ICare-RURAL POC

Improving Care in Rural and URgent care centres for patients with possible Acute coronary syndrome using the Latest Point-of-Care technology

Health research council Ref ID: 22-227

Ethics reference:

ACTRN (registration number):

Version number 1.0

Date: 18 April 2023

Change notes:

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Lay Summary

This quality improvement initiative plans to measure the effect of implementing a chest pain assessment pathway using a point-of-care (near to patient) highly precise blood test to exclude heart attacks, compared with the existing chest pain assessment pathway (the rural accelerated chest pain pathway (RACPP). The context for the study will be people who experience chest pain and attend a community health setting in rural hospitals and general practice and urban urgent care clinics in Aotearoa New Zealand.

The RACPP includes a clinical assessment (the emergency department assessment of chest pain score (EDACS) of less than 16), an ECG (an electrode recording of the heart) and two troponin blood tests two hours apart that are below threshold. This pathway has been shown to be safe and effective at reducing the number of transfers to hospital or hospital admissions.

The new pathway (ICare-RURAL POC) that includes the new blood test (Siemens Atellica VLTi) allows the following changes to the pathway. The threshold for EDACS is able to be raised to 21 and if the episode of chest pain began at least 3-hours ago, a single blood test only will be required. This brings chest pain assessment in-line with urban emergency departments and may enable patients to receive high quality care near to the patient's home, whanau, community and work. The main outcome measure is the length of time in a health facility.

Health facilities will all have at least 6 months on each arm (RACPP or ICare-RURAL POC) and the project will run for 18 months.

Summary

This quality improvement initiative plans to measure the effect of implementing a chest pain assessment pathway using a point-of-care high sensitivity troponin test in rural and community settings (rural hospitals, rural general practice and urgent care clinics) to identify patients with low probability of acute myocardial infarction. This will enable patients to receive high quality care near to the patient's home, whanau, community and work. This project will use a be a prospective randomised stepped wedge design. Facilities will be randomised into clusters and each cluster, with each site using both the current pathway and the updated chest pain pathway. The main outcome measure is the length of time in a health facility. `The quality improvement project will run for 18 months.

Justification

Clinical guidelines recommend that investigation of possible acute myocardial infarction (AMI) involves structured clinical pathways (also known as an accelerated diagnostic pathways, ADPs), which typically use laboratory-based high sensitivity cardiac troponin (hs-cTn) testing to identify patients who have a low probability of AMI.(1) These laboratory-based hs-cTn are largely unavailable in rural areas of New Zealand (NZ) where approximately 20% of non-Māori and 25% Māori live.(2–4) Instead, most rural hospitals (and some rural general practices) rely on much less precise and sensitive conventional bed-side or point-of-care (POC) troponin tests.(2,5) Therefore, ADP commonly used in metropolitan Emergency Departments (EDs) cannot be implemented in the majority of rural hospitals without adaptation. For rural places that do not have access to any POC troponin, patients who develop chest pain require lengthy and potentially expensive, transfers to distant metropolitan centres for testing, only for nearly half of these patients able to be promptly discharged once AMI is excluded.(1,5)

To address this practice gap, a rural ADP was developed (the rural accelerated chest pain pathway - RACPP), which pairs serial troponin tests(≥ 2 tests at least 2 hours apart), with an ECG and a clinical risk score.(5) None of the 1073 low-risk cases went on to suffer a major adverse cardiac events (MACE).(5) More than 40% of patients presenting with chest pain avoided transfer away from their communities, whānau and mahi for further assessment. Additionally, general practices and urgent care facilities that used the RACPP reported that the requirement for serial testing was logistically and financially problematic for both health facilities and patients. The requirement for two POC troponin tests for all patients with chest pain who use the RACPP remains a barrier to widespread adoption of the RACPP.(6)

Hs-cTn POC tests are now available, which are able to exclude AMI with a single blood test.(7–9) This will allow the RACPP to be amended to better suit rural and community settings. We estimate that implementing this single (baseline) test strategy might eliminate the requirement for a second blood test in approximately 50% of patients that present to rural health facilities with chest pain, without compromising safety. For patients with low probability of AMI that do require a second test, this can be deferred (providing it is ≥2hrs between tests).(9) This approach should better fit existing workstreams in rural hospitals,

general practice and urgent care and enable more patients to be assessed closer to their community.(10) POC hs-cTn tests may also identify a group of patients at risk of AMI that are currently being missed by conventional POC tests expediting transfer for investigation, intervention and the initiation of secondary prevention.(11)

Māori have poorer cardiovascular outcomes than non-Māori, and patients that live in rural areas do not get access to the same investigations or treatments compared to patients that live in metropolitan centres.(12–14) Consequently, the availability of POC hs-cTn in rural health facilities, has the potential to improve inequity by ensuring that the optimal investigations and interventions are provided to all patients.

The aims of this quality improvement initiative are to:
(A) implement and evaluate a pathway using POC hs-cTn in rural communities to rapidly identify low-risk patients and provide high quality care near to the patient's whanau, community and work.
(B) explore issues around the implementation of the pathway in rural facilities

Design and Methods

Participants

All people presenting to participating health facilities with recent onset symptoms that could be due to acute myocardial infarction (AMI) in whom the clinician(s) intends to investigate using a cardiac troponin

Settings

Participating health facilities will include rural hospitals as well as rural and urban general practices and urgent care clinics. All facilities will have previously implemented the rural accelerated chest pain pathway using point-of-care troponin (RACPP), which is considered the standard of care.(5)

Initial assessment of patients presenting to these facilities will generally be performed by doctors (rural hospital medicine, general practitioners, urgent care clinicians), nurse practitioners or registered nurses.

Inclusion criteria

- Adults ≥18 years old
- Assessment for possible AMI

Consecutive patients presenting to the health facilities in whom attending clinical staff order cardiac troponin test(s) because there is perceived need (based on presenting symptoms) to

investigate for possible acute myocardial infarction (AMI) will be included. In keeping with the 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain such symptoms may include (but are not limited to): Pain, pressure, tightness, or discomfort in the chest, shoulders, arms, neck, back, upper abdomen, or jaw, as well as shortness of breath and fatigue.(15)

Exclusion criteria

- ST-Segment elevation myocardial infarction (STEMI)
- Patients died in the health facility due to a non-cardiac cause

Design

This quality improvement initiative is a pragmatic multi-centre stepped-wedge cross-sectional cluster randomised trial design (Figure). This will compare usual care (RACPP) with a pathway that incorporates a high-sensitivity POC-cTn, with all sites exposed to both usual care and the intervention.

There will be six clusters (groups) of up to 5 sites each consisting of a combination of rural hospitals, general practices and urgent care clinics. Each cluster will crossover from the control period (usual care) to the intervention at 1-month intervals, with a one-month "run-in" period that is excluded from primary analysis. Each site will be exposed to the control and the intervention for at least 6-months.

This design allows for refinements in the delivery of the implementation to optimise knowledge translation. The initiative will support knowledge translation by utilising the Institute for Health Improvement's Plan-Do-Study-Act (PDSA) cycle model to facilitate introduction and to learn from changes in real-time clinical practice.

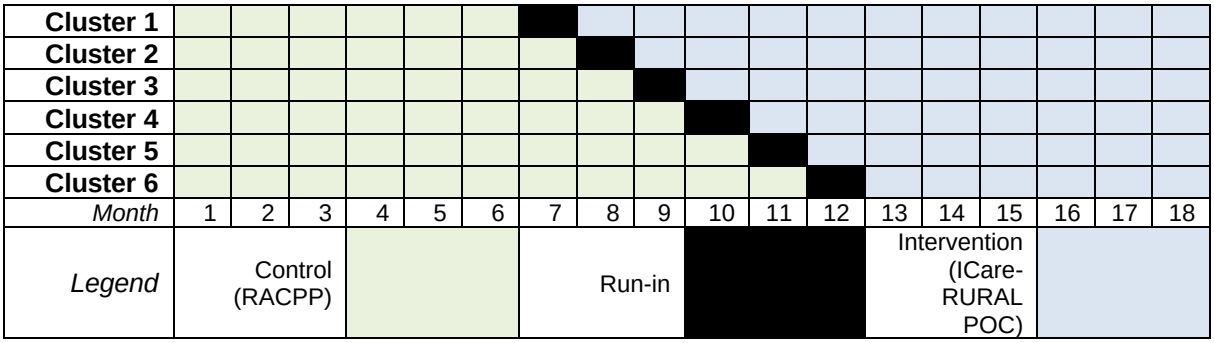

Figure 1: Stepped cluster wedge study design

Control period (usual care)

Each site will have a minimum 6-month control period prior to the intervention phase where usual care is practiced. Usual care is defined as implementing the rural accelerated chest pain pathway (RACPP), which has been proven to be safe and effective in a prospective

study with over 1000 patients enrolled. The pathway was endorsed by the NZ Cardiac Network in 2020.(5)

The RACPP uses the presence of red flags, the emergency department assessment of chest pain score (EDACS), the presence of ECG changes and two troponin concentrations at 0 and 2 hours to identify patients at low probability for AMI. The low probability pathway (Figure 2) is implemented in all facilities and allows the identification of patients who can be discharged home in rural hospital and community settings. Patients who do not have low probability of AMI are assessed using the "Not low-risk" pathway (Figure 3), which aids the identification of those that are at high-risk of AMI and is used in rural hospital settings.

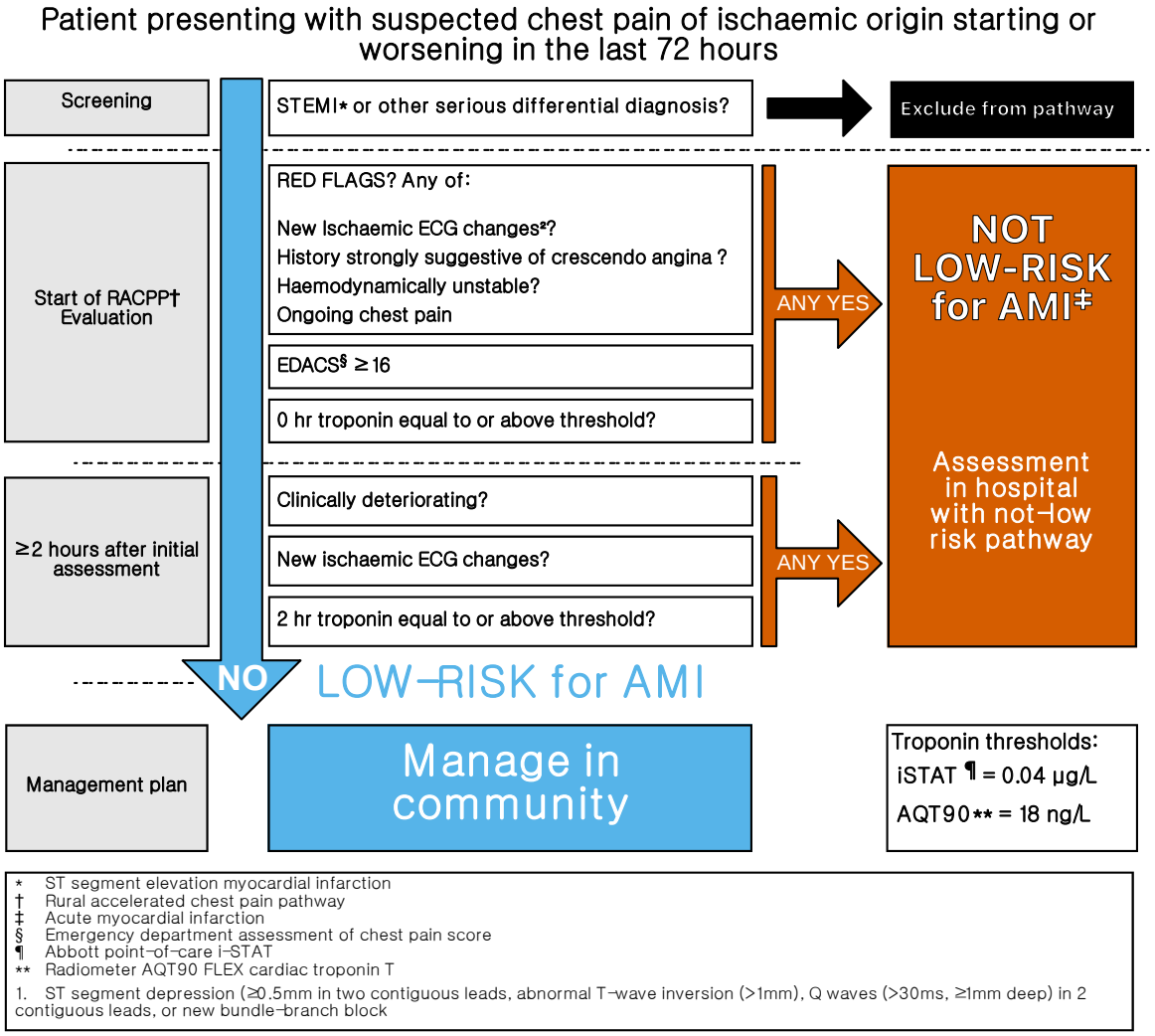

Figure 2: Rural accelerated chest pain pathway - low-risk arm

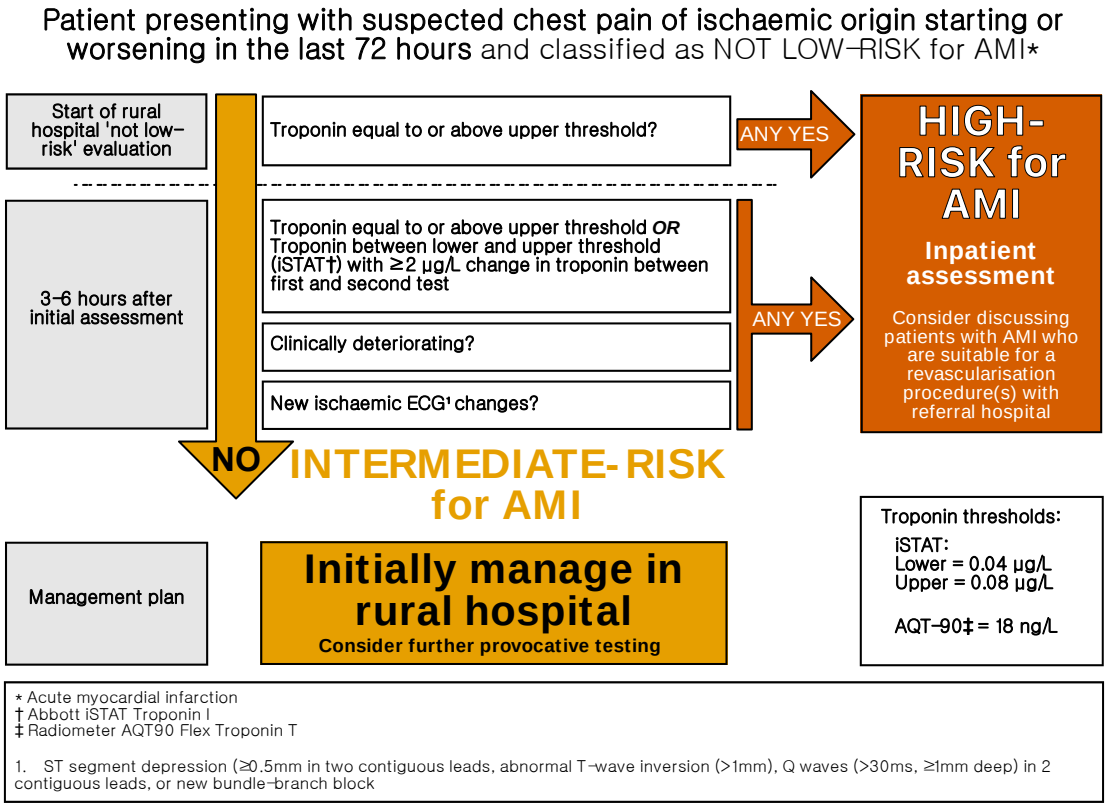

Figure 3: Rural accelerated chest pain pathway - not low-risk arm

Run-in period

The intervention phase will be preceded by a one-month 'run-in' period to allow time for training and confidence with the new intervention. "Teething" issues can be identified and can be addressed.

This period is necessarily flexible and care processes may be adjusted as this is a pragmatic quality improvement initiative, which will also assess the change management process.

The initiative team and the identified clinical lead from each site will co-develop a site-specific framework, with input from the MAG and clinical advisors, which reflects local practice and incorporates lessons learned from implementation at other sites about implementation strategies.

Intervention (implementation) period

The intervention replaces the existing POC troponin test with a high-sensitivity POC troponin test. The higher sensitivity and precision of this test allows a modification of the EDACS threshold to 21 and the opportunity to stratify patients as having low-probability of AMI after a single test, if their chest pain onset was at least 3-hours prior to the presentation.

Patients will be classified as having a low-probability of AMI and suitable for community management if all the below are true: (figure 4)

- EDACS<21,(8,9)

- There is no new ischaemia on ECG
- and either:
    a. Chest-pain onset was ≥3h prior to blood draw and the first (baseline) POC hs-cTn result was below a pre-defined rule-out threshold, or
    b. Serial POC hs-cTn results ≥2h apart are negative (below the upper-reference limit of the assay).

Patients that do not fulfil these criteria are at risk of AMI and should be transferred (if not at a hospital site) and admitted to hospital for further assessment. If there is a rise or fall in cTn of at least 20% then treatment for AMI should commence.

This pathway is designed to assess the probability of AMI and not the underlying risk of coronary artery disease. Once AMI has been excluded, the opportunity should be used to assess and reduce this risk using evidence based assessment and treatment.

The intervention will remain in place at all sites for at least 6 months.

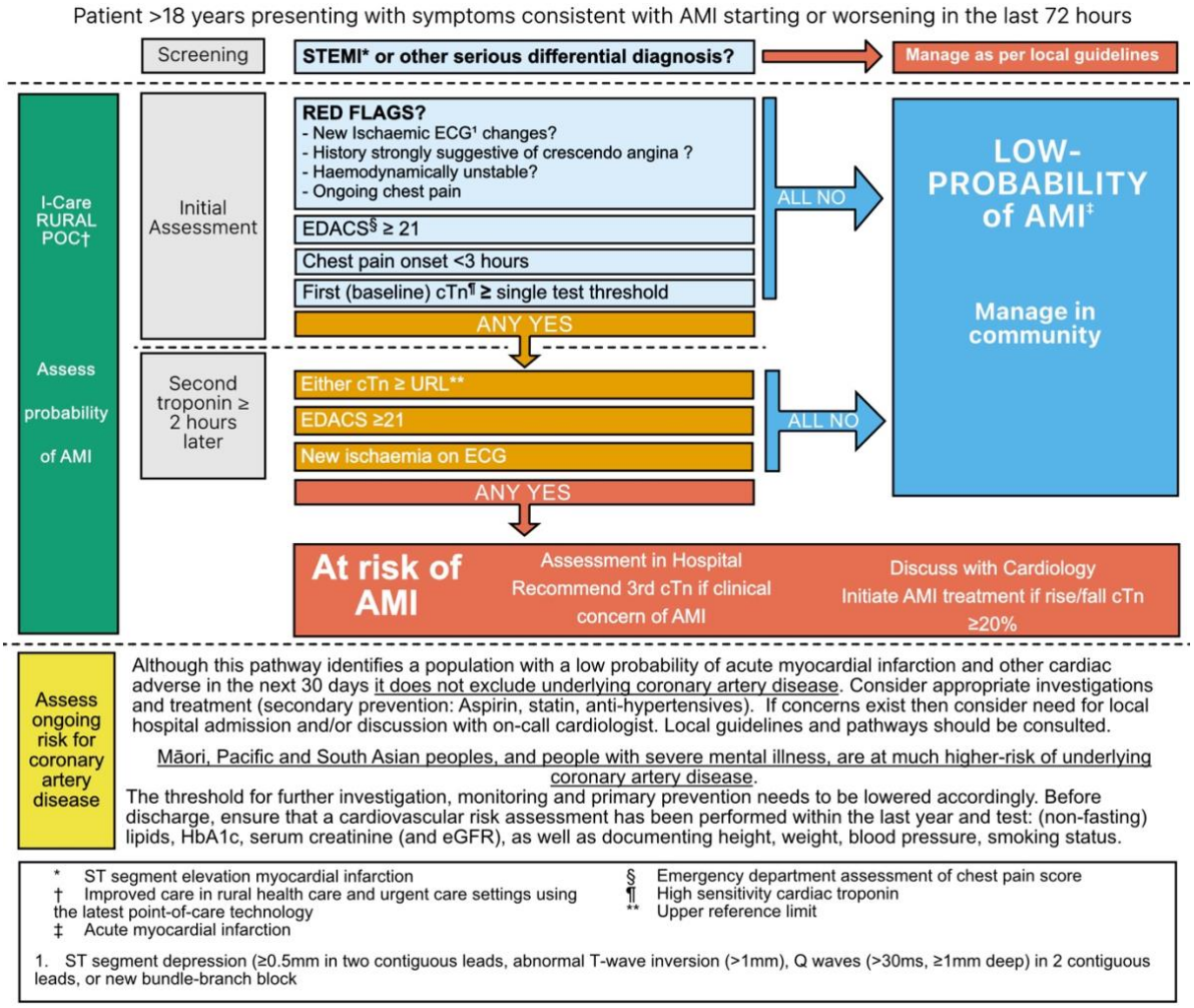

Figure 4: ICare-RURAL-POC pathway

The anticipated effect of the intervention on patient flow is in Figure 5.

Figure 5: patient flow showing difference between usual care (RACPP) and the intervention (ICare-RURAL)

The point-of-care troponin assay

The proposed POC-cTn is the Siemens Atellica VTLi hs-cTnI assay. It has an overall 99th percentile in whole blood of 23 ng/L and sex specific 99th percentiles of 27 ng/L (Males) and 18 ng/L (Females). The limit of detection (LoD) is 1.24 ng/L, 10% CV 6.7 ng/L and limit of quantitation (LoQ: 20%CV) at approximately the LoD.(16,17) The clinical safety of the assay has been determined elsewhere.(16,17) Other high-sensitivity POC assays may be used.

Follow-up

Follow-up data will be collected for patients at all sites for 6-months following the presentation of chest pain.

Site selection

Sites will be identified using existing clinical networks. All facilities will be required to be currently using the rural accelerated chest pain pathway that includes a point-of-care troponin. Thirty sites will be selected, with priority given for facilities that have catchments with a high percentage of Māori, especially those in rural areas. The Māori Advisory Group will have a pivotal role in selecting these sites.

Locality assessment will be performed by each individual site and a letter stating that each locality has the capacity to participate in the project will be obtained by the clinical or managerial lead prior to the commencement of the study.

Likely facilities:

	Facility name	Facility type	Rural/urban	Region	Anticipated volume of patients	Point of care Troponin
1.	Wairoa & Medical centre	Rural GP,Rural hospital	Rural	Central	Medium (50-150)	iSTAT
2.	Kenepuru	Urgent care	Rural	Central	High (>150)	iSTAT
3.	City med medical (Napier)	Urgent care	Urban	Central	Medium (50-150)	iSTAT
4.	Coast to Coast (Wellsford)	Rural GP,Urgent care	Rural	Northern	High (>150)	iSTAT
5.	Hokianga	Rural GP,Rural hospital	Rural	Northern	Medium (50-150)	iSTAT
6.	Shore care	Urgent care	Urban	Northern	Medium (50-150)	iSTAT
7.	Ascott White cross	Urgent care	Urban	Northern	Medium (50-150)	iSTAT
8.	Queenstown	Rural hospital	Rural	Southern	High (>150)	iSTAT
9.	Greymouth	Rural hospital	Rural	Southern	High (>150)	iSTAT
10.	Kaikoura	Rural hospital,Rural GP	Rural	Southern	Medium (50-150)	iSTAT
11.	Westport	Rural GP,Rural hospital	Rural	Southern	Low (<50)	iSTAT
12.	Angelsea	Urgent care	Urban	Southern	High (>150)	iSTAT
13.	Te Anau	Rural GP	Rural	Southern	Low (<50)	iSTAT
14.	Dunstan Hospital	Rural hospital	Rural	Southern	High (>150)	iSTAT
15.	Clutha health trust	Rural hospital,Rural GP	Rural	Southern	Medium (50-150)	iSTAT
16.	Oamaru	Rural hospital	Rural	Southern	Medium (50-150)	iSTAT
17.	Hawera	Rural hospital	Rural	Te Manawa Taki	High (>150)	iSTAT
18.	Te Kaha	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT
19.	Pihanga	Rural GP	Rural	Te Manawa Taki	Low (<50)	None
20.	The Nest	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT

21.	Coromandel Family Health	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT
22.	Kawhia Health	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT
23.	Whangamatā	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT
24.	Raglan	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT
25.	Oakura	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT
26.	Victoria Clinic	Urgent care	Urban	Te Manawa Taki	Medium (50-150)	iSTAT
27.	Te Kuiti	Rural GP,Rural hospital	Rural	Te Manawa Taki	Medium (50-150)	iSTAT
28.	Otorohanga	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT
29.	Three Rivers	Urgent care	Urban	Te Manawa Taki	Medium (50-150)	iSTAT
30.	Thames Hospital	Rural hospital	Rural	Te Manawa Taki	High (>150)	AQT90
31.	Tokoroa Hospital	Rural hospital	Rural	Te Manawa Taki	High (>150)	AQT90
32.	Taumarunui Hospital	Rural hospital	Rural	Te Manawa Taki	Medium (50-150)	AQT90
33.	The Doctors (Te Whare Hāpara)	GP/Urgent care	Urban	Tairawhiti	Low (<50)	iSTAT
34.	Health Te Aroha	Rural GP	Rural	Te Manawa Taki	Low (<50)	iSTAT

Table 1: Potential facilities and the current point-of-care troponin used

Site preparation

Each facility will receive an initiation session with a clinical member of the project team. For practical reasons this maybe virtual. This session will include, but not be limited to:

- Whakawhaungatanga
- Identification of important stakeholders at the local facility and community
- Update on the current evidence on accelerated chest pain pathways
- Explanation of quality improvement documents and materials and adaption to local site
- Demonstration and adaption of the data collection procedures to the local site
- Provision of training on:
    - Clinical use of the POC- hs-cTn
    - Quality assurance procedures with the manufacturer
    - Data collection tool
- Opportunity for questions, concern and feedback from the local team

Prior to the implementation period at each facility, local stakeholders will agree on the pathway that is to be implemented.

The process at each site may include:

(1) a workshop facilitated by a member of the investigating team,
(2) an analysis of gaps in current processes,
(3) identification of process deficiencies and areas for improvement,
(4) identification of potential barriers to change,
(5) plans to change clinical pathway and documentation,
(6) agreement on a process to ensure that change is implemented,
(7) identification of resources implications,
(8) review and reporting procedures, and
(9) identification of local champions responsible for ensuring the new pathway is put in place.

Change management of intervention and identification of barriers

The monitoring of sites and management of change at each facility will be based on the principles laid out by the Plan-Do-Study-Act (PDSA) cycle model for improvement.(18) The PDSA cycle is shorthand for testing a change—by planning it, trying it, observing the results, and acting on what is learned. This is the scientific method used for action-oriented learning.

Facilitators at each site will use a toolkit for change management based upon the PDSA cycle and the principles set out by the Institute of health care improvement (IHI).(18) As each site moves through each phase of the PDSA cycle information on issues encountered and solutions found will collated and fed back into the PDSA cycle of subsequent facilities to implement. The change management process will also be assessed using formal semi-structured qualitative interview as there is little evidence in rural areas.

Outcomes

Primary outcome

Length of stay at health facilities.

Secondary outcomes

- Length of stay of all patients not admitted to hospital
- Proportion of patients able to have AMI excluded with a single cTn result
- Length of health facility stay for patients discharged after a single cTn result
- Rate of AMI or cardiac death within 3 months and 6 months for patients identified as having low probability for AMI and not admitted to hospital
- Rate of myocardial infarction or cardiac death within 3 months and 6 months for all patients
- The proportion of patients not admitted after 1, 2, 3, 4, 5 and 6 hours for those presenting to rural hospitals
- The proportion of patients presenting to general practice and urgent care settings who are transferred for assessment at a hospital

- The time between general practice or urgent care assessment and hospital assessment
- The proportion of patients admitted to hospital
- The rate of index MI to troponin use
- The rate of troponin use (per month)
- Rate of troponin use / patient presentation (rural hospitals only)
- The diagnostic performance of the emergency department of chest pain score (EDACS) in community settings.

AMI is determined by the following ICD10 codes:

- STEMI: I21.0 or I21.1 or I21.2 or I21.3
- NSTEMI: I21.4 or I21.9 or I22.0 or I22.1 or I22.8 or I22.9.

Sensitivity analysis

- By actual times of change of practice at each site
- First presenters only
- Include the 'run-in' period within the intervention period
- Period during which there is overlap of control and run-in or intervention periods

Subgroup analysis

- Stratification by:
    - Ethnicity
    - Facility type (rural hospital, general practice, urgent care)
    - Sex
    - Type of control POC troponin assay used (Abbott i-STAT cTni; Radiometer AQT-90 FLEX cTnI)
    - Type of intervention POC troponin assay used if more than one
- Patients that would have been transferred to an urban hospital regardless of the result of the POC-cTn test.

Additional analyses

- Proportion of patients identified as low probability of AMI using a single rule-out test
- Time from presentation until blood results available

Core data collection

Patients being investigated for possible AMI will have their prospectively data entered in a secure web-based platform.

Data collection will be occur using one of two systems.

1. REDCap: Research Electronic Data Capture (REDCap) is a secure web application for building and managing online surveys and databases and is recommended for recording data, including personal information, that are covered by health information privacy principles, The Privacy Act or ethics committee specifications that

require a secure tool.(19) All REDCap data are securely stored in University of Otago servers.

2. Wayfind: Wayfind is a secure web application specifically designed to support clinical decision using defined clinical pathways. It will be customised for this quality improvement project and will be integrated into existing patients management systems and the POC device's "middleware" platforms. Data is securely stored using the Fast Healthcare Interoperability Resources (FHIR) specification in Amazon Web Services (AWS) data storage.

The National Health Index Identifier (NHI) will be used to identify linked event and outcome data in the New Zealand Ministry of Health's national collections (National minimum dataset of hospital events and mortality collection), including 30-day and 6-month mortality and presentations with AMI. Due to the delay in deaths appearing in the mortality collection, a manual process to check deaths will occur using existing patient management systems. This approach has been used successfully in previous studies.(1,5)

Additional monitoring

The change management process will be monitored closely. Any identified changes to the pathway, can be incorporated throughout the remaining sites.

Safety data will be collated from the Ministry of Health data sets every 6-months. AMI and cardiac death will be determined and all cases reviewed by the project team. A 'dashboard' will be created to track enrolment and safety data. All unexpected AMI or cardiac death will be reviewed by the project team with the Māori Advisory Group (MAG) and clinical advisors, following which a decision to halt the initiative or amend the pathway.

Patient information and consent

Clinicians will be prompted by the REDCap and Wayfind tool to alert patients that a quality improvement project is underway. If there are any queries or a patient wishes not to have their data used in the project, this can be flagged in the data collection tool and the patient will be excluded from analysis and their data deleted from the project's database.

Through REDCap and Wayfind, links to information about the project will be available in a publicly available website, including PDF infographics. This information will also be used as training material.

Consumer engagement

There has been engagement with members of the Health Quality & Safety Commission (HQSC) as well as rural Māori groups (Te Whare Taumata o Whānau Whānui), who have provided feedback on the protocol and patient information. A public website will be developed.

Clinical / Patient risk

This is a quality improvement project. The control and intervention arms both represent the current standard of care for assessing chest pain depending on the available troponin test

available. The safety and performance of the troponin tests and pathways have been documented elsewhere.(7,10,10,16) The implementation of these test will occur regardless of the existence of this project. Therefore the risk to the individual is minimal.

Analysis

Sample size determination

An average reduced LOS of ≥ 20-minute in the patients with low probability of AMI would be clinically meaningful, as this is more than the length of one consultation in general practice.

The RACPP study LOS for all low-risk patients was 3.9h and standard deviation 2.8h.(5) At an α=0.05 with a power of 90% and assuming 6 clusters, an intra-cluster correlation coefficient ρ=0.01 (small; based on the ICare-ACS study),(1) and 50% of patients being low-risk (from the RACPP study) then a sample size of 1,036 patients is required (excluding those in the run-in phase). Based on the RACPP study (3.0 patients per site, per month), with 30 sites and expecting a drop- out of sites and patients of approximately 10%, we estimate that a minimum of 13 months are required (excluding run-in period). We propose a time period of 18 months including the run-in month to roll-out and assess this initiative. The total numbers are estimated at 1,458 (or 1,377 excluding the run-in month). With an estimated 20% Māori in the trial there is adequate power (80%) to identify a 31 minute reduction in length of stay amongst Māori.

In the RACPP study, there were 0.0% (95%CI 0% to 0.3%) MACE within 30-days in the low-risk group. Therefore, the largest acceptable difference between the control arm and intervention arm will be 1% (non- inferiority margin).(20) We estimate there will be 364 patients with low-probability of AMI or cardiac death in the intervention arm, which has >95% power with one-sided alpha of 0.05 to test the hypothesis that the experimental arm is non-inferior to the control arm.

Statistical analysis

The analysis for the primary outcome length of stay (LOS) will be analysed with a generalised linear mixed model with cluster and site as fixed effects, and month of presentation of the patient and arm of the study as random effects. The beta-coefficient for Quality Improvement Arm will be presented with 95% Confidence interval. This represents the adjusted difference in LOS between arms.

The primary analysis will be based on the actual date of change of practice for each site.

Data and outcome metrics will be presented using 95% compatibility (confidence) intervals, and with p-values, s-values, and p-value and s-value graphs for the primary analysis.

Additional analysis will include calculation of the probability of AMI for those stratified to each of the low-probability and at risk of AMI groups. An updated risk stratification tool will be created using the troponin measurements and routine data collected for the ECG and EDACS. This will be created using standard regression and machine learning techniques. This will not be tested in this project and maybe used to inform future studies.

Since this is an implementation quality improvement initiative it will adhere to the Standards for Reporting Implementation studies (StaRI) when reporting results.(21)

Data management and sovereignty

Data will be collected, stored and managed informed by the principles of Māori Data Sovereignty outlined by Te Mana Rarunga: Rangatiratanga; Whakapapa; Whanaungatanga; Kotahitanga; Manaakitanga; Kaitiakitanga.(22) The Māori advisory group will provide guidance on the collection, analysis and the storage of data.

Participant's privacy and confidentiality will be respected. Identifiable participant data will be de-identified using a unique project ID. All data will be stored in password-protected files. The patient's national health index (NHI) will be used to identify outcome data within the national minimum dataset and mortality collection at 6 months. After this step has been completed, the NHI will be de-identified and unlinked from the patient record.

All data will be stored in Aotearoa NZ, either on University of Otago data servers or Amazon Web Services (expected to be in New Zealand in 2024) in accordance with the NZ Government's "Cloud first policy". De-identified data will be moved to University of Otago servers based in Ōtepoti (Dunedin) for analysis and after the project is completed, data will be stored for 10 years on secure University of Otago servers.

A full separate data management plan is include as appendix.

Linked projects

In addition to the described quality improvement initiative, there will be three separate studies connected to the implementation process.

Process evaluation

A qualitative process evaluation in line with current UK MRC complex intervention guidance on both fidelity of intervention delivery and how the intervention is delivered (context; implementation; mechanisms of impact) will be carried out.

Economic evaluation

A cost minimisation study will be performed comparing the costs of the usual practice pathway (RACPP) and the intervention (ICare-RURAL POC). This will consider costs to the patient, the health system and carbon costs.

Advisory Groups

Māori advisory group

The Māori advisory group (MAG) will be led by senior members of the project team and will include the following members who are leaders in Hauora Māori:

- Dr Rawiri Keenan
- Dr Joel Pirini
- Dr Rachel Thomson
- Professor Sue Crengle
- Dr Jason Tuhoe
- Dr Anna Rolleston
- Dr Wil Harrison

The MAG will provide guidance on all aspects of the development of the protocol, as well as the initiation of the intervention at clinical sites. They will have input into the data analysis and ensure that data sovereignty principles are upheld.

Clinical advisory group

The clinical advisory group (CAG) will be led by the principal investigator and includes clinical experts in general practice, urgent care, rural hospital medicine and laboratory science:

- Dr Jo Scott-Jones
- Geoff Herd
- Dr Raewyn Fisher

Site withdrawal

Sites may withdraw voluntarily or the principal investigator may terminate the site participation

Reasons for withdrawal

Sites are free to withdraw from participation at any time upon request

The principal investigator may terminate the site from participation if:

- The site is unable to make the change to the intervention in a reasonable time frame
- The site fails to use the point-of-care device in the manner prescribed. This would be a finding which will inform the second primary outcome (optimisation).

If any site withdrawals efforts will be made to continue to follow-up 30 day events and utilise all data collected up to the date of withdrawal.

Adverse Events (AEs)

An adverse event is any untoward or unfavourable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the project, whether or not considered related to the subject's participation in the project.

Serious Adverse Events

A serious adverse event (SAE) is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the subject at immediate risk of death from the event as it occurred)
- MACE event
- Results in a persistent or significant disability or incapacity
- Results in a congenital anomaly or birth defect

An important medical event that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

For the purpose of the evaluation of this quality improvement initiative in patients discharged from ED by the pathway any unplanned hospitalisation within 30 days for any reason related to ischemic heart disease and/or the patient's original presentation will be considered a SAE.

Time Period and Frequency for Event Assessment and Follow-Up

Unanticipated problems will be recorded. The site champions will record all reportable events with start dates occurring any time after informed consent is obtained until 30 days after the last day of study participation.

Characteristics of the event

As a pragmatic quality improvement initiative only events that the site champions deem possible, probable or definitely related to the quality improvement will be recorded. This requires a temporal relationship between the patient visit to the ED and the event.

Severity of Event

The following scale will be used to grade adverse events:
Common Terminology Criteria for Adverse Events v4.0 (CTCAE)
Publish Date: May 28, 2009

Grades

Grade refers to the severity of the AE. The CTCAE displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated;
Grade 2 Moderate; minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living (ADL);
Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL;
Grade 4 Life-threatening consequences; urgent intervention indicated;
Grade 5 Death related to AE.

Reporting of events

These will be reported to the principal investigator within 7 days of the event. Reports will include:

- Grade of event
- Date and time of ED visit
- Details of ED investigations and biochemistry
- Date and time of event
- Description of event
- The site champion's assessment of the relatedness (possible, probable, or definite) to the ED visit.

Review of events

A multi-disciplinary clinical governance committee will review any adverse events at each site. Following review events will be acted upon depending on severity and in keeping with the standard governance processes for that health institution.

References

1. Than MP, Pickering JW, Dryden JM, Lord SJ, Aitken SA, Aldous SJ, et al. ICare-ACS (Improving Care Processes for Patients With Suspected Acute Coronary Syndrome): A Study of Cross-System Implementation of a National Clinical Pathway. Circulation. 2018 Jan 23;137(4):354–63.

2. Miller R, Stokes T, Nixon G. Point-of-care troponin use in New Zealand rural hospitals: a national survey. New Zealand Medical Journal. 2019;132(1493):13.

3. Whitehead J, Davie G, de Graaf B, Crengle S, Fearnley D, Smith M, et al. Defining Rural In Aotearoa New Zealand: A Novel Geographic Classification For Health Purposes. New Zealand Medical Journal [Internet]. 2022 Aug 5 [cited 2022 Aug 6];135(1559). Available from: https://www.researchsquare.com/article/rs-817117/v1

4. Ministry of Health. Mātātuhi Tuawhenua: Health of Rural Māori. MInistry of Health. Wellington; 2012.

5. Miller R, Nixon G, Pickering JW, Stokes T, Turner RM, Young J, et al. A prospective multi-centre study assessing the safety and effectiveness following the implementation of an accelerated chest pain pathway using point-of-care troponin for use in New Zealand rural hospital and primary care settings. European Heart Journal Acute Cardiovascular Care. 2022 Apr 4;zuac037.

6. Herd G, Musaad S. Point-of-Care Testing in Rural and Remote Settings to Improve Access and Improve Outcomes. Archives of Pathology & Laboratory Medicine. 2020 Nov 25;

7. Carlton E, Greenslade J, Cullen L, Body R, Than M, Pickering JW, et al. Evaluation of High-Sensitivity Cardiac Troponin I Levels in Patients With Suspected Acute Coronary Syndrome. JAMA Cardiology. 2016 Jul 1;1(4):405.

8. Pickering JW, Young JM, George PM, Watson AS, Aldous SJ, Troughton RW, et al. Validity of a Novel Point-of-Care Troponin Assay for Single-Test Rule-Out of Acute Myocardial Infarction. JAMA Cardiology [Internet]. 2018 Oct 17 [cited 2018 Nov 1]; Available from: http://cardiology.jamanetwork.com/article.aspx?doi=10.1001/jamacardio.2018.3368

9. Young JM, Sage JN, Pickering JW, Bannister L, Aldous S, George PM, et al. Next-Day Troponin Tests in Real-World Implementation of Baseline Troponin Rule-Out of Myocardial Infarction Demonstrates Minimal Delayed Troponin Rises. Circulation. 2021 Jan 12;143(2):202–4.

10. Pickering JW, Than MP, Cullen L, Aldous S, ter Avest E, Body R, et al. Rapid Rule-out of Acute Myocardial Infarction With a Single High-Sensitivity Cardiac Troponin T Measurement Below the Limit of Detection: A Collaborative Meta-analysis. Annals of Internal Medicine. 2017 May 16;166(10):715.

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

12. Lee S, Miller R, Lee M, White H, Kerr AJ. Outcomes after ST-elevation myocardial infarction presentation to hospitals with or without a routine primary percutaneous coronary intervention service (ANZACS-QI 46). New Zealand Medical Journal. 2020;133(1524):18.

13. Grey C, Jackson R, Wells S, Marshall R, Mehta S, Kerr AJ. Ethnic differences in case fatality following an acute ischaemic heart disease event in New Zealand: ANZACS-QI 13. European Journal of Preventive Cardiology. 2016 Nov;23(17):1823–30.

14. Mazengarb J, Grey C, Lee M, Poppe K, Mehta S, Harwood M, et al. Inequity in one-year mortality after first myocardial infarction in Maori and Pacific patients: how much is associated with differences in modifiable clinical risk factors?(ANZACS-QI 49). The New Zealand Medical Journal (Online). 2020;133(1521):40–5.

15. Gulati Martha, Levy Phillip D., Mukherjee Debabrata, Amsterdam Ezra, Bhatt Deepak L., Birtcher Kim K., et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain. Journal of the American College of Cardiology. 2021 Nov 30;78(22):e187–285.

16. Gunsolus IL, Schulz K, Sandoval Y, Smith SW, Lindgren B, Okeson B, et al. Diagnostic performance of a rapid, novel, whole blood, point of care high-sensitivity cardiac troponin I assay for myocardial infarction. Clinical Biochemistry. 2022 Jul;105–106:70–4.

17. Apple FS, Schulz K, Schmidt CW, van Domburg TSY, Fonville JM, de Theije FK. Determination of sex-specific 99th percentile upper reference limits for a point of care high sensitivity cardiac troponin I assay. Clinical Chemistry and Laboratory Medicine (CCLM). 2021 Aug 26;59(9):1574–8.

18. Institute for Healthcare Improvement. Model for Improvement [Internet]. 2022 [cited 2022 Sep 16]. Available from: https://www.ihi.org/resources/Pages/HowtoImprove/default.aspx

19. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. Biomed Inform. 2009 Apr;42(2):377–81.

20. Than M, Herbert M, Flaws D, Cullen L, Hess E, Hollander JE, et al. What is an acceptable risk of major adverse cardiac event in chest pain patients soon after discharge from the Emergency Department? International Journal of Cardiology. 2013 Jul;166(3):752–4.

21. Pinnock H, Barwick M, Carpenter CR, Eldridge S, Grandes G, Griffiths CJ, et al. Standards for Reporting Implementation Studies (StaRI) Statement. BMJ. 2017 Mar 6;i6795.

22. Te Mana Parunga. Principles of Māori Data Sovereignty: Brief #1 [Internet]. Te Mana Parunga: Māori Data Soverignty Netowrk; 2018 [cited 2021 Nov 22]. Available from: https://static1.squarespace.com/static/58e9b10f9de4bb8d1fb5ebbc/t/5bda208b4ae237cd89ee16e9/1541021836126/TMR+Māori+Data+Sovereignty+Principles+Oct+2018.pdf