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

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Aims
Most rural hospitals and general practices in New Zealand (NZ) are reliant on point-of-care troponin. A rural accelerated chest pain pathway (RACPP), combining an electrocardiogram (ECG), a structured risk score (Emergency Department Assessment of Chest Pain Score), and serial point-of-care troponin, was designed for use in rural hospital and primary care settings across NZ. The aim of this study was to evaluate the safety and effectiveness of the RACPP.

Methods and results
A prospective multi-centre evaluation following implementation of the RACPP was undertaken from 1 July 2018 to 31 December 2020 in rural hospitals, rural and urban general practices, and urgent care clinics. The primary outcome measure was the presence of 30-day major adverse cardiac events (MACEs) in low-risk patients. The secondary outcome was the percentage of patients classified as low-risk that avoided transfer or were eligible for early discharge. There were 1205 patients enrolled in the study. 132 patients were excluded. Of the 1073 patients included in the primary analysis, 474 (44.0%) patients were identified as low-risk. There were no [95% confidence interval (CI): 0–0.3%] MACE within 30 days of the presentation among low-risk patients. Most of these patients (91.8%) were discharged without admission to hospital. Almost all patients who presented to general practice (99%) and urgent care clinics (97.6%) were discharged to home directly.

Conclusion
The RACPP is safe and effective at excluding MACEs in NZ rural hospital and primary care settings, where it can identify a group of low-risk patients who can be safely discharged home without transfer to hospital.
Graphical Abstract

**Aim:** To evaluate the safety and effectiveness of the rural accelerated chest pain pathway (RACPP) adapted for point-of-care troponin.

1073 patients

- Rural Hospitals 80%
- GP 16%
- Urgent Care 4%

27 locations

474 low-risk

- F: 60%
- M: 40%
- 55 years (13)

599 not-low-risk

- M: 61%
- F: 41%
- 70 years (12)

Major Adverse Cardiac Events (MACE) in low-risk patients

- Overall 91.8%
- GP 99.0%
- Rural Hospitals 88.8%
- Urgent Care 97.6%

Majority of low-risk patients discharged or avoided transfer to hospital
Introduction

Chest pain is a common reason for patients to access healthcare, accounting for up to 10% of non-injury-related presentations to emergency departments (EDs) and 1–3% of general practice (GP) presentations. While fewer than 20% of these patients will have a final diagnosis of acute myocardial infarction (AMI), the potential consequences of missing AMI typically prompts a cautious approach to the assessment of chest pain. Historically, this has led to prolonged ED stays for observation and serial investigations.

Accelerated diagnostic chest pain pathways (ADPs), typically combine a clinical risk score, electrocardiogram (ECG), and cardiac troponin, and have been developed to facilitate the rapid identification of low-risk patients who can be safely discharged without the need for further in-hospital assessment.

In metropolitan EDs, ADPs have been shown to increase the proportion of chest pain patients discharged within 6 h from 8.3 to 18.4%, with no increase in major adverse cardiac events (MACEs).

Approximately 20% of New Zealanders live in rural and remote areas and have limited access to metropolitan EDs and central laboratory services. When patients in these communities develop chest pain, their initial assessment is frequently undertaken in a nearby rural hospital or by a local GP.

In New Zealand (NZ), 65% of rural hospitals lack timely access to laboratory-based troponin assays and instead rely on existing point-of-care troponin (POC-cTn) assays. Similarly, the vast majority of rural GPs also lack ready access to laboratory-based troponin with a small number able to access POC-cTn. In NZ, the available POC-cTn assays are less precise and have lower clinical sensitivity than laboratory troponin assays.

While all of NZ’s metropolitan EDs have adopted ADPs that use highly sensitive troponin (with good analytical precision), these cannot be directly translated into rural contexts without specific adaptation to account for the use of POC-cTn. There are no point-of-care high-sensitivity troponin assays currently available for clinical use in NZ. To date, many of the rural hospitals reliant on POC-cTn have employed a variety of unstructured and unvalidated strategies to exclude AMI.

To fill the practice gap a cross-specialty panel of experts modified existing metropolitan-based ADP for rural primary care and hospital settings using POC-cTn and developed the rural accelerated chest pain pathway (RACPP). A pilot implementation study in rural general practice demonstrated the feasibility and potential efficacy of the RACPP. Hospital admissions were avoided by 61.7% of the patients presenting with chest pain and there were no MACEs in the 111 patients classified as low-risk and managed in the community.

The aim of this study is to evaluate the safety and effectiveness of the RACPP in a larger cohort of patients at multiple rural hospital and primary care sites across NZ.

Methods

Study design

A prospective multi-centre evaluation of the safety and effectiveness following implementation of the RACPP was undertaken between 1 July 2018 and 31 December 2020. The full study protocol has been published elsewhere.

Setting and location(s)

All the study sites were within NZ and included rural hospitals, general practices, and urgent care clinics. All sites were reliant on point-of-care troponin at least some of the time. The sites were deliberately chosen to represent the diversity of rural communities and their health services. The rural study sites were at least 45 min (up to 4 h 20 min) drive from the nearest metropolitan hospital with specialist care and central laboratory services.

Most sites provide 24-h on-call or on-site care (see Supplementary material online, Table S1). New Zealand rural hospitals have diverse locations, sizes, patient demographics, and resources. They are staffed by generalist doctors with broad scopes of practice who often work in both hospital and primary care settings. Sites were given education, training, and support to implement the pathway by the study authors (R.M., M.T., G.N., and M.S.).

Participants

Inclusion criteria

All patients aged >18 years were included if they:

1. had chest pain that the treating clinician considered could be due to cardiac ischaemia or AMI that began or worsened within the last 72 h and
2. would have ordinarily required transfer for an urgent hospital-based assessment if presenting to a primary care setting (GP or urgent care).

Exclusion criteria

Patients were excluded from the RACPP if they:

1. presented with ST-segment elevation myocardial infarction (STEMI),
2. a proven or suspected non-coronary artery pathology cause of the chest pain,
3. required transfer to a metropolitan hospital regardless of the result of the RACPP due to other medical conditions, or
4. had an anticipated problem with follow-up (e.g. overseas tourist leaving within 30 days).

These exclusion criteria are consistent with other studies.

Point-of-care troponin

Manufacturer’s reported analytical characteristics

Two POC-cTn assays were used:

1. Abbott iSTAT cTnI (iSTAT) (IL, USA): The upper reference limit (URL) based at 99th percentile 0.08 μg/L, limit of blank = 0.02 μg/L. The coefficient of variation (CV) at the 99th percentile was 16.5%.

2. Radiometer AQ-ST FLEX cTnT (AQ-T90) (Bronshøj, Denmark): URL = 0.17 μg/L (17 ng/L), limit of detection = 0.008 μg/L. The CV at the 99th percentile was 5.2%.

The manufacturers of the POC-cTn installed the necessary hardware, training, and certified competency for users (pre-dominantly nurses) of the devices. Ongoing quality control included daily electronic and liquid quality control sampling.

Rule-out thresholds for the rural accelerated chest pain pathway

For the iSTAT: patients were considered low-risk if the troponin concentration was below a decision-making threshold of 0.04 μg/L (lower rule-out threshold). Compared with the 99th percentile, this lower threshold improves the clinical sensitivity of the iSTAT cTnI, and was used in the pilot study and is consistent with guidelines. Patients were
considered high-risk if they had (i) any troponin concentration above the URL (0.08 μg/L) or (ii) a troponin concentration $\geq 0.04$ μg/L but $<0.08$ μg/L with a difference between the first and second concentrations of $\geq 0.02$ μg/L.\textsuperscript{10}

For the AQT90, there was a single decision-making threshold at 18 ng/L.\textsuperscript{10,20}

**The rural accelerated chest pain pathway**

Identification and management of patients categorized as:

**Low-risk**

Patients were defined as low-risk if they met all the following criteria (Figure 1):

1. No ‘red flags’ (crescendo angina, haemodynamic instability, or ongoing chest pain),
2. The absence of potentially significant ECG changes suggestive of cardiac ischaemia at 0 and 2 h,
3. Emergency Department Assessment of Chest Pain Score (EDACS) $<16$\textsuperscript{16,22} and
4. Serial point-of-care troponin concentrations below the lower rule-out threshold at 0 and 2 h.

If all criteria were met the patient was eligible to be discharged home. Clinicians were encouraged to arrange further out-patient testing or cardiology referral based on individual patient factors and local guidelines.

**Not low-risk**

Patients who did not fulfil all the low-risk criteria entered the not low-risk arm of the pathway. Patients that presented to primary care settings were transferred to their usual referral centre and those that presented to rural hospitals were admitted to that facility (Figure 2).

**Follow-up**

Patients were followed up 30 days after their presentation. Health events, based on International Classification of Diseases, 10th Revision (ICD-10) codes, were collected from the National Minimal Dataset of
public hospital admissions, NZ Ministry of Health (MOH). Mortality data were retrieved from the National Mortality Collection (MOH). Events were linked using a unique national health identifier that is assigned to all people who access publicly funded healthcare in NZ and is used throughout NZ's health system.

Data collection

Data were collected from participating urgent care clinics and general practices using an electronic template developed for the practice's patient management system. In rural hospitals, data were entered into a customized form using the Research Electronic Capture (REDCap) database. All REDCap data were stored securely on University of Otago servers.

Outcome measures

The primary outcome was the presence of a 30-day MACE in patients who were identified as low-risk by the accelerated pathway. MACE was defined as 'death, cardiac arrest, emergency revascularization procedure, cardiogenic shock, ventricular arrhythmia, ventricular fibrillation, high-degree atrio-ventricular block needing intervention, or acute myocardial infarction'. Relevant ICD-10 codes are shown in Supplementary material online, Table S2.

Secondary outcome measures considered the effectiveness of the pathway and included (i) the percentage of low-risk patients who were able to be immediately discharged from either primary healthcare settings or rural hospital facilities after their assessment and (ii) the percentage of patients in the group identified as not low-risk who developed a 30-day MACE.

Sample size

A 30-day MACE rate of <1% was chosen as an acceptable threshold to demonstrate the safety of an ADP based on consensus opinion from the NZ Cardiac Network (NZCN) and a published survey. The NZCN is a national multi-disciplinary clinical stakeholder network endorsed by the NZ MOH, established with the goal of ensuring 'equity of access to high quality cardiac services for all New Zealanders'. Assuming a 30-day MACE rate of 1%, 410 low-risk patients would generate a 95% confidence interval (95% CI) between 0.27 and 2.5%. The NZCN agreed that this sample size would be sufficient for them to endorse the RACPP and recommend its use as a national clinical practice guideline if the rate was <1%. An estimated total sample size of 1000 patients was considered necessary to ensure inclusion of at least 410 patients at low-risk of developing MACE.

Statistical analyses

All data management and statistical analysis were performed using R version 4.1.1 (2021-10-8). Descriptive analyses were presented using mean and standard deviation (SD) or median and interquartile range for continuous variables. Frequency and percentage were presented for categorical variables. Patients were excluded from the primary analysis if they were managed as low-risk but the protocol was breached by clinicians either (i)

Figure 2 Not low-risk arm of the rural accelerated chest pain pathway.
ordered only a single troponin test or (ii) the interval between troponin tests was <120 min. The excluded patients were analysed separately.

The percentages of patients identified as low-risk with a 30-day MACE and those able to be immediately discharged from either primary healthcare or rural hospital facilities after their assessment (secondary outcomes) were calculated. The percentage of not low-risk patients with MACE was also determined.

Sensitivity, specificity, and positive and negative predictive values as well as likelihood ratios were determined with a 30-day MACE as the reference standard and the risk determined by the pathway (low- or not low-risk) as the ‘test’.

For each outcome measure, a 95% CI was calculated.

Ethics
The Health and Disability Ethics Committee approved the protocol as an Audit-Related Activity (16/CEN/107/AM03). As this was a study of the implementation of an evidence-based pathway, patient consent was not required, although patients were informed about the study. Consultation with indigenous Māori was undertaken via the University of Otago Ngāi Tahu Research Consultation Committee.

Results
There were 1205 patients enrolled in the study from 29 study sites between 1 July 2018 and 31 December 2020 (Figure 3). Most patients presented to rural hospitals (915/1205, 75.9%) with the remainder presenting to general practice (243/1205, 20.2%) or urgent care clinics (47/1205, 3.9%).

There were 132 (11.0%) patients excluded from the analysis. Three patients were excluded from the pathway due to either STEMI (2/132, 1.5%) or because the clinician thought the patient’s presentation had a non-coronary cause (1/132, 0.8%). The remaining 129 patients were excluded retrospectively from the primary analysis due to protocol breaches, either the failure to (i) collect a second troponin (88/132, 66.7%) or (ii) wait the minimum 2 h between tests (41/132, 31.1%). Therefore, 1073 patients were included in the primary analysis. The mean age of the participants was 63 years (SD: 15 years) and approximately half the patients (515/1072, 48.0%) were female. Most patients were NZ European (822/1073, 77.0%) with 15.0% (158/1073) identifying as NZ Māori. The median time from pain onset to assessment was 4 h and 36 min (interquartile range: 2–14 h and 30 min). Further demographic information is presented in Table 1.

There were 474 patients (474/1073, 44.2%) who were identified and managed as low-risk for AMI. The remainder (599/1073, 63.8%) were not low-risk and further classified as intermediate-risk (363/599, 60.6%) or high-risk (236/599, 39.3%).

Primary outcome
No patient identified and managed as low-risk had a MACE within 30 days of presentation (0/474, 0%; 95% CI: 0–0.3%).

Secondary outcomes
Disposition for low-risk patients
Most patients managed as low-risk (435/474, 91.8%; 88.8–93.9%) were discharged without hospital admission. When considered by facility type, 293 patients (293/330, 88.8%; 84.9–91.9%) were discharged after their initial assessment from rural hospitals, while nearly all patients who presented to general practice (101/102, 99.0%; 94.7–99.8%) and urgent care clinics (41/42, 97.6%; 87.7–99.9%) were discharged home.
Major adverse cardiac events in not low-risk patients

There were 138 (13.0%) patients with a 30-day MACE with just over half the patients identified as high-risk (124/236, 52.5%) and a minority (14/363, 3.9%) as intermediate-risk. Most MACEs (102/138, 73.9%) occurred during the index admission. The majority of patients with MACE had an ICD-10 code of AMI (125/138, 90.6%) and more than a third of such patients received an emergency revascularization procedure (51/138, 37.0%). There were three deaths (3/138, 2.2%) recorded within 30 days of the chest pain presentation.

Among patients who experienced a MACE, 23.2% (32/138) had an EDACS of ≤15, more than two-thirds (95/138, 68.8%) had an ECG without ischaemic features and 19 (13.8%) had a troponin that was below the decision-making threshold (Figure 4).

Four (3%) of the 132 patients who were excluded from the primary analysis experienced MACE. These four patients all received appropriate treatment (details are presented in Supplementary material online, Table S3).

Sensitivity and specificity

The sensitivity, negative predictive value, and negative likelihood ratio of the pathway for detecting a 30-day MACE were 100% (97.3–100%), 100% (99.2–100%), and 0 (not able to estimate a CI), respectively. The specificity, positive predictive value, and positive likelihood ratio were 50.7% (47.5–53.9%), 23.0% (19.8–26.6%), and 2.0 (1.9–2.2) respectively. The diagnostic performance of each component of the pathway is presented in Supplementary material online, Table S4.

Discussion

This study has demonstrated that the RACPP, incorporating currently available POC-cTn, ECG, and EDACS, is safe and effective in rural and primary care settings. There was no MACEs within 30 days of presentation recorded in the 474 patients (44.2% of all presenting patients) that were assessed and treated as low-risk. Almost all these

| Characteristic | Low-risk, n = 474 | Not low-risk, n = 599 | Overall, n = 1073 |
|---------------|-----------------|-------------------|---------------|
| Age (years), mean (standard deviation) | 55 (13) | 70 (12) | 63 (15) |
| Sex, n (%) | | | |
| Female | 284 (60) | 231 (39) | 515 (48) |
| Male | 190 (40) | 368 (61) | 558 (52) |
| Ethnicity, n (%) | | | |
| New Zealand European | 323 (68) | 499 (83) | 822 (77) |
| New Zealand Maori | 96 (20) | 62 (10) | 158 (15) |
| Cook Island Maori | 10 (2.1) | 4 (0.7) | 14 (1.3) |
| Other/unstated | 45 (9.4) | 34 (5.7) | 79 (7.4) |
| Assays used, n (%) | | | |
| Radiometer AQT-90 Flex Troponin T | 112 (24) | 188 (31) | 300 (28) |
| Abbott iSTAT cardiac troponin I | 362 (76) | 411 (69) | 773 (72) |
| Location category, n (%) | | | |
| General practice | 102 (22) | 65 (11) | 167 (16) |
| Rural hospital | 330 (70) | 533 (89) | 863 (80) |
| Urgent care | 42 (8.9) | 1 (0.2) | 43 (4.0) |
| Clinical factors | | | |
| Hypertension, n (%) | 164 (35) | 337 (56) | 501 (47) |
| Dyslipidaemia, n (%) | 105 (22) | 216 (36) | 321 (30) |
| Diabetes, n (%) | 48 (10) | 118 (20) | 166 (15) |
| Current smoker, n (%) | 88 (19) | 68 (11) | 156 (15) |
| Family history of pre-mature coronary artery disease, n (%) | 94 (20) | 56 (9.3) | 150 (14) |
| Obesity, n (%) | 44 (9.3) | 72 (12) | 116 (11) |
| Emergency Department of Chest Pain Score (EDACS), median [interquartile range (IQR)] | 10 (7, 13) | 19 (16, 22) | 14 (10, 19) |
| Time of pain onset to assessment (h:min), median (IQR) | 4:36 (2:00, 14:30) | 4:20 (2:08, 10:09) | 4:30 (2.04, 12:07) |
| Time between first and second troponin (h:min), median (IQR) | 2:13 (2:0, 3:00) | 3:97 (2:20, 4:19) | 2:45 (2:04, 3:42) |
low-risk patients (91.8%) were discharged home, avoiding transfer or admission to hospital.

These findings are important because to date, most patients living in NZ’s rural areas who suffer an episode of chest pain have not been able to access modern evidence-based ADPs, unless they travelled to a distant metropolitan ED. Reducing hospital admissions and transfers to distant EDs (40.3% of patients in this study) have benefits for both patients (travel and time away from home or work) and to the healthcare system (fewer ambulance transfers and hospital assessments).

Strengths and limitations
A key strength of this study is the number, distribution, and diversity of study sites with most rural areas in NZ represented. It is significant that nearly 20% of the low-risk population identified as Māori (the indigenous peoples of NZ). Māori has poorer cardiovascular outcomes than New Zealanders of European descent and compared with metropolitan areas, a higher proportion of the rural population is Māori. Ensuring that the RACPP is safe for rural Māori patients is therefore crucial.

This study was a pragmatic ‘real-world’ evaluation following the implementation of the RACPP, providing reassurance that the RACPP performs in routine clinical practice. There are some weaknesses with this real-world approach. The final decision to include patients in the study was left to the judgement of participating clinicians. It is likely that some patients judged to be high-risk, were referred directly to hospital, or that very low-risk patients were managed using clinical gestalt. The number of these patients not enrolled in the study is unknown; however, given the results of this study are similar to other published literature, the effect maybe small.

Point-of-care testing was already being undertaken at the majority of the study sites and the researchers had no direct control of the quality standards being employed. However, quality control procedures were in place at all sites, mitigating this risk.

The clinical score used in this study (EDACS) was initially derived and validated in metropolitan emergency departments and has not yet been optimized in a population outside of this context. It is possible that the clinical risk was overestimated by the pathway in this study population. While this may have increased the number of patients who were identified as not low-risk and potentially referred to or admitted to hospital unnecessarily, the safety of the pathway will not have been affected.

It is possible that re-presentation with MACEs may have occurred after the 30-day follow-up period this study used; however, a 30-day MACE is a common outcome used in other similar studies.
Implications for clinical practice

To our knowledge, this is the first large study to assess the implementation of an ADP in a rural and general practice population. The safety of ADPs that incorporate high-sensitivity laboratory troponin assays is well established. Although POC-cTn has poor sensitivity for detecting AMI in isolation, its safety when combined with clinical assessment has previously been demonstrated in metropolitan EDs. However, it is not possible to directly translate this evidence to the NZ rural context because of the low-resource environment (a feature of rural and primary care clinical settings), as well as possible differences in the available troponin assays, the sociodemographic profile and underlying risk of ischaemic heart disease in the patient populations. This study and the preceding pilot have demonstrated that the safety of the RACPP is similar to that achieved by ADPs that use more sensitive troponin assays in metropolitan EDs. Rural clinicians can therefore identify and discharge low-risk chest pain patients with confidence that the RACPP has been validated in their context.

Acceptance of these results by the NZCN and endorsement of the RACPP as a clinical practice guideline should ensure more locations can implement the pathway successfully. Current funding models could prove a barrier to widespread adoption of the RACPP, despite the likely savings to both the health system and patients. The requirement for two blood tests 2 h apart within the low-risk arm of the RACPP places a significant time and financial burden on primary care providers, which in most instances is passed on to patients. While ED visits are free in NZ, many rural patients face a co-payment when accessing local GP or urgent care facilities. This represents an obvious inequity in the way that healthcare is delivered to many rural NZ communities. If, as anticipated, a high-sensitivity POC-cTn becomes available in NZ, a second test may no longer be necessary, with initial clinical studies of ED patients showing comparable diagnostic performance of these assays to laboratory-based tests. Adoption of these high-sensitivity POC-cTn may reduce the time and costs associated with the current generation of POC-cTn and incentivise the adoption of future rural chest pain assessment pathways, including in other pre-hospital settings.

Nearly 11% of patients were excluded due to protocol breaches either because only one troponin was drawn or there was an inadequate amount of time between samples (although all MACEs in this group were identified and managed appropriately). The results of this study highlight the important role all three components (ECG, EDACS, and POC-cTn) of the RACPP have in ensuring MACE is not missed. We do not know the reasons why clinicians may have chosen to over-ride the protocol. A qualitative study on the implementation of chest pain pathways in rural settings would allow this to be explored in more depth.

Additional opportunities for research include (i) refining a structured clinical assessment tool specifically for rural and general practice populations, (ii) evaluating a single-test pathway when high-sensitivity POC-cTn assays become available, and (iii) undertaking a formal economic evaluation of ADPs in a rural context. International evidence of a successful implementation of an ADP in a general practice and rural context is needed to ensure that this ADP can be applied outside of NZ.

Conclusion

This study has demonstrated the safety and efficacy of an accelerated chest pain pathway incorporating a point-of-care troponin in rural and primary care settings. The outcomes of RACPP are at least equivalent to those achieved with the metropolitan-based ADPs that use high-sensitivity troponin assays.

Authors’ contribution

All authors had a role in study design, planning, grant application submission, conducting the study, and authoring this paper. R.M. was the lead investigator and author. Project management was performed by A.W., J.Y., and T.N. Data assimilation and management was performed by R.M. Data analysis was performed by R.M., R.M.T., and J.W.P. Data interpretation was performed by all authors. Specialist input was provided: cardiology (G.D.), rural health and primary care (R.M., G.N., and M.S.), emergency medicine (M.T. and M.G.), statistics (R.T. and J.W.P.), chemical pathology (S.D.T. and P.G.). R.M. is the guarantor of this manuscript and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted; and any discrepancies from the study as planned have been explained.

Supplementary material

Supplementary material is available at European Heart Journal: Acute Cardiovascular Care.

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Data availability

Relevant de-identified data will be provided on reasonable request to the corresponding author (R.M.).
