Original Investigation

A 2-Hour Diagnostic Protocol for Possible Cardiac Chest Pain in the Emergency Department
A Randomized Clinical Trial

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**IMPORTANCE**
Patients with chest pain represent a high health care burden, but it may be possible to identify a patient group with a low short-term risk of adverse cardiac events who are suitable for early discharge.

**OBJECTIVE**
To compare the effectiveness of a rapid diagnostic pathway with a standard-care diagnostic pathway for the assessment of patients with possible cardiac chest pain in a usual clinical practice setting.

**DESIGN, SETTING, AND PARTICIPANTS**
A single-center, randomized parallel-group trial with blinded outcome assessments was conducted in an academic general and tertiary hospital. Participants included adults with acute chest pain consistent with acute coronary syndrome for whom the attending physician planned further observation and troponin testing. Patient recruitment occurred from October 11, 2010, to July 4, 2012, with a 30-day follow-up.

**INTERVENTIONS**
An experimental pathway using an accelerated diagnostic protocol (Thrombolysis in Myocardial Infarction score, 0; electrocardiography; and 0- and 2-hour troponin tests) or a standard-care pathway (troponin test on arrival at hospital, prolonged observation, and a second troponin test 6-12 hours after onset of pain) serving as the control.

**MAIN OUTCOMES AND MEASURES**
Discharge from the hospital within 6 hours without a major adverse cardiac event occurring within 30 days.

**RESULTS**
Fifty-two of 270 patients in the experimental group were successfully discharged within 6 hours compared with 30 of 272 patients in the control group (19.3% vs 11.0%; odds ratio, 1.92; 95% CI, 1.18-3.13; \( P = .008 \)). It required 20 hours to discharge the same proportion of patients from the control group as achieved in the experimental group within 6 hours. In the experimental group, 35 additional patients (12.9%) were classified as low risk but admitted to an inpatient ward for cardiac investigation. None of the 35 patients received a diagnosis of acute coronary syndrome after inpatient evaluation.

**CONCLUSIONS AND RELEVANCE**
Using the accelerated diagnostic protocol in the experimental pathway almost doubled the proportion of patients with chest pain discharged early. Clinicians could discharge approximately 1 of 5 patients with chest pain to outpatient follow-up monitoring in less than 6 hours. This diagnostic strategy could be easily replicated in other centers because no extra resources are required.

**TRIAL REGISTRATION**
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Patients with symptoms suggestive of acute coronary syndromes (ACS) compose approximately 5% to 10% of annual presentations to emergency departments (EDs) and up to 25% of hospital admissions. Assessment and safe disposition of these patients is a major challenge for clinicians because a missed diagnosis of ACS can lead to death or other adverse outcomes. International guidelines for the investigation of ACS recommend serial measurements of contemporary (non-high sensitivity) cardiac troponin during 6 to 12 hours from the time of symptom onset or presentation to the ED. Consequently, safe patient workup generally requires considerable time, even though less than 25% of patients with chest pain finally receive diagnoses of ACS. A combination of the high numbers of patients assessed and prolonged observation contributes to ED overcrowding, which is associated with high costs and adverse patient outcomes, including increased mortality. A study of more than 14 million patients showed significantly worse outcomes for patients staying in the ED longer than 6 hours compared with those who remain only 1 hour. A reliable diagnostic strategy is needed using serial troponin testing over a short time frame to identify a low-risk patient group who could avoid prolonged observation.

Diagnostic strategies incorporating point-of-care panels or sensitive and highly sensitive troponins have been shown to identify subgroups of low-risk patients with chest pain who may be eligible for early discharge from the hospital with high sensitivities and negative predictive values. The observational ADAPT study described a 2-hour accelerated diagnostic protocol (ADP) combining 0- and 2-hour cardiac troponin tests, electrocardiograms (ECGs), and an adaptation of the Thrombolysis in Myocardial Infarction (TIMI) score. The ADP classified 20% of chest pain presentations as low-risk with a subsequent 0.3% rate of short-term adverse events. These low-risk patients might therefore be discharged early to outpatient follow-up investigation or proceed more quickly to further inpatient testing, potentially shortening hospital length of stay. The efficacy of implementing this type of intervention has not been evaluated in a patient population.

Clinicians do not always adhere to clinical pathways or guidelines. For example, a study including 117 EDs found that international guidelines for the investigation of suspected pulmonary embolism were not followed for 47% of patients. It is therefore important to determine whether the ADP will work within a clinical pathway implemented in daily hospital care where the attending clinician has final decision-making authority. We designed a trial using the Consolidated Standards for Reporting of Trials (CONSORT) group pragmatic trials guidance to test for the existence and size of any beneficial effect of using the ADAPT ADP in the conditions in which it usually would be applied. We conducted a randomized clinical trial comparing use of the ADP with conventional diagnostic assessment. We compared the rate of successful ED discharge within 6 hours (defined as without a major adverse cardiac event occurring within 30 days).

**Methods**

**Study Design and Participants**

This study was a single-center randomized clinical trial (1:1 allocation ratio) designed to compare the effectiveness of 2 investigative pathways for the assessment of patients with possible cardiac chest pain. The trial design was based on the CONSORT extension statement for pragmatic trials, and clinical management therefore was not strictly controlled. Although pathways for the intervention and control arms were provided, the final clinical management decision, based on either subjective or structured risk assessment, as well as on test results, was at the discretion of the attending clinician. Research staff documented, but did not intervene in, clinical decisions. The research protocol received regional ethics committee approval, and informed consent was obtained from all patients.

Recruitment occurred from October 11, 2010, to July 4, 2012, between 8 AM and 10 PM, 7 days a week. Consecutively consenting patients who presented acutely to the Christchurch Hospital ED with possible cardiac chest pain were enrolled. Eligible patients were those aged 18 years or older who had symptoms consistent with ACS and for whom the attending physician planned further observation/ admission and troponin testing to investigate for possible acute myocardial infarction. The American Heart Association case definitions for possible cardiac symptoms were used (ie, acute chest, epigastric, neck, jaw, or arm pain, or discomfort or pressure without an apparent noncardiac source). All eligible patients were randomized regardless of their likely final TIMI score, and perceived high risk of ACS was not used as an exclusion criterion. Patients were excluded for any of the following reasons: ST-segment elevation myocardial infarction, an initial clear cause other than ACS for the symptoms (eg, pneumonia), inability to provide informed consent, staff considered recruitment to be inappropriate (eg, receiving palliative treatment), chest pain symptoms began more than 12 hours before presentation, persisting chest pain, transfer from another hospital, pregnancy, previous inclusion in the study, or inability to be contacted after discharge.

**Study Setting**

Christchurch Hospital is the general and tertiary hospital for approximately 450 000 people. The ED has approximately 75 000 new patient attendances per year. Patients arriving at the ED with chest pain do so mainly by self-presentation or via a call to ambulance services, or after referral from primary care physicians. Patients who present to the ED with possible cardiac symptoms usually are entered into a special cardiac chest pain clinical pathway containing specific steps and guidance. Clinicians are expected to follow the guidance in the pathway unless they can document good clinical reasons not to. The hospital used a troponin assay that has a manufacturer-specified limit of detection of less than 0.01 ng/mL, 99th percentile of 0.028 ng/mL, and 10% coefficient of variation of 0.032 ng/mL (ARCHITECT troponin I [TnI] assay; Abbott). At Christchurch Hospital, results were rounded to 2 decimal places; results re-
ported as greater than 0.03 ng/mL were classified as positive. (Conversion of TnI to micrograms per liter is 1:1.)

Randomization and Blinding
A computer-generated block randomization sequence (permuted blocks of 20) was used to populate consecutively numbered sealed envelopes, placed within closed study packs. The recruiting personnel were unaware of this sequence. The 3 senior clinicians (S.A. and R.T.) who adjudicated for the presence of any major adverse cardiac event (MACE) were blinded to study group allocation. Adjudications were entered into a database separate from other trial information. It was not possible to blind the patients or clinical staff.

Interventions
In the control group of the trial, patients were entered into the hospital’s standard-care cardiac chest pain pathway. On arrival, patients received an initial ECG and a blood sample was obtained for the first TnI test. The blood sampling for the second TnI test was timed so that it took place 6 to 12 hours after the onset of the possible cardiac symptoms.3-7 Standard care usually involved observation/admission under the care of an inpatient team. Plans for follow-up investigations (eg, exercise stress test) were at the discretion of the senior clinician. Discharge advice was provided to patients on recommended lifestyle modifications, and guidance was given on how to respond to any future symptoms. Patients were encouraged to visit their primary care physician within 7 days.

In the experimental group of the trial, patients received an initial ECG and a blood sample was obtained for TnI on their arrival at the hospital, and their modified TIMI score25 was calculated (Table 1). If there was no new ischemia observed on the first ECG, the initial TnI test result was normal, and the TIMI score was 0, patients were moved to an ED observation bed without ECG monitoring. At 2 hours after the initial tests (approximately 2 hours after presentation to the ED), another ECG was obtained and blood was drawn for a second TnI test. If all test results were negative, patients were classified as low risk and discharged. All patients who were discharged early on the basis of the ADP were scheduled to return to the hospital within 72 hours as outpatients for a stress test (usually an exercise treadmill test) using the same slot they would have been allocated as an inpatient. If any diagnostic factor was positive or the TIMI score was 1 or more, patients were not classified as low risk and their care was managed according to the standard cardiac chest-pain clinical pathway with a TnI test performed 6 to 12 hours after symptom onset (Supplement eFigure). Discharge arrangements were otherwise the same as for the control group.

Outcome Measures
The primary end point of the study was successful discharge, defined as discharge from the hospital within 6 hours of ED arrival and without a subsequent MACE within 30 days. A time point was chosen for the primary outcome rather than admission/discharge rate because hospital admission is defined differently in different locations/countries. Six hours was selected as the time point for the primary outcome because it is an upper limit of time that a patient can remain in the ED without an effect on overcrowding and adverse patient outcomes.11 For all patients in the study, MACE was reported if any of the following 7 predefined published ACS-related diagnoses26 were made during the initial hospital admission or during the 30-day follow-up period: (1) death (unless clearly noncardiac), (2) cardiac arrest, (3) emergency revascularization procedure, (4) cardiogenic shock, (5) ventricular arrhythmia needing intervention, (6) high-degree atrioventricular block needing intervention, and (7) acute myocardial infarction.5,26 Patients were followed up to determine the occurrence of MACE within 30 days after presentation using all of the following methods: telephone contact, review of patient medical records, and a national death and health events search. Patients in New Zealand have a unique alphanumerical identifier for tracking of all hospital inpatient and outpatient events within the nation’s health system.

Table 1. ADP Criteria for Patient Classification as Low Risk26

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>All factors had to be negative for the patient to be classified as low risk and suitable for early discharge with outpatient stress test.</td>
<td></td>
</tr>
<tr>
<td>1. Modified TIMI score, 0 (ie, all 7 criteria absent)*</td>
<td></td>
</tr>
<tr>
<td>a. Age ≥65 y</td>
<td></td>
</tr>
<tr>
<td>b. ≥3 Risk factors for coronary artery disease: family history of coronary disease, hypertension, hypercholesterolemia, diabetes mellitus, or current smoker</td>
<td></td>
</tr>
<tr>
<td>c. Use of aspirin in the past 7 d</td>
<td></td>
</tr>
<tr>
<td>d. Significant coronary stenosis (eg, previous coronary stenosis ≥50%)</td>
<td></td>
</tr>
<tr>
<td>e. Severe angina (eg, ≥2 angina events in past 24 h or persisting discomfort)</td>
<td></td>
</tr>
<tr>
<td>f. ST-segment deviation of ≥0.05 mV on first ECG</td>
<td></td>
</tr>
<tr>
<td>g. Increased initial troponin level*</td>
<td></td>
</tr>
<tr>
<td>2. Negative troponin test result at 0 and 2 h*</td>
<td></td>
</tr>
<tr>
<td>3. No new ischemic ECG changes*</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ADP, accelerated diagnostic protocol; ECG, electrocardiogram; TIMI, Thrombolysis in Myocardial Infarction.

*Assessment of the modified TIMI score for unstable angina and non-ST elevation acute coronary syndrome and ECG was done by the attending clinician. With the TIMI score, 1 point is given for each criterion from a to g. If any criterion is positive, the score is greater than 0 and the patient is not considered low risk.

Assessment of the modified TIMI score and negative if equal to or below cutoff. The results of the 0-hour troponin I testing were used for calculation of the TIMI score in this study. The score criteria for points 1f and 1g are effectively redundant in the ADP because of the broader troponin and ECG criteria in points 2 and 3.

Ischemic ECG changes with no evidence that they were preexisting. Electrocardiographic changes were defined as ST-segment depression of at least 0.05 mV in 2 or more contiguous leads (including reciprocal changes), T-wave inversion of at least 0.1 mV, or Q-waves greater than 30 milliseconds in width and 0.1 mV or greater in depth in at least 2 contiguous leads.26-28 Patients with other abnormal ECG findings (eg, pacing artifact and left bundle-branch block) that were present on preexisting ECGs were not defined as high risk.

Abnormal vital signs were classified as pulse rate less than 50 or greater than 100 bpm, systolic blood pressure less than 100 or greater than 200 mm Hg, and respiratory rate greater than 30 per minute.

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Sample Size
We estimated a 5% early discharge rate in the control group and a 17% early discharge rate in the experimental group (95% CI lower boundary, 14%). The study was powered to detect a 9% difference between the randomized groups in the primary outcome of early discharge rate with 90% power and a 2-tailed \( \alpha = .05 \), requiring 250 patients per group.

Statistical Analysis
Successful discharge and occurrence of MACE were compared between study groups using the \( \chi^2 \) test or Fisher exact test and the odds ratio with 95% CI. The primary analysis was undertaken on an intention-to-treat basis.

Results
Study Patients
Of the 544 patients who underwent randomization, 2 were removed from the trial because they were included twice. All remaining 542 patients were successfully monitored for 30 days (Figure 1). Participants were predominantly older men of New Zealand European origin (white) and commonly had cardiovascular risk factors and prior cardiovascular disease (Table 2).

Accelerated diagnostic protocol (ADP) included Thrombolysis in Myocardial Infarction (TIMI) score for unstable angina and non-ST elevation acute coronary syndrome of 0, electrocardiogram, and 0- and 2-hour troponin testing. Three patients assigned to the control pathway received treatment via the experimental pathway and were discharged early. Forty-one patients assigned to the experimental pathway and classified as low-risk received standard care. These patients were admitted for further inpatient investigation for acute coronary syndrome (n = 35) or because an alternative diagnosis requiring admission had become apparent (n = 6). None of these patients had an acute coronary syndrome. No study patients were lost to follow-up or excluded from the analysis.

Early Discharge
Significantly more patients were successfully discharged within 6 hours of arrival using the experimental pathway (52 of 270 [19.3%]) than using the standard-care pathway (30 of 272 [11.0%]) (Table 3). The difference of 8.3% was statistically significant (95% CI, 1.8-14.0; odds ratio, 1.92; 95% CI, 1.18-3.13; number needed to treat, 13). With use of the standard-care pathway, 20 hours was required to discharge the same proportion of patients discharged in 6 hours with use of the experimental pathway (Figure 2). Thirty-five patients (13.0%) in the experimental group who were classified as low risk were admitted to an inpatient ward for further investigation for possible ACS; none received that diagnosis.

Secondary Outcomes
There were no significant differences in numbers of MACEs experienced by the patients assigned to either diagnostic pathway (Table 3). Eighty-one of the 542 patients (14.9%) had at least 1 of the 7 diagnoses related to MACE during their initial hospital attendance. One of the 542 patients (0.2%) experienced a MACE during the 30-day follow-up period. This patient was
among those in the experimental group discharged within 6 hours and therefore was not regarded as having a successful discharge. The patient was a 63-year-old man who arrived at the ED 6.5 hours after chest pain onset. The morning following discharge, he had an exercise treadmill test, and the results were misinterpreted. The test was reported as normal by a junior resident and the patient was released without follow-up; he returned 7 days later with an ST-segment elevation myocardial infarction. No adverse events occurred in patients discharged within 6 hours in the control group. There were no adverse events in either group between the time of discharge and the time of the exercise stress testing, which occurred within 72 hours for 99% of the patients in both groups.

Additional Observations

Three patients (1.1%) who were assigned to the standard-care pathway underwent the ADP and were discharged early; none of these patients had a MACE. Two patients (0.7%) in the experimental group were discharged from the ED between 6.6 and 8.2 hours after arrival resulting from delays in clinician review. Six patients (2.2%) in the experimental group classified as low risk were admitted because an alternative diagnosis requiring admission had become apparent (Supplement [eTables 2 and 3]).

Discussion

In this randomized trial, almost twice as many patients with chest pain were discharged early when clinicians used the experimental pathway rather than the standard-care pathway. To our knowledge, this is the first randomized trial incorporating troponin as the sole biomarker in an ADP within a clinical pathway. The findings are consistent with those of the large observational ADAPT study, in which the same ADP applied post hoc classified 20% of 1975 patients as low risk. Increased early discharge was also shown by the Randomised Assessment of Treatment Using Panel Assay of Cardiac Marker trial, which investigated the impact of point-of-care blood tests in a population with 5 times lower prevalence of MACE than in the present study (2.8% vs. 15.1%). The rate of MACE in our cohort was higher than that recorded by other centers. Introducing the experimental pathway in locations where the risk of ACS is lower might be expected to achieve higher early discharge rates.

The trial finding has important health resource implications. From a clinical perspective, increasing early discharge rates can help to decrease overcrowding in EDs and hospitals and avoid duplication of staff time. Reducing the time that patients with chest pain spend in the hospital will lessen the pressure on resources and finances. Such savings could have an immense impact in a country such as the United States, where more than 6 million patients present to EDs with chest pain annually.

This study provides the first evidence of the effective use of the experimental pathway in a real-life setting. It was conducted without enforcement of the allocated study protocol so that a realistic measurement of the impact of introducing the experimental pathway could be obtained. It may seem logical that provision for earlier troponin testing will lead to earlier discharge. However, clinicians may not follow such an approach with sufficient numbers of patients to make implementation of the experimental pathway worthwhile. This effect was illustrated by the high number of patients (in the experimental group) classified as low risk but still admitted to the hospital (without subsequent diagnosis of ACS). This had an important effect on the difference between primary outcomes for each group and suggests that a higher early discharge rate might be achievable with greater acceptance of the protocol by clinicians.

Table 2. Patient Demographics and Risk Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (Standard Care) (n = 272)</th>
<th>Experimental (Incorporating ADP) (n = 270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>60.5 (13.0)</td>
<td>60.5 (12.6)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>166 (61.0)</td>
<td>171 (63.3)</td>
</tr>
<tr>
<td>Female</td>
<td>106 (39.0)</td>
<td>99 (36.7)</td>
</tr>
<tr>
<td>Ethnic origin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Zealand European</td>
<td>249 (91.5)</td>
<td>251 (93.0)</td>
</tr>
<tr>
<td>New Zealand Maori</td>
<td>7 (2.6)</td>
<td>11 (4.1)</td>
</tr>
<tr>
<td>Pacific island</td>
<td>3 (1.1)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (0.7)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Other or not stated</td>
<td>11 (4.0)</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>121 (44.5)</td>
<td>116 (43.0)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>67 (24.6)</td>
<td>68 (25.2)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>14 (5.1)</td>
<td>10 (3.7)</td>
</tr>
<tr>
<td>Stroke or transient ischemic attack</td>
<td>27 (9.9)</td>
<td>27 (10.0)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>11 (4.0)</td>
<td>15 (5.6)</td>
</tr>
<tr>
<td>Coronary artery bypass grafting</td>
<td>18 (6.6)</td>
<td>24 (8.9)</td>
</tr>
<tr>
<td>Coronary angioplasty</td>
<td>79 (29.0)</td>
<td>73 (27.0)</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>12 (4.4)</td>
<td>12 (4.4)</td>
</tr>
<tr>
<td>Atrial arrhythmia</td>
<td>24 (8.8)</td>
<td>26 (9.6)</td>
</tr>
<tr>
<td>Other</td>
<td>45 (16.5)</td>
<td>54 (20.0)</td>
</tr>
<tr>
<td>Risk factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>124 (45.6)</td>
<td>120 (44.4)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>38 (14.0)</td>
<td>43 (15.9)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>145 (53.3)</td>
<td>134 (49.6)</td>
</tr>
<tr>
<td>Family history of coronary artery disease</td>
<td>169 (62.1)</td>
<td>162 (60.0)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>51 (18.8)</td>
<td>42 (15.6)</td>
</tr>
<tr>
<td>Recent ex-smoker (&gt;1 mo to 1 y)</td>
<td>8 (2.9)</td>
<td>8 (3.0)</td>
</tr>
<tr>
<td>Ex-smoker (&gt;1 y)</td>
<td>102 (37.5)</td>
<td>107 (39.6)</td>
</tr>
<tr>
<td>TIMI score, 0</td>
<td>3.08 (2.00-5.81)</td>
<td>3.42 (1.96-7.15)</td>
</tr>
</tbody>
</table>

Abbreviations: ADP, accelerated diagnostic protocol; IQR, interquartile range; TIMI, Thrombolysis in Myocardial Infarction; Tni, troponin I.
In addition, to make the experimental pathway more reproducible, there was no provision of extra staff, bed, or capital resources to the experimental group. It is therefore possible that logistical constraints (eg, availability of medical staff to review patients) might have prevented timely discharge of many low-risk patients, but this occurred only twice. All the components needed for implementation of the experimental pathway are widely available internationally. Consequently, it could provide a screening process that could be integrated with existing chest-pain assessment processes at other hospitals to create significant benefits without financial investment.

Many centers have or will soon have high-sensitivity cardiac troponin (HS-cTn) assays instead of the TnI assay used in the present trial. If HS-cTn were incorporated into the ADP, fewer patients might be identified as low risk because of the potential for increased numbers of positive results with HS-cTn.
compared with assays that are not highly sensitive. Evidence is now available that this ADP also works when used with HS-cTnI or HS-cTnT assays. In recent studies using HS-cTnT, 15.3% of patients were identified as low risk, with a negative predictive value of 99.3% for acute myocardial infarction. Using HS-cTnI, 19.6% to 25.3% of patients were identified as low risk with a negative predictive value for MACE of 100%.31

There are some limitations of the present study. This was a single-center trial, which may limit the generalizability of the findings. The single-center design also limited the sample size, so it was not possible to make subgroup comparisons. Although the rates of MACE did not differ significantly between the study groups, we cannot exclude a small difference in the risk of MACE following early discharge because our study was not powered to compare rates of MACE between the intervention and control groups. However, the safety of the ADP was demonstrated in the 1975 patients participating in the ADAPT observational study16 and has been confirmed using HS-TnI in 909 patients from the Advantageous Predictors of Acute Coronary Syndrome Evaluation cohort in Germany and Switzerland.31 Although larger observational studies need to further evaluate the safety of the ADP when fully implemented, our study is an important first step in proving that its use is feasible and will facilitate early discharge from the ED. This experimental pathway has been successfully implemented at Christchurch Hospital and Nambour Hospital, Australia, and Queen Elizabeth II Hospital in Hong Kong and has been running for almost a year without adverse events.32

In the ADAPT16 and APACE31 groups, the negative predictive values of the ADP were 99.7% and 100%, respectively. In the experimental arm of our trial, of 94 patients classified as low risk, I had a MACE on follow-up, giving a similar negative predictive value at 98.9%. An attempt to achieve a zero rate of missed MACE may be very difficult without creating a considerable increase in health system costs. For the single patient with MACE in our study, the event occurred following clinician error that could have happened in either pathway. The second TnI was performed 8.5 hours after symptom onset, making the same outcome likely had randomization of that patient been to the control group. Local procedures were modified for both pathways so that senior clinicians now interpret stress tests. This case emphasizes that there is still a need for a follow-up test for ischemic heart disease, such as a stress test, after the ADP is completed.

This trial demonstrated that the experimental pathway is an effective and practical strategy to improve early discharge rates for some patients with chest pain. The strategy can easily be replicated. Use in the clinical setting would allow discharge of more patients with chest pain to outpatient follow-up within 6 hours of presentation. The reduction in time required to assess some patients could have significant benefits in terms of reduced consumption of health resources, costs, and patient anxiety and inconvenience.

ARTICLE INFORMATION
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Author Contributions: Dr Than had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Than, Aldous, Goodacre, Frampton, George, Ardagh, Jardine, Cullen, Richards, Hamilton, Deely.
Acquisition of data: Than, Aldous, Troughton, George, Florkowski, Smyth, Richards.
Analysis and interpretation of data: Than, Lord, Goodacre, Troughton, George, Ardagh, Peacock, Young, Deely, Cullen, Richards.
Drafting of the manuscript: Than, Lord, Young, Deely, Cullen.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Lord, Frampton.
Obtained funding: Than, Goodacre, Troughton, Hamilton, Richards.
Administrative, technical, and material support: Than, Aldous, Troughton, George, Florkowski, Ardagh, Smyth, Jardine, Deely, Richards.
Study supervision: Troughton, George, Ardagh, Jardine, Cullen.
Conflict of Interest Disclosures: Dr Than has received funding from Alere, Abbott, Beckman, and Roche for speaking and support for other research. Dr Goodacre has received funding from the UK National Institute for Health Research for chest pain trials. Dr George receives funding from Abbott, Beckman Coulter, and Roche for speaking. Dr Ardagh has received funding from the Health Research Council, New Zealand (HRCNZ) for unrelated research. Dr Peacock has received research grants from Abbott, Alere, Brahms, Novartis, Roche, and The Medicines Company; has been a consultant for Abbott, Alere, Lilly, The Medicines Company; has been a speaker for Bureau Abbott, Alere, and EiJnR; and had ownership interest in Comprehensive Research Associates LLC. Vital Sensors, and Emergency Services in Medicine LLC. Dr Deely receives funding from the Emergency Care Foundation for medical writing and HRCNZ for unrelated research. Dr Cullen has received funding from Abbott Diagnostics, Roche, Alere, Siemens, and Radiometer Pacific for clinical trials, and from Alere, Boehringer Ingelheim, Pfizer, AstraZenica, Abbott Diagnostics, and Radiometer Pacific for speaking and education. Dr Richards receives speaker honoraria from Roche Dx and Alere. No other disclosures were reported.
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