have been approved for use by Health Canada.

TABLE 1: IDENTIFIED POC TROPONIN DEVICES

Manufacturer	Device name	Test results (min.)	Date of approval by Health Canada
Abbott	i-STAT (cTnl)	12	2005-10-18
Alere	Following troponin tests: <ul style="list-style-type: none"> • Cardio2 Panel (cTnl+BNP) • Cardio3 Panel (cTnl+BNP+CKMB) • Troponin I To be used with Triage MeterPro-testing platform (monitor)	15 to 20	2010-08-09 2010-08-09 2010-08-09 2002-10-11
LifeSign/Princeton Biomeditech Corp	<ul style="list-style-type: none"> • LifeSign MI Troponin I • LifeSign MI CKMB/Myoglobin/Troponin I 	15	2013-02-11
Radiometer	AQT90 Flex (cTnl and cTnT)	10 to 20	2014-10-14
Response Biomedical	RAMP (cTnl)	15 to 20	2012-07-17
Roche	<ul style="list-style-type: none"> • CARDIAC Troponin T (Cardiac T) – test to be used with Cobas h 232 testing platform • Sensitive Troponin T strip (doesn't require instrument) 	12 12	2009-01-08 2007-08-10
Siemens	Stratus CS (cTnl)	14	2004-06-09
ZBX Corporation/Innova	<ul style="list-style-type: none"> • ZAP Troponin I • Zap Troponin I/Myoglobin 	15	2009-01-15 2010-05-12

BNP = B-type natriuretic peptide; CKMB = creatine kinase MB; cTn = cardiac troponin; cTnl = cardiac troponin I; cTnT = cardiac troponin T; MI = myocardial infarction; min. = minutes.

Cost of the Technology

A CADTH report cited an estimate of 818,847 Canadian emergency room visits were made in 2009 for suspected ACS.⁴ A one-year economic model was also generated that found that from time of presentation at the emergency department to one year later, the costs per patient, after undergoing standard laboratory testing of cTn, ranged from \$2,018 to \$2,186 per patient per year, which included the costs of false-positive hospitalizations. Multiplying the total emergency visits by \$2,018 leads to an estimated annual cost of C\$1,652,433,246 to care for patients presenting to emergency departments with suspected ACS and who undergo laboratory testing for cTn. This model also assumed that each patient would receive two tests at either \$3.00 (for cTnT) or \$6.75 (for cTnl) per test. A 2013 CADTH environmental scan found that 77% of hospitals were using cTnl testing. POC cTn is more expensive compared with laboratory testing, with one manufacturer citing \$12.50 per test. However, a cost-per-test approach is not an informative cost comparison; rather, the question is how POC compares with laboratory testing when examining factors beyond the costs of reagents to including the costs of running the POC program (for example, training, quality assurance and quality control, maintenance, and data management) and savings from avoiding the costs of patient transfers and hospital admissions.

It is unknown whether cost savings and health benefits can be realized in various Canadian health care settings (such as community hospitals, remote locations, various test administrators, hospitals without central laboratories, rural/remote nursing stations, medical clinics, long-term care settings, and emergency medical services). The estimated cost savings or costs incurred in Canada can be better understood if calculations are made with knowledge of Canadian

information concerning the costs of devices, reagents, staff overhead, how POC tests for cTn are being used and by whom, costs of training, quality control, quality assurance, opportunity costs associated with demands on nurse time, and whether and where the use of the technology is increasing or decreasing.

OBJECTIVES

The aim of this health technology assessment (HTA) is to inform decision-making about the appropriate use of POC cTn testing. Policy questions such as appropriate settings (rural or remote, ambulance, hospital, emergency room), the timing of testing, and population suitable for POC cTn testing have been raised in Canadian jurisdictions. This HTA will address these questions by evaluating the diagnostic accuracy, clinical utility, and cost-effectiveness of POC cTn testing in patients presenting with ACS. The proposed HTA will address the following research questions:

1. What is the diagnostic accuracy of POC cTn testing, using POC cTn devices approved by Health Canada, compared with central laboratory methods, in patients presenting with symptoms of ACS?
2. What is the clinical utility of POC cTn testing in altering the treatment and outcomes of patients presenting with symptoms of ACS?
 - a. As compared with standard care in settings where a central laboratory is not available (pre-hospital setting; rural/remote settings)
 - b. As compared with central laboratory methods in settings where a central laboratory is available (emergency departments, in hospital)
3. What is the cost-effectiveness of POC cTn testing in patients presenting with symptoms of ACS?
 - a. As compared with standard care in settings where a central laboratory is not available (pre-hospital setting; rural/remote settings)
 - b. As compared with central laboratory methods in settings where a central laboratory is available (emergency departments, in hospital)

Questions 1 and 2 will be addressed through a systematic review of available clinical evidence. Question 3 will be addressed through a primary economic evaluation. Other factors such as the ethical, legal, and social implications of POC cTn testing will be addressed through the clinical review.

The HTA will be peer-reviewed by external clinical experts.

METHODS — CLINICAL REVIEW

Literature Search Strategy

The literature search will be performed by an information specialist using a peer-reviewed search strategy. Published literature will be identified by searching the following bibliographic databases: MEDLINE (1946–) with in-process records and daily updates via Ovid; Embase (1974–) via Ovid; The Cochrane Library (2015, Issue 1) via Wiley; and PubMed. The search strategy will be comprised of both controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings) and keywords. The main search concepts will be cardiac troponin and point-of-care.

No filters will be applied to limit the retrieval by study type. Where possible, retrieval will be limited to the human population. Retrieval will not be limited by publication year or language. Conference abstracts will be excluded from the search results. The initial search was completed on January 14, 2015. Regular alerts will be established to update the search until the publication of the final report. Regular search updates will be performed on databases that do not provide alert services. Grey literature (literature that is not commercially published) will be identified by searching sources identified in the CADTH Grey Matters checklist (<http://www.cadth.ca/resources/grey-matters>), which includes the websites of regulatory agencies, HTA agencies, clinical guideline repositories and professional associations. Google and other Internet search engines will be used to search for additional Web-based materials. These searches will be supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry.

Selection Criteria and Methods

Two reviewers will independently screen the titles and abstracts of all citations retrieved from the literature search and, based on the selection criteria (Table 2), will order the full text of any articles that appear to meet those criteria. The reviewers will then independently review the full text of the selected articles, apply the selection criteria, and compare the independently chosen studies. Disagreements will be resolved through discussion until consensus is reached. Multiple publications of the same trial will be excluded unless they provide additional outcome information of interest. A prisma flow diagram of studies inclusion and exclusion will be presented.

TABLE 2: CLINICAL REPORT SELECTION CRITERIA

	Diagnostic Accuracy (Question 1)	Clinical Utility (Question 2)
Settings	Medical centres where central laboratory testing is available (such as hospital emergency departments)	<ul style="list-style-type: none"> Medical centres where central laboratory testing is available (such as hospital emergency departments) Medical centres where central laboratory testing is not available (such as pre-hospital settings, rural/remote medical clinics)
Population	Adults presenting with chest pain or other symptoms suggestive of ACS	Adults presenting with chest pain or other symptoms suggestive of ACS
Intervention	POC cTn assays/tests approved for use in Canada by Health Canada that use the 99 th percentile cut-off threshold	Any POC cTn test
Comparator	Central laboratory methods	<ul style="list-style-type: none"> For settings where a central laboratory is available: central laboratory methods either alone or in addition to POC cTn For settings where central laboratory is not available: standard care (e.g., transfer to facility with testing capabilities)
Outcomes	Clinical validity of POC cTn tests, including: sensitivity, specificity, positive predictive value, and negative predictive value of POC cTn testing in the detection of AMI	<ul style="list-style-type: none"> Benefits and risks of POC cTn testing such as: turnaround time, time to clinical decision-making, time to discharge or transfer (length of hospital stay, length of emergency department stay), number of hospital admissions, adverse events rate, mortality rate, repeat emergency department visits Behaviour/treatment patterns of health care professionals Availability of the test, acceptability of and interest in the test for patients Ethical, legal, and social implications of POC cTn testing Recommendations from evidence-based guidelines
Study design	Randomized controlled trials, cohort studies, retrospective studies	Randomized controlled trials, cohort studies, evidence-based guidelines, surveys (for outcomes related to behaviour/treatment patterns, and availability and acceptability of tests)

ACS = acute coronary syndrome; AMI = acute myocardial infarction; cTn = cardiac troponin; POC = point-of-care.

Exclusion Criteria

Studies will be excluded if they do not meet the selection criteria, or if preliminary results are presented in abstract form. Duplicate publications, narrative reviews, case studies, and editorials will be excluded. Studies will be excluded if they are not published in English or French.

Data Extraction

A draft data extraction form for the diagnostic accuracy and clinical utility reviews is provided in Appendix 1. The form will be designed a priori to document and tabulate relevant study characteristics (e.g., study design, eligibility criteria, patient characteristics, setting, and other such factors and measures of clinical utility, as outlined above) in the selected studies. Data will be extracted by one reviewer and checked for accuracy by a second reviewer.

Critical Appraisal of Included Studies

Quality of the included studies in terms of diagnostic accuracy and clinical utility of the tests will be assessed by one reviewer and checked for accuracy by a second reviewer, using QUADAS-2¹² and the Downs and Black checklist,¹³ respectively. The quality of the included guidelines will be assessed by one reviewer and checked for accuracy by a second reviewer, using the AGREEII¹⁴ checklist. Disagreements will be resolved through consensus.

Data Analysis and Synthesis Methods

Diagnostic Accuracy

The diagnostic accuracy of POC cTn testing will be assessed based on the ability of POC cTn testing to predict acute MI (clinical validity), using central lab methods as the reference standard.

For diagnostic accuracy outcomes, a meta-analysis will not be performed due to the expected heterogeneity of the studies. Based on a scoping review, the studies that assessed diagnostic accuracy varied in terms of criteria for reference standards (WHO [World Health Organization] or ESC/ACC [European Society of Cardiology/American College of Cardiology]) and POC products from different manufacturers, therefore pooling will not be appropriate. Rather, studies that are identified that report on diagnostic accuracy will be reviewed, and results reported narratively in tables with ranges. Findings on the identification of patients who have acute MI (sensitivity), those who do not have acute MI (specificity), those who truly have acute MI from among those who tested positive (positive predictive value), and those who do not truly have acute MI from among those who tested negative (negative predictive value) will be reported. Study details that contributed to heterogeneity will be explored and reported. Results of the critical appraisal will be summarized in a table.

Clinical Utility

The clinical utility of POC cTn testing will be based on findings about the benefits (how testing influences management of ACS, and whether or not the choice of treatment based on testing results alters clinical outcomes) and risks resulting from test use.

Unlike for diagnostic accuracy outcomes that are device-specific, meta-analyses are planned for clinical utility outcomes to evaluate these outcomes from a POC cTn concept in general using studies that fulfill the selection criteria. If meta-analyses are not feasible due to the nature of the data — for example, due to clinical diversity among included studies — a review that includes a

narrative synthesis and summary of study findings will be conducted. Presenting results through a summary table of findings will help to determine the direction and size of observed effects in the absence of a meta-analysis. Studies will be appraised for quality, with results of the appraisal summarized in a table.

When meta-analyses are performed using Review Manager Version 5.0, the random effects model will be used to account for expected variation among devices and manufacturers. Clinical utility outcomes from randomized controlled trials and cohort studies will be pooled separately. The I^2 test will be used to explore heterogeneity between studies, with $I^2 \geq 75\%$ indicating high heterogeneity across trials. Forest plots will be presented for all meta-analyses to supplement reported estimates. The measures of effect for dichotomous data such as mortality rates will be expressed as relative risk with 95% confidence intervals (CI). The measures of effect for continuous data such as turnaround time will be expressed as weighted mean differences with 95% CIs. Findings will be reported as “not statistically significant” if the 95% CI of the overall estimate includes unity for dichotomous data or includes zero for continuous data.

Recommendations from evidence-based guidelines will also be reported. The literature search results will be screened for studies regarding behaviour and treatment patterns of health care professionals for POC cTn testing, availability of testing, interest and acceptability of testing to the patient, and ethical, legal, and social implications of POC cTn testing. Results of relevant articles will be summarized descriptively using frequencies, means, or qualitative categories, depending on the nature of data.

Subgroup Analyses

Subgroup analysis for the clinical utility outcomes will be conducted when available to increase the robustness of the findings. Stratification factors for subgroup analysis will include testing methods (cTnI, cTnT), type of health care providers who conducted the test, location (emergency department with 24/7 access to a central laboratory, emergency department with “working hours only” access to a central laboratory, rural/remote), three-hour or six-hour protocols, and other factors such as funding source (private versus public).

If required measures of variance are not available, variances will be imputed if possible.

METHODS — ECONOMIC EVALUATION

Primary Economic Evaluation

In collaboration with the CADTH clinical review team and clinical experts for the Health Technology Expert Review Panel (HTERP), the HTA Unit, University of Calgary will develop a decision analytic model for this economic evaluation. The patient population, intervention, and comparators reflect the criteria specified in Table 2.

- a) **Intervention:** POC cTn testing devices approved by Health Canada.
- b) **Comparators:** The comparators are dependent on the contexts reported in Table 3.

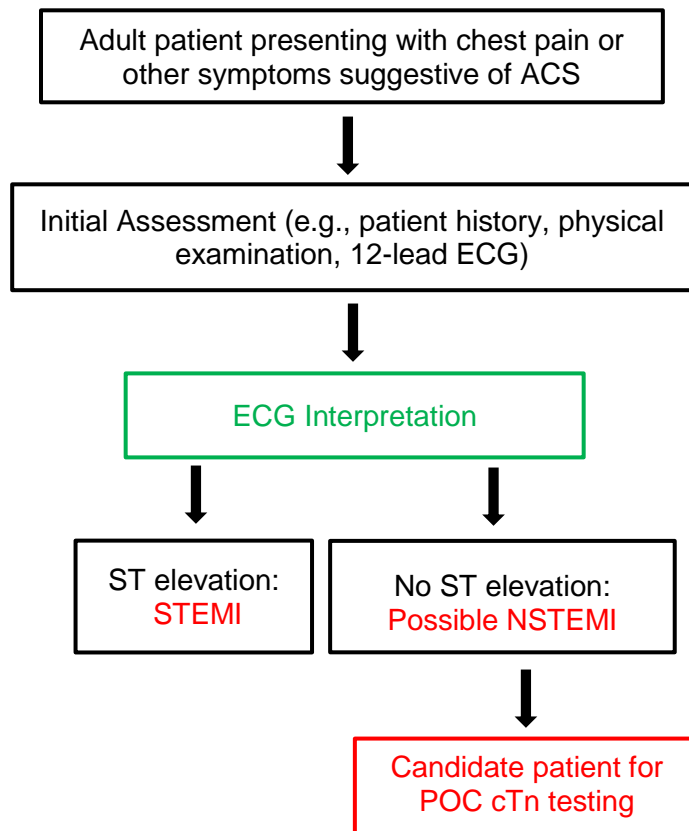
TABLE 3: COMPARATORS FOR THE ECONOMIC ANALYSIS BASED ON CONTEXT

	Context 1	Context 2
Comparator	Central laboratory testing of cTn available e.g., emergency department settings	Standard care (no cTn testing available via a central laboratory) e.g., non-hospital settings, rural/remote hospitals without a central laboratory, smaller hospitals without cTn testing in central laboratory
Alternative	POC cTn plus central laboratory cTn testing	POC cTn on-site

- c) **Patient population:** Among adult patients presenting with chest pain or other symptoms suggestive of ACS, the target population for the economic evaluation are patients identified as having non-ST elevation from ECG testing. These may include patients suspected of having possible NSTEMI or UA (Figure 1).
- d) **Model structure:** A simple decision-tree model will be built to determine the cost-effectiveness of implementing POC cTn testing in two different contexts: central laboratory testing of cTn available and no cTn testing available via a central laboratory. The structure of the model is dependent on the following information: the prevalence of individuals with NSTEMI; the sensitivity and specificity for the cTn testing strategies; the probabilities for clinical decision-making (e.g., early treatment/transfer, discharge, hold/re-test and late treatment/transfer, discharge); and the probabilities and utilities of the health states of being alive or dead after one year. Appendix 2 provides two schematics of the proposed economic model for the two different contexts.

The HTA Unit will work with the CADTH clinical review team as well as clinical experts from HTERP to ensure that current clinical literature and relevant POC practices/scenarios are accurately reflected in the economic model. In accordance with published guidelines,^{15,16} the internal and external validity of the decision analytic model will be assessed for any logical discrepancies. STATA 13 will be used for all statistical analysis and TreeAge Pro 2014 will be used to perform the decision analysis.

FIGURE 1: PATIENT POPULATION FOR THE ECONOMIC EVALUATION OF POINT-OF-CARE CARDIAC TROPONIN TESTING



e) Economic outcomes of interest: These may include the incremental cost-effectiveness ratio (ICER) based on the cost per hospital admissions avoided, cost per appropriate diagnosis made, and the cost per quality-adjusted life-year (QALY) gained. The potential bed hours saved from implementing POC cTn testing may also be examined in the proposed budget impact analysis (see below).

f) Model inputs:

- **Costs:** Cost estimates for POC cTn devices, testing materials (e.g., strips), and running the POC program (e.g., staff, training, quality assurance and quality control, maintenance) will be obtained from the manufacturer, provincial reimbursement data, and/or the literature. Costs related to central laboratory testing, standard care (i.e., clinical assessment, ECG), emergency department visits, length of stay, transfers, or hospitalizations in addition to procurement costs will be obtained from the literature, appropriate formularies and/or physician schedules.

- **Clinical inputs:** The clinical systematic review of the literature (to be conducted by the CADTH team) will inform these parameters and may include turnaround time, time to clinical decision-making, time to disposition, and repeat emergency department visits. These estimates will be summarized as odds ratios, relative risks, or weighted mean differences, depending upon the nature of underlying evidence. Consultation with the CADTH clinical team and/or clinical experts for HTERP will ensure that all relevant clinical events are included.
 - **Health-related quality of life estimates:** Each of the model health states for all the strategies (central laboratory testing, POC cTn testing, and standard care [no cTn testing]) will be associated with utility estimates. These estimates will be obtained either from published literature or available secondary data sources (i.e., from the use of the EuroQol 5-Dimensions Questionnaire [EQ-5D] or Short Form (36) Health Survey [SF-36] instruments).
 - **Sensitivity and specificity of POC cTn testing:** It is likely that the sensitivity and specificity of POC cTn testing will vary between devices, and from central laboratory testing and standard care. Depending upon the availability of this data, the economic analysis will incorporate the sensitivity and specificity estimates from the clinical systematic review.
 - **Time horizon:** A lifetime horizon will be used for the economic model.
- g) Perspective and audience:** The primary perspective will be that of a publicly funded health care system in a Canadian province. The target audience of this analysis will be health care practitioners and decision-makers.
- h) Base-case analysis:** An incremental cost-effectiveness analysis will be performed to determine the value for money of POC cTn testing relative to central laboratory cTn testing or standard care (no cTn testing) for patients with symptoms of ACS and possible non–ST-elevation.
- i) Sensitivity analyses:** In accordance with published guidelines, one-way and probabilistic sensitivity analyses will be conducted to assess the uncertainty of the model parameters and robustness of results from the primary analysis. Depending on the data available, the sensitivity analyses may examine uncertainty in parameters such as the estimates of clinical utility, hand-held versus desktop devices, different test costs, timing of testing, and sensitivity and specificity of testing devices.
- j) Assumptions:** During the course of model development, major assumptions and limitations will be identified and duly acknowledged in the final report.

Budget Impact Analysis

A budget impact analysis using a provincial health care context — decided in conjunction with the CADTH project team — will be conducted as part of the economic evaluation. Demographic variables and cost data specific to the province of interest will be used to compare the overall budgetary impact of strategies of implementing POC cTn testing with standard care.

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APPENDIX 1: DATA EXTRACTION FORM FOR DIAGNOSTIC ACCURACY AND CLINICAL UTILITY REVIEW

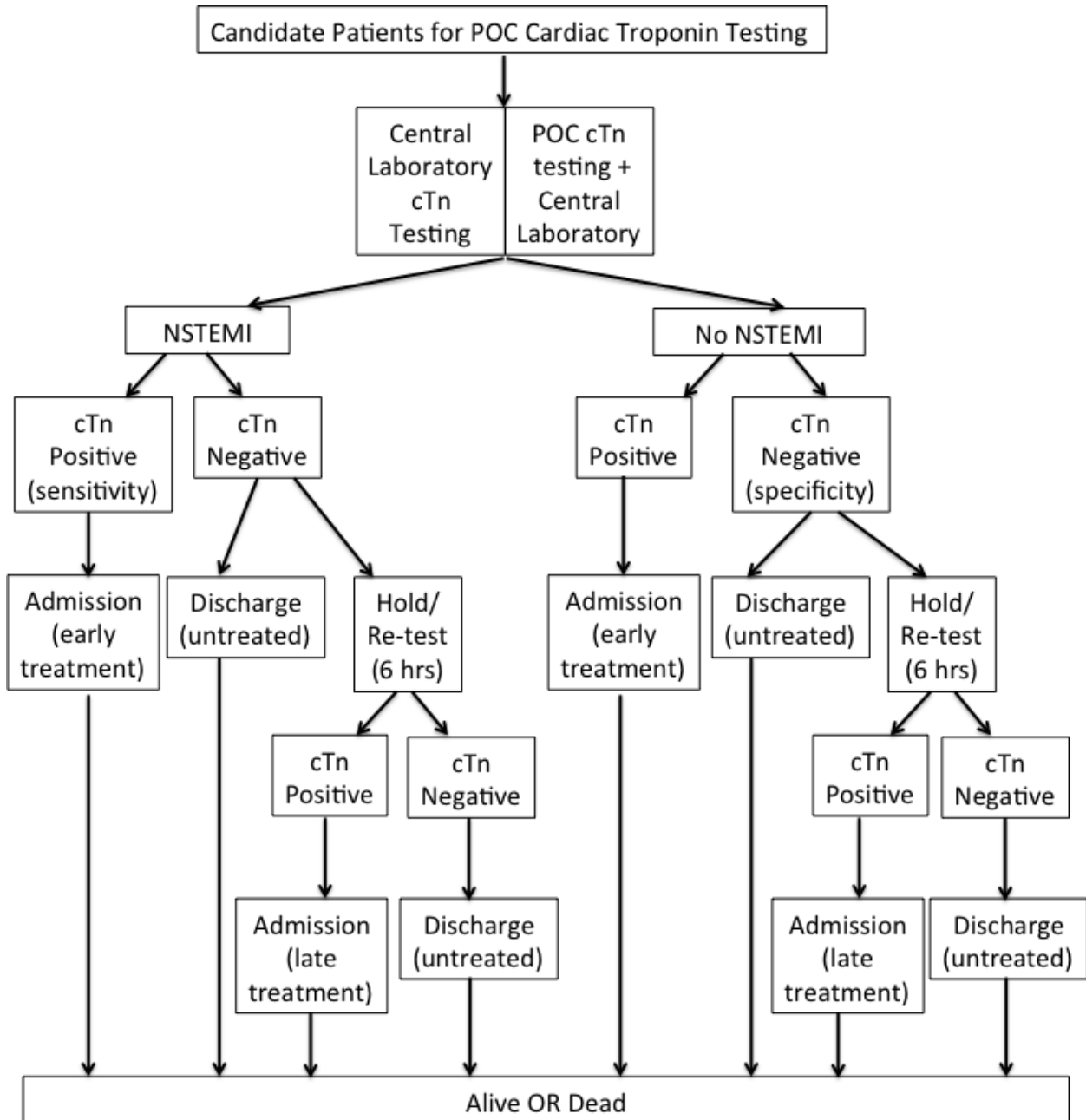
Reviewer		
RefID		
Author, date		
Country of origin		
Study characteristics		
Study setting		
Study design		
Study duration		
Inclusion/exclusion criteria		
Type of POC assay (cTnT, cTnI, hand-held, desktop); Manufacturer AMI criteria; Test protocol		
Type of central lab assay (cTnT, cTnI, high sensitivity-cTnT, high sensitivity-cTnI); Manufacturer; AMI criteria; Test protocol		
Description of central lab (e.g., on-site or off-site, distance from patient, etc.)		
Health care personnel conducting POC tests		
Conflict of interests (yes, no, none declared, not mentioned)		
Funding status		
Other (other lab diagnostic work up...)		
Patient characteristics		
	Intervention: • POC Testing	Comparators: • Central lab testing for emergency department setting • Standard care for settings where central lab is not available
Number enrolled Number completing study		
Age, sex		
Symptoms and comorbidities		
Time from symptom onset to testing (“pre-analytic time”)		

Other		
Outcomes		
Diagnostic accuracy		
Sensitivity		
Specificity		
PPV		
NPV		
Clinical utility		
	Intervention: • POC Testing	Comparators: • Central lab testing (for emergency department setting) • Standard care for settings (where central lab is not available)
Benefits and risks: • turnaround time • time from testing to clinical decision-making (“turnaround time”) • time to discharge • adverse events • mortality rate • repeat ED visit • others		
Evidence-based guidelines recommendations		
Behaviour/treatment patterns of physicians		
Availability		
Acceptability		
Interest		
Ethical, legal, social implications		
Other		
Notes		

AMI = acute myocardial infarction; cTnl = cardiac troponin I; cTnT = cardiac troponin T; ED = emergency department; NPV = negative predictive value; POC = point-of-care; PPV = positive predictive value.

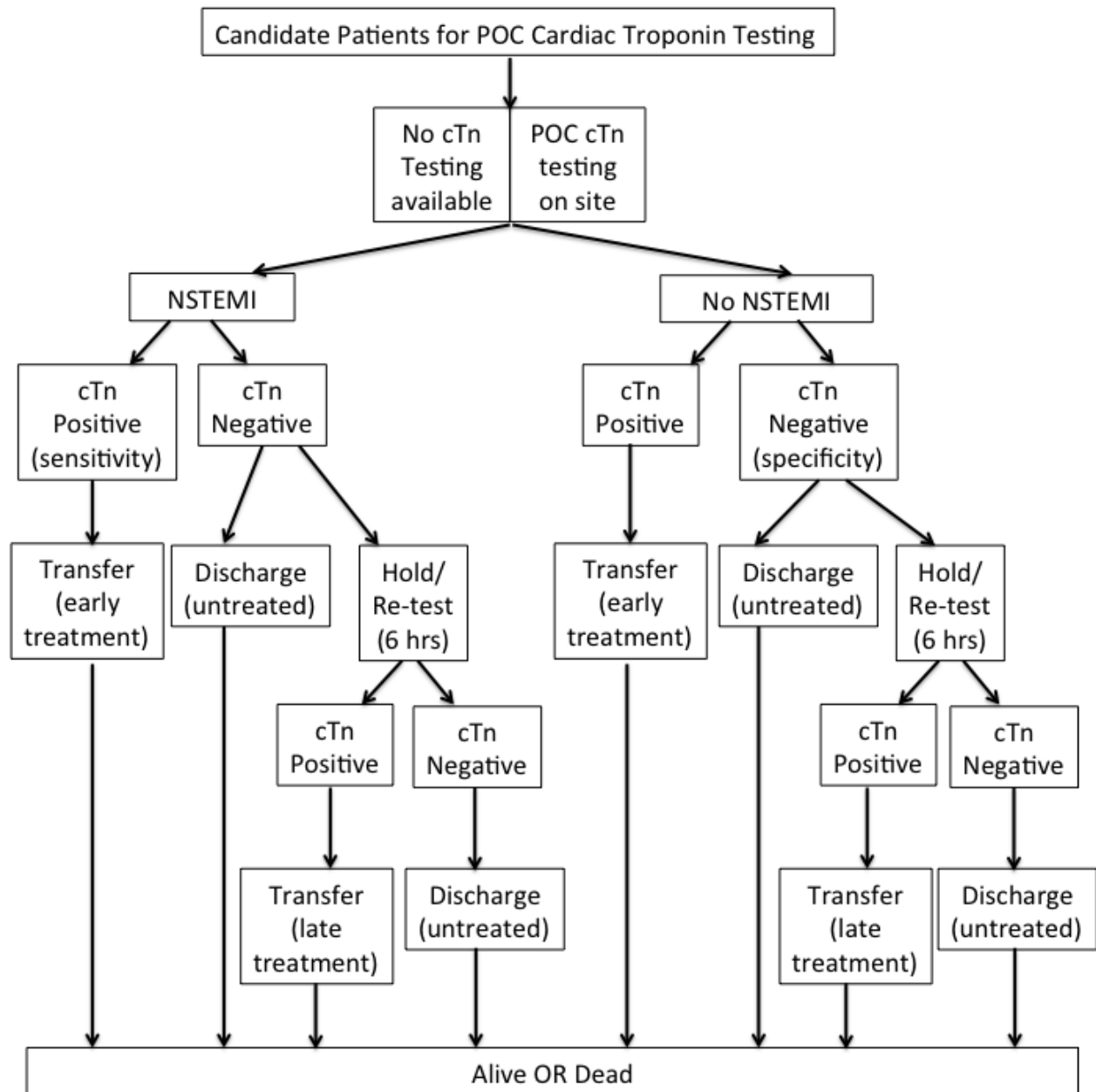
APPENDIX 2: PROPOSED MODEL SCHEMATIC FOR THE ECONOMIC EVALUATION OF POC CARDIAC TROPONIN TESTING

CONTEXT 1: Central Laboratory cTn testing available



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

CONTEXT 2: Standard care (no cTn testing available)



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