THE UNIVERSITY OF QUEENSLAND

AUSTRALIA

Examination of troponin testing following implementation of the IMProved Assessment of Chest pain Trial (IMPACT) Protocol, an accelerated chest pain assessment strategy

Ariel Ho

BSc, MBBS

A thesis submitted for the degree of Master of Philosophy at
The University of Queensland in 2020
Faculty of Medicine

Abstract

Background

The 2006 National Heart Foundation and Cardiac Society of Australia and New Zealand (NHFA/CSANZ) guidelines on the management of acute coronary syndrome (ACS) recommended stratifying patients with possible ACS into low-, intermediate- and high-risk cohorts. Low- and intermediate-risk patients were assessed with serial cardiac biomarkers and electrocardiography (ECG). If negative results were obtained, further objective testing for intermediate-risk patients was required while low-risk patients may be discharged. High-risk patients required admission, which often included early invasive interventions as part of management. Biomarker testing was recommended on presentation (zero hours) and then six to eight hours later when using sensitive (contemporary) troponin assays. Such practice was resource-intensive and time-consuming.

Local Problem

The Emergency Department (ED) at the Royal Brisbane and Women's Hospital (RBWH), a large tertiary hospital in Australia, had recently implemented the IMProved Assessment of Chest pain Trial (IMPACT) protocol, an accelerated diagnostic protocol for assessing patients presenting to the ED with possible ACS. The IMPACT protocol was evaluated in the IMPACT study, an intervention trial between February 2011 and March 2014. The IMPACT protocol was then immediately translated into clinical practice as the standard protocol for use at all hours (during and out of working hours) at the RBWH from April 2014. The IMPACT protocol utilised zero- and two-hour troponin testing for low- and intermediate-risk patients. Troponin ordering for high-risk patients was unchanged at zero and six hours.

This study sought to investigate whether the troponin ordering practices detailed by the IMPACT protocol were translated into clinical care in the post-implementation period.

Methodology

This was an observational study of adult patients presenting to the RBWH ED with chest pain between April 2014 and June 2016. The study included patients who had at least two troponins ordered, with the first being within four hours of presentation to the ED. Troponin data was obtained from the hospital pathology database. The proportion of patients in the overall cohort who had zero- and two-hour troponin testing was calculated along with median ED and short stay unit (SSU) length of stay, and proportion of patients admitted into hospital.

Results

The proportion of patients that had zero- and two-hour troponin testing, which was considered the accelerated cohort, increased rapidly over the first six months. The overall proportion of patients who underwent accelerated assessment during this study period was 49.2%. It reached a predicted 53.7% of the overall cohort by the end of this study, a figure less than that of the 75.6% reported by the IMPACT study.

The overall cohort was older than that recruited into the IMPACT study. After adjustment for age and sex (to the average age of the IMPACT cohort), the predicted proportion of accelerated patients was 66.7% for males and 72.7% for females by the end of the study period. The median ED and SSU length of stay was 7.2 hours for accelerated patients. The median hospital length of stay was 9.8 hours for accelerated patients and 23.9 hours for all patients. The proportion of patients admitted into hospital was 23.3% for accelerated patients, and 53.5% for the overall cohort.

Conclusions

This study demonstrated that the IMPACT protocol was rapidly being adopted and utilised in a clinical setting following conclusion of the original trial. The initial increase in proportion of patients being accelerated, followed by a plateau before the end of the study period, indicated acceptability, adoption and sustainability of the IMPACT protocol. The secondary outcomes of ED and SSU length of stay and admission rates remained unchanged for accelerated patients across the post-implementation period, demonstrating sustainability and consistency in the use of the IMPACT protocol at the RBWH ED.

Declaration by author

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

I have clearly stated the contribution of others to my thesis as a whole, including statistical assistance, survey design, data analysis, significant technical procedures, professional editorial advice, financial support and any other original research work used or reported in my thesis. The content of my thesis is the result of work I have carried out since the commencement of my higher degree by research candidature and does not include a substantial part of work that has been submitted to qualify for the award of any other degree or diploma in any university or other tertiary institution. I have clearly stated which parts of my thesis, if any, have been submitted to qualify for another award.

I acknowledge that an electronic copy of my thesis must be lodged with the University Library and, subject to the policy and procedures of The University of Queensland, the thesis be made available for research and study in accordance with the Copyright Act 1968 unless a period of embargo has been approved by the Dean of the Graduate School.

I acknowledge that copyright of all material contained in my thesis resides with the copyright holder(s) of that material. Where appropriate I have obtained copyright permission from the copyright holder to reproduce material in this thesis and have sought permission from co-authors for any jointly authored works included in the thesis.

Publications included in this thesis

No publications included.

Submitted manuscripts included in this thesis

No manuscripts submitted for publication.

Other publications during candidature

No other publications.

Contributions by others to the thesis

Professor Louise Cullen and Associate Professor Jaimi Greenslade had provided contributions to the conception and design of the project. A/Prof Jaimi Greenslade contributed to the statistical analysis of research data. Ms Jadwiga Chabrowska was responsible for data linkage.

Statement of parts of thesis submitted to qualify for the award of another degree

No works submitted towards another degree have been included in this thesis.

Ethical considerations

This study is part of the low risk research project:

> Examination of health care assessment practices and costs pre- and post-implementation of an accelerated chest pain assessment strategy: a marker of translational research success.

The reference number is: HREC/15/QRBW/429.

The RBWH Human Research Ethics Committee has granted ethical approval of this low risk research project. The waiver of consent and breach of the Australian Privacy Principles were considered justified in accordance with National Statement 2.3.10 and are approved.

Acknowledgements

Firstly, I must express my appreciation to both my supervisors, Professor Louise Cullen and Associate Professor Jaimi Greenslade, for their continual support and kind encouragement.

I am thankful to Prof Louise Cullen for allowing me to join her research team as an inexperienced first year medical student many years ago. Without that opportunity, this MPhil would not exist.

Completion of this thesis would not have been possible without the advice and expertise of A/Prof Jaimi Greenslade. I am immensely grateful for her patience while bearing with my many, many, many questions.

I thank my parents and sister for their love and lifelong support, and their constant reminders that I need to submit my thesis and get more sleep.

Lastly, I thank Ben for his unwavering belief in me even when mine falters. During the more difficult moments, even though he could not carry it for me, he did carry me.

Financial support

Keywords

acute coronary syndrome (ACS), accelerated diagnostic protocol (ADP), chest pain, emergency department (ED), translational research, troponin

Australian and New Zealand Standard Research Classifications (ANZSRC)

ANZSRC code: 110305 Emergency Medicine, 60%

ANZSRC code: 111709 Health Care Administration, 40%

Field of Research (FoR) Classification

FoR code: 1103 Clinical Sciences, 60%

FoR code: 1117 Public Health and Health Services, 40%

Table of Contents

List of Figures and Tables

Figure 1: IMPACT protocol (based on study by Cullen et al.[1])

Figure 2: Flow diagram of study participants

Figure 3. Percentage of patients intended for accelerated assessment by time. The black line represents the predicted proportion of patients undergoing accelerated assessment across time. The blue line represents actual percentages accelerated by week.

Figure 4. Percentage of patients intended for accelerated assessment adjusted for age and sex. Data are plotted for an average age of 51 years. The blue and purple lines represent the predicted proportion of female and male patients respectively undergoing accelerated assessment across time.

Figure 5. Proportion of patients admitted to hospital by time

Figure 6. Adjusted probability to being admitted to hospital for accelerated patients. Data presented for an average age of 51 years.

Figure 7. Median ED and SSU length of stay by time

Figure 8. ED and SSU length of stay by time for accelerated patients. Data presented for an average age of 51 years.

Table 1. Baseline characteristics of the study cohort

Table 2. Health care utilisation by presentation time

Supplementary Figure 1. Proportion of patients accelerated by age

Supplementary Figure 2. Proportion of patients admitted by age

Supplementary Figure 3. ED and SSU length of stay by age

Supplementary Table 1: Comparison of risk stratification criteria from the 2006 National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand (NHFA/CSANZ) guideline and IMPACT protocol

List of Abbreviations

- ACRE – Accelerated Chest pain Risk Evaluation

- ACS – Acute Coronary Syndrome

- ACS-AP – Acute Coronary Syndrome Accelerated Pathway

- ADP – Accelerated Diagnostic Pathway

- AMI – Acute Myocardial Infarction

- CDR – Clinical Decision Rule

- ECG – Electrocardiogram

- ED – Emergency Department

- EDIS – Emergency Department Information System

- eGFR – estimated Glomerular Filtration Rate

- EST – Exercise Stress Test

- HBCIS – Hospital Based Corporate Information System

- IMPACT – IMProved Assessment of Chest pain Trial

- LVEF – Left Ventricular Ejection Fraction

- NHFA/CSANZ – National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand

- NSTEMI – Non-ST Elevation Myocardial Infarction

- RBWH – Royal Brisbane and Women's Hospital

- SSU – Short Stay Unit

- STEMI – ST Elevation Myocardial Infarction

Introduction

Each year in Australia, an estimated 500,000 patients present to hospital Emergency Departments (EDs) with possible cardiac chest pain.[2] The most common serious aetiology of this symptom is acute coronary syndrome (ACS), which includes ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina. In 2012, there were an estimated 68,200 acute coronary events in Australia.[3] It is often difficult to distinguish an ACS from alternative aetiologies, including serious conditions such as pulmonary embolism and less life-threatening diagnoses such as gastro-oesophageal reflux.

The assessment of chest pain in the ED focuses not only on the rapid diagnosis of ACS, but also on the exclusion of ACS and other serious conditions that may cause significant morbidity and mortality. Most patients undergoing investigations for ACS do not have the condition,[4] but the serious consequences of a missed diagnosis encourage extensive investigations in patients with possible ACS.

The diagnosis of ACS is based on history, clinical assessment, serial cardiac biomarker measurements, serial electrocardiography (ECG) and possibly cardiac imaging.[5] The main biomarker used is cardiac troponin. Cardiac troponin is released in the event of myocardial cell damage and its degree of elevation correlates to the amount of myocardial cell death. Serial troponin testing is critical for the evaluation of ACS; troponin elevations are seen in multiple chronic cardiac and non-cardiac conditions, but a change in serial troponin levels is indicative of an acute cardiac injury and is an important component of acute myocardial infarction diagnosis.[6,7] This underpins the importance of serial measurement of cardiac troponin. In addition, serum troponin levels are most commonly elevated six to eight hours after myocardial injury, with a peak at twelve to twenty-four hours, and remaining in circulation in the blood

for seven to ten days.[8] If the initial troponin test was performed too close to the time of myocardial insult, the test may be reported as a normal result. Thus it is imperative for serial tests after an appropriate interval.[7]

The 2006 National Heart Foundation and Cardiac Society of Australia and New Zealand (NHFA/CSANZ) guidelines[9] on the management of ACS utilised serial troponin testing as part of stratifying patients into low-, intermediate- and high-risk categories.[9,10] Serial troponin testing was recommended over a six to eight hour period when using sensitive (contemporary) troponin assays. The guidelines recommended that patients with low-risk clinical features, normal serial troponin and normal ECG results could be discharged from ED. Patients with intermediate-risk clinical features, normal serial troponin and normal ECG results were sent for further objective testing, the most commonly used being an exercise stress test (EST). Other more expensive investigations may include stress echocardiography, computed tomography coronary angiography, myocardial perfusion scanning and invasive coronary angiography. Patients with high-risk clinical features, elevated troponin or abnormal ECGs required admission to hospital and intensive management, often including early invasive strategies. Overall this process resulted in extended emergency stays and a high rate of admission, yet up to 67.2% of patients were ultimately diagnosed as having pain of non-cardiac origin and a further 20.8% were diagnosed with non-ACS cardiac conditions.[4] Processes for the assessment of chest pain using the 2006 NHFA/CSANZ guidelines were expending valuable time and resources. Overcrowding and extended length of stay in EDs increased mortality.[11,12] On the other hand, timeliness did not affect safety.[13]

A recent intervention trial had shown that patients who were at low- or intermediate-risk of ACS could safely undergo an accelerated diagnostic protocol. The protocol, termed the

IMProved Assessment of Chest pain Trial (IMPACT) protocol (Figure 1),[1] aimed to safely accelerate the assessment of low- and intermediate-risk patients. Firstly, the IMPACT protocol redefined low- and intermediate-risk characteristics (Supplementary Table 1), enabling a higher proportion of patients to be categorised as low risk. Secondly, it enabled serial troponin testing at zero and two hours for low- and intermediate-risk patients, rather than the zero and six hours recommended by traditional clinical guidelines. This allowed low-risk patients to be discharged earlier, and intermediate-risk patients to undergo objective testing earlier. The IMPACT trial was facilitated by research nurses during working hours, between 0800 and 1700 hours on Monday to Friday between February 2011 and March 2014. The protocol was immediately translated into clinical practice, and became the standard protocol at all hours (during and out of working hours) at the Royal Brisbane and Women's Hospital (RBWH) from April 2014.

The IMPACT protocol was shown to be a safe and cost-effective strategy within the confines of a clinical trial; the average cost per patient managed by the IMPACT protocol was $1229 less than the traditional NHFA/CSANZ approach, and saved twenty-six hours in hospital.[1,14] However, translation of research findings into guidelines is often difficult.[15] As such, an evaluation of the usage of the IMPACT protocol was necessary. Further, an evaluation of its effectiveness in terms of secondary outcomes such as length of stay and admission rates was required.

Available knowledge

The 2006 NHFA/CSANZ guidelines[9] on the management of ACS recommended stratifying patients into low-, intermediate- and high-risk categories. Cullen et al.[4] found that for patients presenting to an Australian ED with at least five minutes of chest pain suggestive of an ACS (acute chest, epigastric, neck, jaw, or arm pain; discomfort or pressure without an apparent non-cardiac source), the final cause of chest pain was a non-cardiac condition in 67.2% of 926 patients. Non-ACS cardiovascular disease, including pericarditis and heart failure, was diagnosed in 20.8% of patients. ACS was diagnosed in 11.1% of patients, with the most common pathology being NSTEMI (51.5% of the ACS group).

Using the 2006 NHFA/CSANZ guidelines, the total cost for assessing 580 intermediate-risk patients during this study was $1,916,100, and such assessment resulted in the identification of eleven ACS patients. This equated to $174,191 to identify and treat one ACS patient in the intermediate-risk group. In the high-risk group, the total cost of assessment was $2,934,317. Ninety-two patients out of 329 were diagnosed with ACS in the high-risk group, resulting in an average of $31,895 spent in identifying and treating one ACS event. Therefore, even though the high-risk group incurred the highest total cost, identifying the 1.9% of patients with ACS in the intermediate risk cohort was resource-intensive, with the costs expended to diagnose and treat a very small proportion.[4]

Alongside high assessment costs, there had been evidence that the process of risk stratification for patients with ACS was often not strictly performed, with variation in test ordering and timing of tests. Resistance by emergency physicians to the use of the NHFA/CSANZ guidelines had been observed in some Australian hospitals.[16] As such, a revised assessment approach for ED patients with chest pain that maintained safety while improving efficiency was warranted.

Accelerated chest pain protocols had been trialled and had facilitated early discharge both safely and effectively.[17-19] An ideal accelerated diagnostic protocol would reduce unnecessary testing in patients who were low-risk for ACS and would streamline the overall assessment process for patients at intermediate-risk. This would save resources but with no adverse impact on health outcomes. Ideally, the protocol would also allow for a much shorter time frame for assessment of serial troponins.

The IMPACT protocol is an alternative strategy to the 2006 NHFA/CSANZ protocol for assessing chest pain.[1] The IMPACT protocol stratifies patients into low-, intermediate- and high-risk groups using demographic and clinical features (Figure 1). On presentation (zero hours), troponin testing and ECG are performed on all patients. For low- and intermediate-risk patients, this is repeated at two hours. Low-risk patients can be discharged upon normal results for troponin and ECG. Intermediate-risk patients with normal results in troponin and ECG undergo an inpatient EST. A negative EST allows the patient to be discharged; while positive or equivocal ESTs require patients to be referred to internal medicine or cardiology. High-risk patients receive serial troponin testing and ECG at zero and six hours, and are admitted as inpatients for further investigations and treatment.
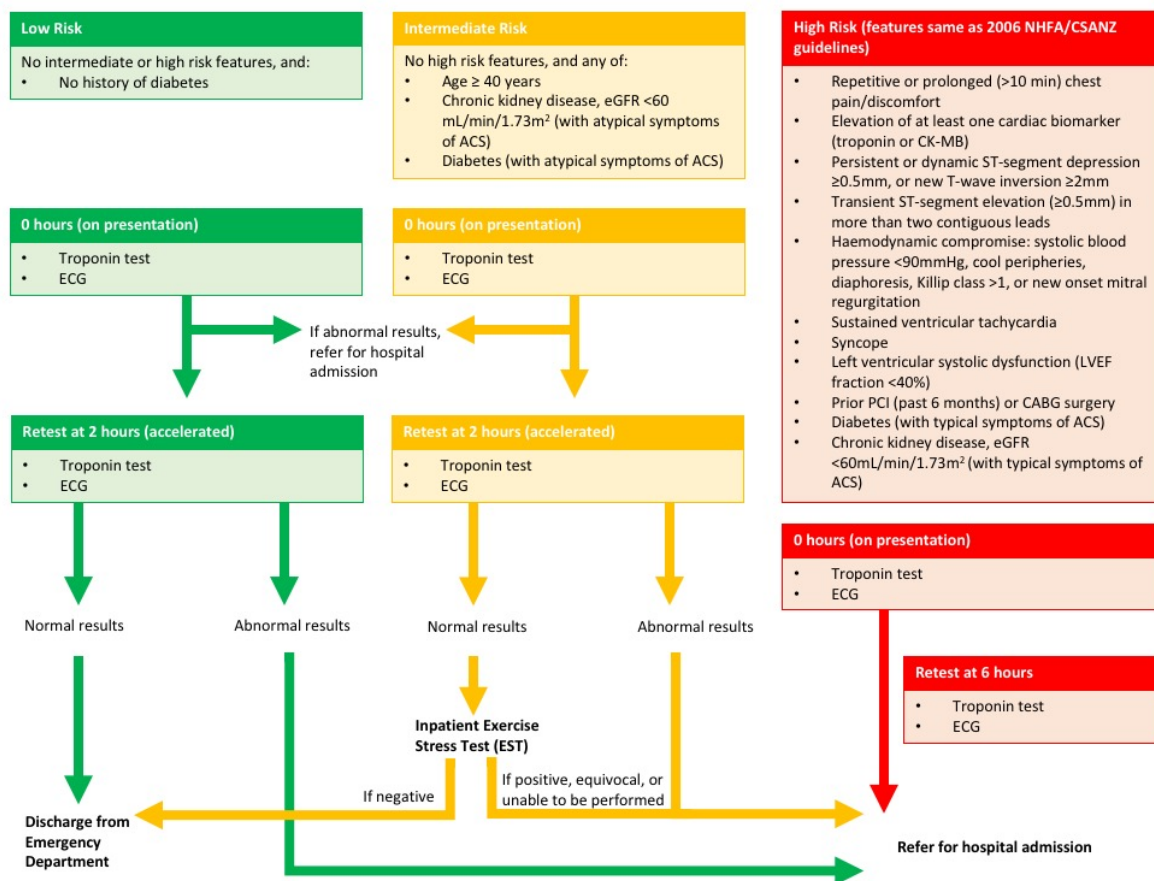
Low Risk

No intermediate or high risk features, and:
- No history of diabetes

Intermediate Risk

No high risk features, and any of:
- Age ≥ 40 years
- Chronic kidney disease, eGFR <60 mL/min/1.73m^2 (with atypical symptoms of ACS)
- Diabetes (with atypical symptoms of ACS)

High Risk (features same as 2006 NHFA/CSANZ guidelines)

- Repetitive or prolonged (>10 min) chest pain/discomfort
- Elevation of at least one cardiac biomarker (troponin or CK-MB)
- Persistent or dynamic ST-segment depression ≥0.5mm, or new T-wave inversion ≥2mm
- Transient ST-segment elevation (≥0.5mm) in more than two contiguous leads
- Haemodynamic compromise: systolic blood pressure <90mmHg, cool peripheries, diaphoresis, Killip class >1, or new onset mitral regurgitation
- Sustained ventricular tachycardia
- Syncope
- Left ventricular systolic dysfunction (LVEF fraction <40%)
- Prior PCI (past 6 months) or CABG surgery
- Diabetes (with typical symptoms of ACS)
- Chronic kidney disease, eGFR <60mL/min/1.73m^2 (with typical symptoms of ACS)

0 hours (on presentation)
- Troponin test
- ECG

0 hours (on presentation)
- Troponin test
- ECG

If abnormal results, refer for hospital admission

Retest at 2 hours (accelerated)
- Troponin test
- ECG

Retest at 2 hours (accelerated)
- Troponin test
- ECG

0 hours (on presentation)
- Troponin test
- ECG

Retest at 6 hours
- Troponin test
- ECG

Normal results   Abnormal results   Normal results   Abnormal results

Inpatient Exercise Stress Test (EST)

If negative   If positive, equivocal, or unable to be performed

Discharge from Emergency Department

Refer for hospital admission

Figure 1: IMPACT protocol (based on study by Cullen et al.[1])

A study by Cheng et al.[14] found that using the 2006 NHFA/CSANZ guidelines,[9] 62% of patients were classed as intermediate-risk. 56% of this intermediate-risk cohort did not have an EST and were admitted to the ward for further investigations, incurring higher costs. In contrast, using the IMPACT protocol, 55% of patients were classed as intermediate-risk; 82% in this group had an EST and thus a smaller proportion of patients required admission for further, more expensive and potentially invasive investigations.[14] Furthermore, the 2006 NHFA/CSANZ guidelines classified <1% of patients presenting with chest pain into the low-risk cohort, a category that was associated with lower costs due to less extensive investigations required. In comparison, the IMPACT protocol stratified 18% into the low-risk category. There was no increase in adverse events using the IMPACT protocol in comparison to the

NHFA/CSANZ protocol, and the IMPACT protocol allowed a higher proportion of low- and intermediate-risk patients to be discharged from ED within 4 hours (72% vs 51%).[14]

Clinical Decision Rules (CDRs), such as the IMPACT protocol, are major applications of clinical research. They integrate clinical or laboratory results to provide a quantitative probability of a diagnosis or clinical outcome.[20] The use of CDRs can improve the accuracy of risk stratification and usage of appropriate evidence-based therapies, and can decrease the number of unnecessary referrals.[16,21,22] When used appropriately, CDRs can reduce overcrowding in EDs, improve access to EDs and decrease patient mortality.[11,23] CDRs have a high level of acceptability among most physicians,[24] and have been shown to increase efficacy and decrease cost.[25]

However, adherence to well-established rules is at times inconsistent, leading to a negative impact both on healthcare expenditure and patient care.[19,26] Non-adherence is a common problem. Mahler et al.[19] evaluated adherence to the HEART pathway for assessment of chest pain. They found that non-adherence occurred in 28 of 141 patients (20%), with under-testing occurring in 9 patients and over-testing in 19 patients. Although none of the 28 patients suffered a major adverse cardiac event at 30 days, the net effect of non-adherence was 10 additional hospital admissions among patients identified as low-risk and appropriate for early discharge. The decreased discharge rate of 7% is clinically significant; with an estimated 500,000 chest pain presentations to Australian EDs,[2] a 7% reduction in discharges would result in 35,000 avoidable hospitalisations per annum.

Inconsistent adherence to accelerated pathways was also observed in a study[26] comparing the novel Emergency Department Assessment of Chest Pain Score accelerated diagnostic pathway

(EDACS-ADP) to a controlled accelerated diagnostic pathway (ADAPT-ADP). None of the patients in the low risk groups in either arm had a major adverse event within 30 days. The EDACS-ADP identified 11.8% more low-risk patients than ADAPT-ADP. Despite this, the discharge rate between the two arms was not significantly different, suggesting non-adherence to the protocols.

Barriers to adherence of CDRs include physician disagreement with the rules, physicians' view that the rules are over-simplifications or too time-consuming to apply, patients' insistence on an investigation or intervention, and misinterpretation of the rules.[21,25,27] Recommendations on how to improve CDRs utilisation include continuing education to maintain and improve practice performance,[28] and use of clinical decision support systems to ensure the use of CDRs.[29]

When appraising the short- and long-term utilisation of the IMPACT protocol within the ED setting, the protocol should be evaluated in the context of translational research. Translational research is a complex, multi-stage process of applying research findings to improve clinical practice or promote health benefits.[30,31] There had been increasing interest in the field of translational research, with one of the most significant motivations arising from the protracted period of time it took to transform basic scientific ideas into clinical practice and health impacts.[32] The translation of major findings to clinical applications is often sluggish and inefficient.[33] Morris et al.[15] evaluated the literature on translational research and found that it required an average of seventeen years for research evidence to reach clinical practice. In addition, only 14% of original research turned into interventions of benefit to patient care.[34] Contopoulos-Ioannidis et al.[35] examined 101 articles in six major science journals that studied technology with promising therapeutic or preventative uses, and found that the median

translation lag was twenty-four years between first description and earliest highly cited article. Only five new technologies had been licensed for clinical use and only one was used extensively for the licensed indications. It required an average of nine years for interventions to be implemented even after they were recommended as evidence-based practice in systematic reviews and guidelines.[34]

To improve the success of translational research, which is determined by minimising time while preserving quality and cost to maximise the returns from research,[31] many studies had looked to identifying "time lags" that caused delay in research results being translated into clinical interventions.[36,37] Green et al.[34] suggested that long periods of delay were partially due to the process of how research became clinical practice, with multiple stages such as acceptance, publication, indexing, and inclusion in systematic reviews.

In addition, treatment effectiveness may not convey implementation effectiveness, which relies on the interplay of acceptability, adoption, appropriateness, costs, feasibility, fidelity, penetration and sustainability.[38] The majority of research included in systematic reviews with influence in recommending evidence-based practices had been conducted in highly controlled environments. This maximised internal validity but restricted external validity. Acceptability (the perception among stakeholders that a given innovation is agreeable), appropriateness (the perceived fit, relevance or compatibility of the innovation for a given setting, provider or consumer) and feasibility (the extent to which the new innovation can be successfully used within a given setting) may hence be limited.[34,38] Sustainability, the extent to which a newly implemented innovation is maintained within a service setting's ongoing operations, is also difficult to ascertain within clinical trials, but greatly influences the success of translating research findings into clinical practice.[38] Basic research has led to many notable advances, but

there are a multitude of hurdles between promising findings and successful implementation of those results in a clinical setting. Consequently, there has been a trend towards increasing the focus on applied clinical research, which had been demonstrated to have greater immediate health, social and economic effects than basic research.[37] To maximise the applicability of research, studies should be informed by burden of disease, with a focus on answering relevant and important questions in areas of need and minimising time lags.[34,37]

Implementation effectiveness of an accelerated diagnostic pathway, the ADAPT-ADP, was evaluated in the Accelerated Chest pain Risk Evaluation (ACRE) Project.[39] The implementation of the ADAPT-ADP was found to be associated with a reduction in ED length of stay, total hospital length of stay and the need for hospital admission. The implementation was accomplished across a variety of hospital types including metropolitan centres and regional hospitals. Of note, the implementation had been achieved within four years of publication of the original evidence, a shorter time frame than the average of seventeen years as reported by Morris et al.[15] A range of factors had been identified by stakeholders to have contributed to the successful implementation of the ADAPT-ADP.[40] Acceptability was achieved through the stakeholders' knowledge and awareness of the accelerated diagnostic pathway, its supporting evidence and how the pathway was used in practice. Adoption was aided by the ADAPT-ADP being an adaptation, rather than replacement, of pathways and guidelines in current use, as well as being simple to use and the belief by stakeholders that it was easily accessible. It was interesting to note that although fidelity (the degree to which an intervention was implemented as prescribed by the original protocol) was suggested to be a component of a successful implementation by Procter et al.[38], the ACRE authors attributed some success of the ADAPT-ADP's implementation to being able to be flexible in order to adapt to local processes.[40]

However, despite its successful implementation, ACRE identified areas of difficulties regarding the implementation process.[40] The ADAPT-ADP was a pathway utilised in the ED, but required the engagement of various other specialties, such as cardiology and internal medicine. In addition, despite its ease of use, sustainability may prove to be difficult due to the high turnover of both senior and junior medical staff in the ED. Similar difficulties may prevent the successful use of the IMPACT protocol outside of a trial setting, despite promising results during its implementation stage.

Rationale

The IMPACT protocol had been shown to be promising in its implementation phase as an accelerated protocol for the assessment of chest pain. It was found to be safe, with no adverse impact on health outcome.[1] It was also cost and resource efficient, classifying a larger proportion of patients presenting to ED with chest pain as low-risk (18% with the IMPACT protocol (previously named Brisbane protocol) vs <1% with the 2006 NHFA/CSANZ guidelines) and thus decreasing the proportion of patients who require further investigations (55% vs 62%). Using the IMPACT protocol resulted in spending an average $1229 less than the traditional approach per patient, saved an average of twenty-six hours in hospital per patient, and allowed for a higher discharge rate of low- and intermediate-risk patients from ED within four hours (72% vs 51%).[14] Despite the desirable outcomes achieved by the IMPACT protocol during its trial period, the IMPACT protocol required evaluation in its post-implementation stage.

Specific aims

In this study, we sought to provide an initial investigation into the implementation effectiveness of the IMPACT protocol. The IMPACT protocol included zero- and two-hour troponin testing for all low- and intermediate-risk patients. Thus, this study investigated troponin ordering practices of clinicians in the post-implementation period. The proportion of patients undergoing zero- and two-hour testing was examined and compared to that reported by the IMPACT study.[1] We also reported ED and SSU length of stay and proportion of patients admitted in the post-implementation period.

Methods

Study Design

This was an observational study of adult patients presenting to the ED of the RBWH, a large tertiary hospital in Australia, between April 2014 and June 2016. This study period commenced immediately after the trial period of the IMPACT protocol. The IMPACT protocol was implemented as the standard chest pain assessment protocol at the RBWH ED for use at all hours (during and out of working hours) via several approaches, including formal and informal education sessions, and large posters on display.

Participants

The study included adult patients who had a minimum of two troponins ordered within 24 hours, with at least one troponin ordered within four hours of presentation to the ED. Patients with only one troponin were excluded, as the ordering of a single troponin test suggested that the patient was not being investigated for ACS.

Measurements

Patients met the criteria for hospital admission if they were admitted to an inpatient unit from either the ED or SSU. Intention to undergo an accelerated chest pain assessment process was defined as having a non-elevated troponin test on presentation (zero hours) and at two hours. Intention to undergo accelerated assessment was evaluated because patients were no longer being enrolled onto the study via a consent process. No clinical data directly indicated the classification of a patient's risk group. Cardiac troponin testing is integral in the diagnosis of ACS, and a rise in serial troponin testing indicates acute myocardium damage. Thus, the inclusion of patients undergoing serial troponin testing soon after presentation to ED would identify the group of patients being investigated for ACS with a high degree of accuracy. In

addition, obtaining pathology testing data would be more reliable and accessible than determining the differential diagnoses being considered during a patient's presentation. Troponin was measured using the Beckman Coulter AccuTnI+3 assay, with values exceeding 0.040mg/L deemed to be elevated.

It was recognised that within the clinical context, troponins may not be performed exactly within the recommended time period. Errors in the time entered on the database were also possible. As such, a presentation troponin (zero-hour troponin) was considered to be any troponin taken within 1.5 hours of presentation and a two-hour troponin was any troponin taken within four hours of presentation. Patients were also considered to have accelerated assessment if they had two troponins taken less than three hours apart within the first 4.5 hours after presentation. Data were analysed on an intention-to-treat basis. As such, patients meeting the criteria above were considered as part of the accelerated group even if they had further troponin testing or were admitted for other cardiac testing.

Data Linkage

Data was obtained from a number of hospital databases. Data on ED arrival and discharge time, patient demographics and discharge disposition were collected from the Emergency Department Information System (EDIS). Troponin results and the date and time that the troponin test was ordered were obtained from the state-wide pathology database (Auslab). Finally, hospital discharge time and diagnosis were obtained from the hospital based corporate information system (HBCIS). Deterministic linkage was used to link these three databases. This linkage method involved linking records based on exact agreement of selected match variables and was recommended where direct identifiers were available and were of good

quality. Each of the databases contained a unique patient record number (UR) and this was used in combination with date and time data to link the patient data.

Statistical Analysis

Data were analysed using Stata 14 (StataCorp, 2015, College Station, TX) and included 116 weeks of data between 6th April 2014 and 25th June 2016. Descriptive statistics were calculated to define the baseline characteristics of the cohort. The proportion of patients in the overall cohort assessed using an accelerated strategy (zero- and two-hour troponin testing) was calculated along with median ED and SSU length of stay and the proportion of patients admitted. Such characteristics were also reported by presentation time (during or after work hours), to examine whether healthcare utilisation differed after hours when fewer resources are available (e.g. exercise stress testing). Working hours were defined as 0800 to 1700 hours on Monday to Friday.

Regression analyses were conducted to examine the odds of having accelerated assessment, the odds of being admitted, and ED and SSU length of stay over the 116-week observation period. We sought to describe whether the outcomes changed across time and thus incorporated the number of weeks post-implementation as an independent variable. There was the possibility of non-independence within the data (e.g. patients presented multiple times). Thus, for the dichotomous outcomes (accelerated and hospital admitted), generalized estimating equations (GEE) were fit with an exchangeable working correlation and robust standard errors. A binomial error distribution and a logit link function were specified. For length of stay, the median length of stay was modelled using quantile regression with robust standard errors.

Regression models were fit in several steps. The first stage was examining the unadjusted relationship between each outcome and time. As the purpose of this analysis was to describe the data, rather than future prediction, we did not have a hypothesis about the nature of the relationship (i.e., linear, curvilinear). As such, restricted cubic splines were fit, enabling the relationship to be dictated by the data. Knots were set at May (the start of winter season in ED) and September (end of winter season in ED) each year. A sensitivity analysis was conducted with splines placed the 5th, 35th, 65th, and 95th percentile, as recommended by Harrell.[41] This knot placement yielded similar results and so results were not reported here.

The second stage included the regression of each outcome on time after adjustment for age and sex. This analysis was conducted to allow for adjustment of the regression equation to enable a comparison with the original IMPACT study. A non-linear association between age and each of the endpoints was postulated. This was because age was a key factor within the risk stratification system used for identifying patient risk and whether a patient can undergo accelerated care. To account for such non-linearity, restricted cubic splines were again fit. Knots were set at 30, 50, 65, and 85 years. These knots were chosen as they represented the 5th, 35th, 65th, and 95th percentile, as recommended by Harrell.[41]

Results

There were 11327 presentations in this study period (5239 during work hours and 6088 after hours) with one or more troponin tests taken within four hours of presentation to the ED. There were 3733 presentations with only one (non-elevated) troponin taking during the patient's first twenty-four hours in hospital. These presentations were excluded from the current analysis as the ordering of a single troponin test suggested that the patient was not being investigated for ACS. This left 7594 presentations for analysis.

Baseline characteristics of the cohort were shown in Table 1. Of this cohort, 15% of patients were discharged from the ED, with the remaining patients being admitted to the SSU or directly to the ward. An elevated troponin on presentation was present in 18% of the cohort. There were 3805 patients with a presentation troponin <99th percentile who had a two-hour troponin; of these, 71 (1.87%) had a two-hour troponin >99th percentile. As with the IMPACT study, only patients with non-elevated zero- and two-hour troponins were considered accelerated; they remained in the accelerated group even if they had further troponin testing or were admitted for other cardiac testing. This deemed 3734 patients as accelerated patients.
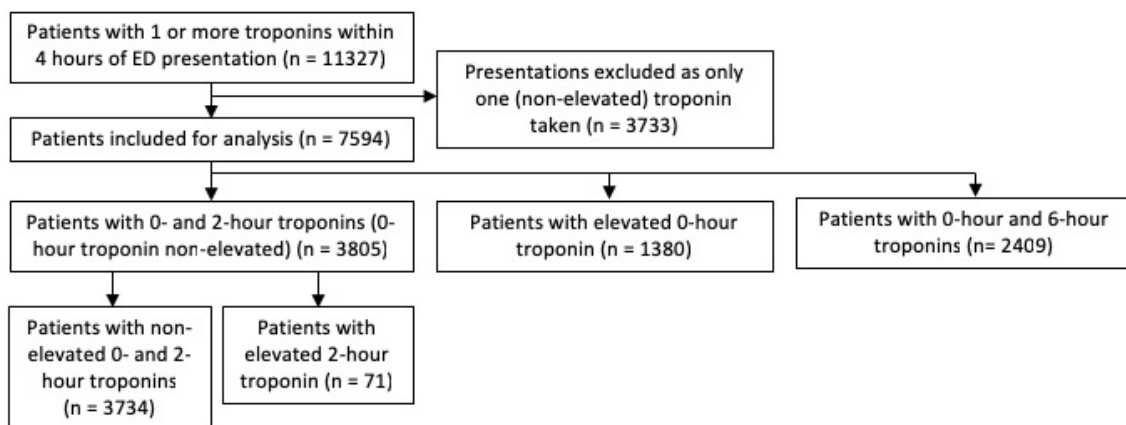
Figure 2. Flow diagram of study participants

Table 1. Baseline characteristics of the study cohort

	Post-IMPACT (n=7594)
Mean Age (SD)	58.09 (17.1)
Male Sex, n (%)	3185 (42.0%)
Disposition from ED, n (%)	
Admitted to ward	3654 (48.1%)
Admitted to short stay	2715 (35.8%)
Discharged Home	1119 (14.7%)
Left against medical advice	59 (0.8%)
Inter-hospital transfer (IHT)	39 (0.5%)
Died in the ED	8 (0.1%)
Median (IQR) time to zero-hour troponin, hours	0.5 (0.3-0.8)
Median (IQR) time from arrival to second troponin for accelerated patients, hours	2.7 (2.4-3.2)
Median (IQR) time to six-hour troponin in non-accelerated patients, hours	7.0 (6.3-8.6)
Presented after work hours, n (%)	4120 (54.3%)
Troponin >99th percentile on presentation, n (%)	1380 (18.2%)

Data on healthcare utilisation is provided in Table 2. The median hospital length of stay for the overall cohort was just less than one day. Patients intended for an accelerated protocol had a shorter hospital length of stay, particularly when presenting during working hours. One quarter of patients intended for an accelerated chest pain protocol were admitted to hospital. These patients were admitted to specialised cardiac units (26.5%) or general medical units (73.5%).

Table 2. Health care utilisation by presentation time

	Overall Cohort (n=7,594)	During working hours (n=3,474)	Outside of working hours (n=4,120)	Difference during versus outside of working hours (95% CI)
Median (IQR) Hospital length of stay for all patients, hours	23.9 (7.9-75.7)	24.8 (7.1-74.4)	21.9 (9.1-78.6)	-2.9 (-4.9 to -0.8)
Hospital admission n (%)	4,066 (53.5%)	1863 (53.6%)	2203 (53.5%)	-0.2% (-2.4 to 2.1%)
Patients accelerated, n (%)	3734 (49.2%)	1797 (51.7%)	1937 (47.0%)	-4.7% (-7.0 to -2.4%)
Accelerated patients admitted, n (%)	876 (23.3%)	419 (23.3%)	457 (23.6%)	0.3% (-2.5 to 3.0%)
Median (IQR) hospital length of stay for accelerated patients, hours	9.8 (4.9-22.7)	8.0 (5.0-24.0)	11.6 (4.8-20.9)	3.5 (1.6 to 5.5)
Median (IQR) ED and SSU length of stay for accelerated patients, hours	7.2 (4.7-14.8)	6.7 (4.7-16.6)	8.1 (4.6-14.7)	1.4 (0.8 to 1.9)

CI = confidence interval, IQR = interquartile range; 95% CI calculated using clustered robust standard errors to account for patients presenting multiple times.
Hospital length of stay includes ED and SSU length of stay

Figure 3 provides the predicted proportion of accelerated patients each week following regression of accelerated care over time. The original IMPACT study reported that 75.6% of patients were placed on an accelerated protocol.[1] There was an association between weeks after implementation (entered as cubic splines) and the proportion of patients accelerated (χ^2=76.2, p <0.001). Specifically, the proportion of patients deemed suitable for accelerated assessment increased rapidly over the first six months after implementation of the IMPACT protocol. Accelerated assessment then slowly increased for a further year, before plateauing to an expected 53.7% (95% CI: 49.6-57.8%) by the end of the study period (Figure 3).
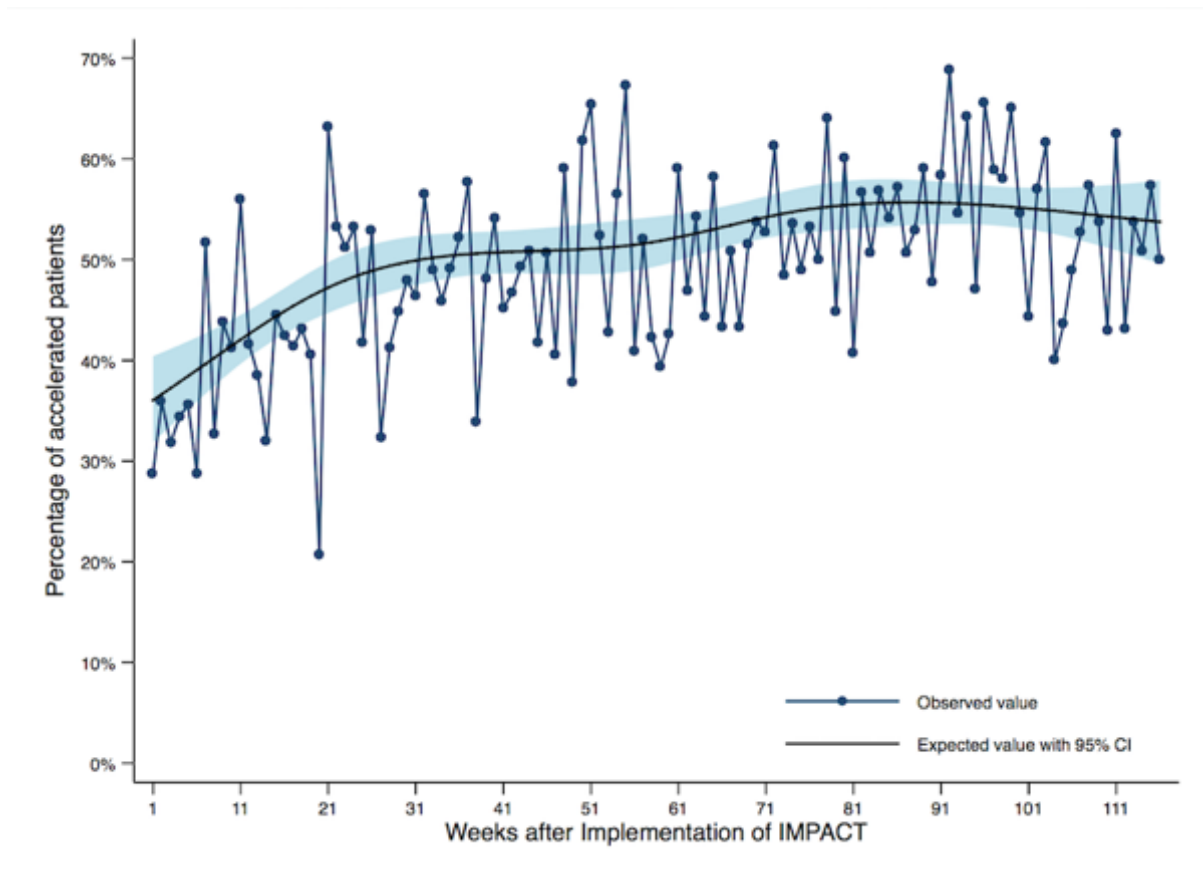
Figure 3. Percentage of patients intended for accelerated assessment by time. The black line represents the predicted proportion of patients undergoing accelerated assessment across time. The blue line represents actual percentages accelerated by week.

A second regression examined the odds of being accelerated following adjustment for age and sex. The odds of being accelerated were 25% lower for males compared to females (OR=0.75, 95% CI: 0.67-0.84) and decreased with increasing age (Supplementary Figure 1). Figure 4 provides the probability of being accelerated by week at an average age of 51 years (the average age of the original IMPACT cohort). This figure shows that, after adjustment for age, the expected proportion of accelerated patients was 66.7% (95% CI: 61.8-71.4%) for males and 72.7% (95% CI: 68.2-76.9%) for females by the end of the study period.
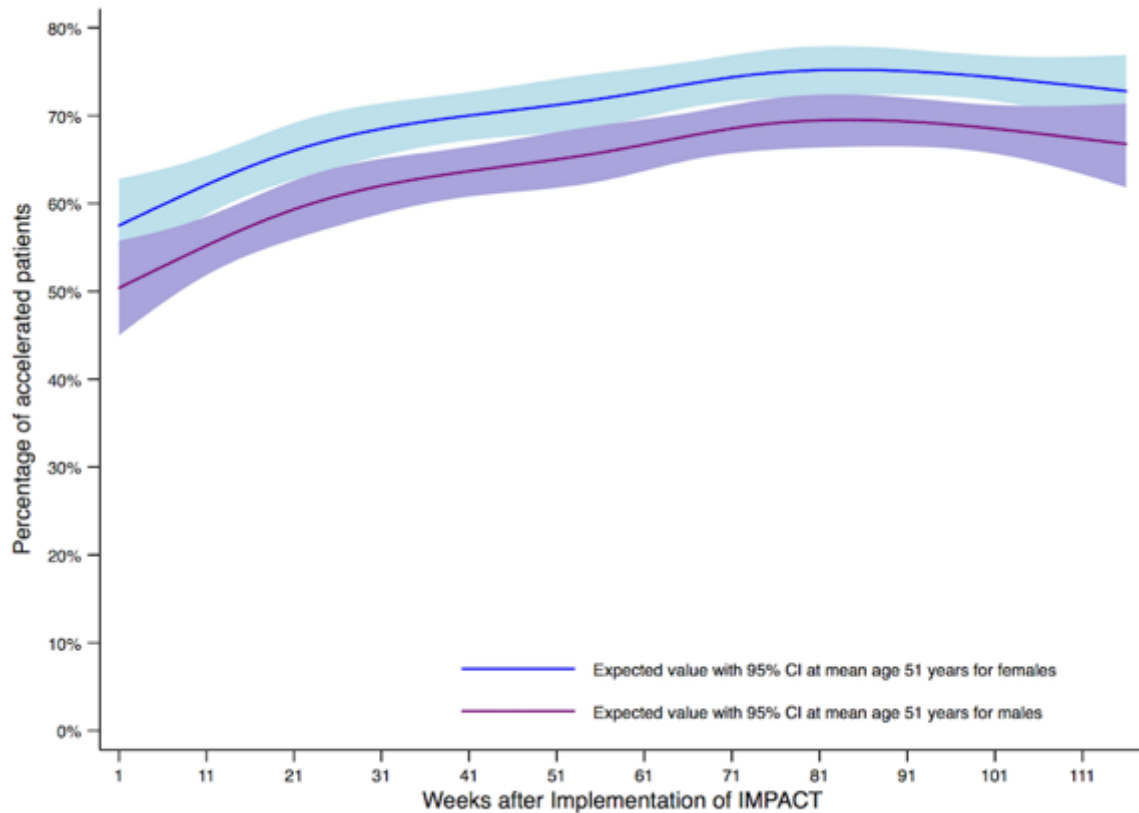
Figure 4. Percentage of patients intended for accelerated assessment adjusted for age and sex. Data are plotted for an average age of 51 years. The blue and purple lines represent the predicted proportion of female and male patients respectively undergoing accelerated assessment across time.

For the overall cohort, regression of the proportion of patients admitted to hospital on weeks after implementation (as cubic splines) indicated that hospital admission changed across time (χ^2=10.3, p=0.04). Hospital admission slightly decreased over the first six months post implementation of IMPACT and then plateaued over the remaining period (Figure 5). The expected proportion of patient admitted to hospital by the end of the observation period was 50.4% (95% CI: 46.4-54.4%).
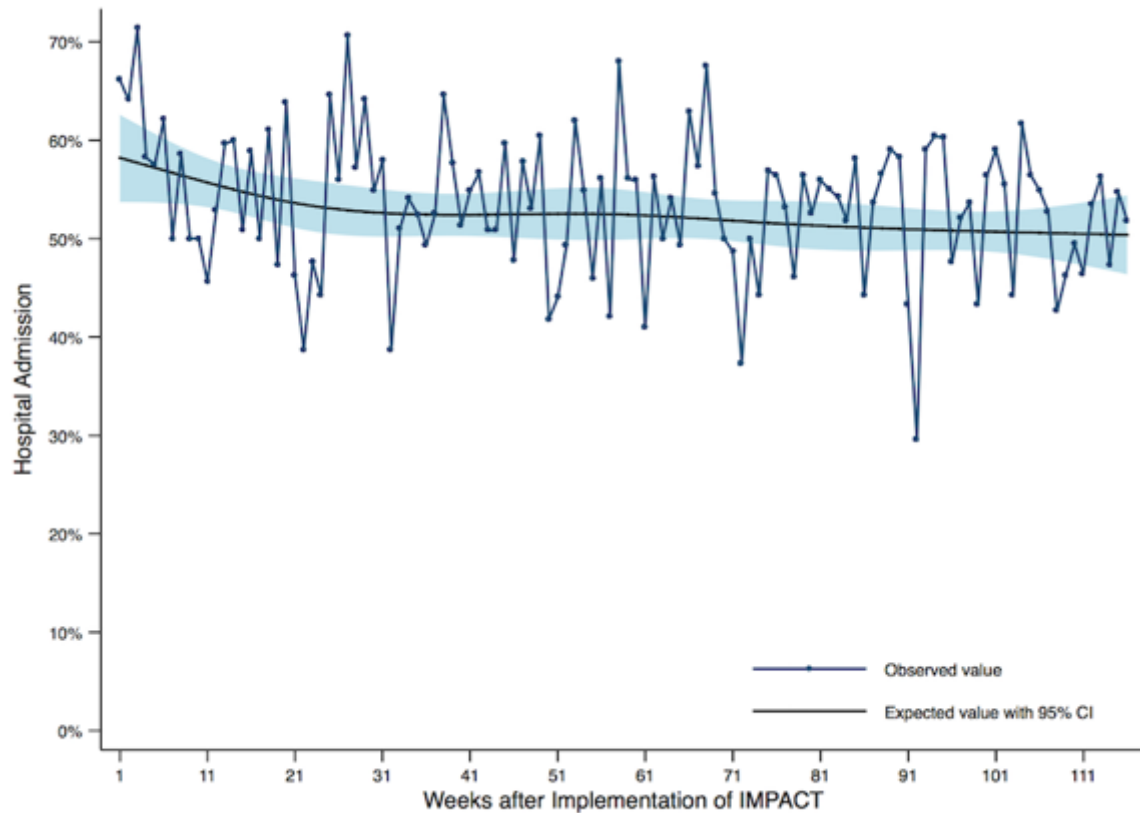
Figure 5. Proportion of patients admitted to hospital by time

A second regression was conducted examining the odds of being admitted for accelerated patients only, including adjustment for age and sex. The odds of being admitted were similar for males and females (Male OR=1.1, 95% CI: 0.96-1.3) and increased with increasing age (Supplementary Figure 2). Weeks after implementation was not associated with admission rates (χ^2=7.9, p=0.09), indicating that the proportion of accelerated patients admitted did not change across this study period. Figure 6 provides the probability of being admitted by week at an average age of 51 years (the average age of the original IMPACT cohort). The expected proportion of patients admitted to hospital at the end of the study period was 19.1% (95% CI: 14.9-24.1%) for females and 21.1% (95% CI; 16.5-26.5%) for males.
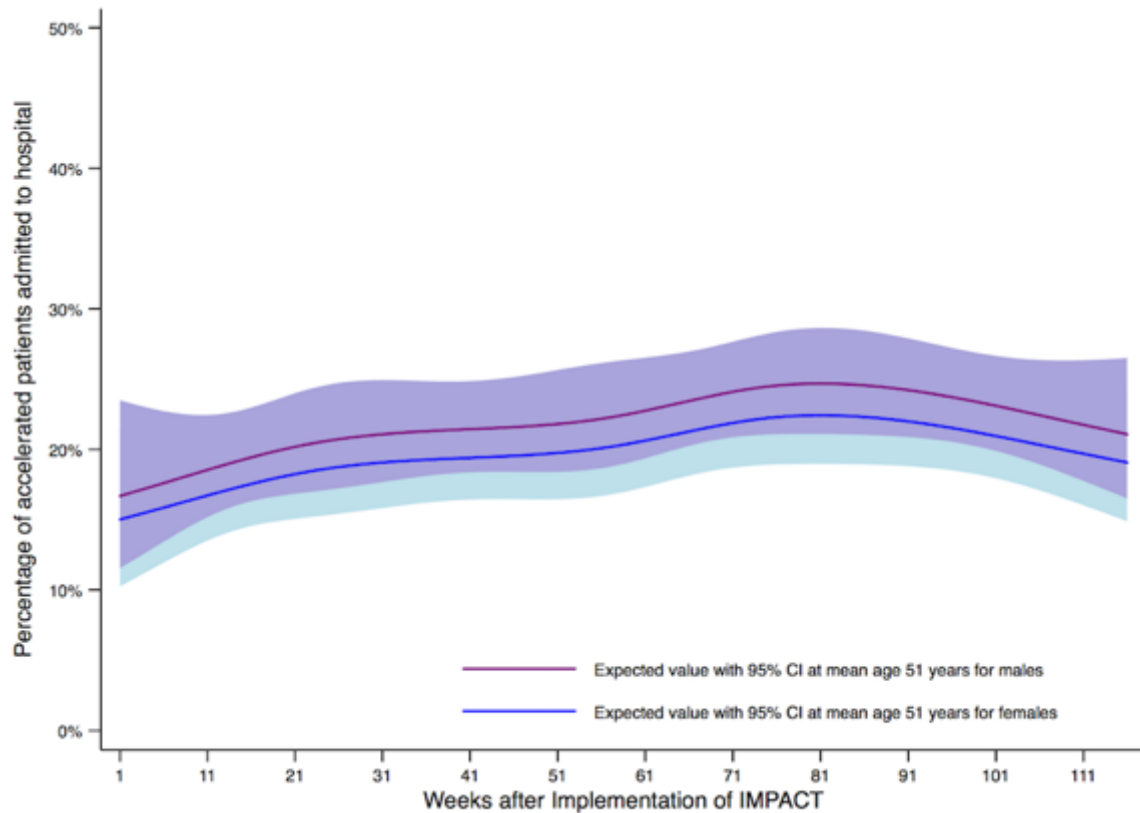
Figure 6. Adjusted probability to being admitted to hospital for accelerated patients. Data presented for an average age of 51 years.

ED and SSU length of stay changed across time (F=3.29, p =0.01). There was a slight decrease in ED and SSU length of stay for the first year after the introduction of IMPACT, but length of stay increased again during the second year (Figure 7). For accelerated patients, after adjusting for age and sex, the time after implementation did not have a clear association with ED and SSU length of stay (F=2.3, p=0.06). At the end of the study period, predicted median ED and SSU length of stays for accelerated patients was 8.7 hours (95% CI: 8.0-9.4) for males and 8.4 hours (95% CI: 7.7-9.1 hours) for females (Figure 8). Length of stay did not differ by sex (median difference=-0.35, 95% CI: -0.72 to 0.02) but increasing age was associated with increasing length of stay (Supplementary Figure 3).
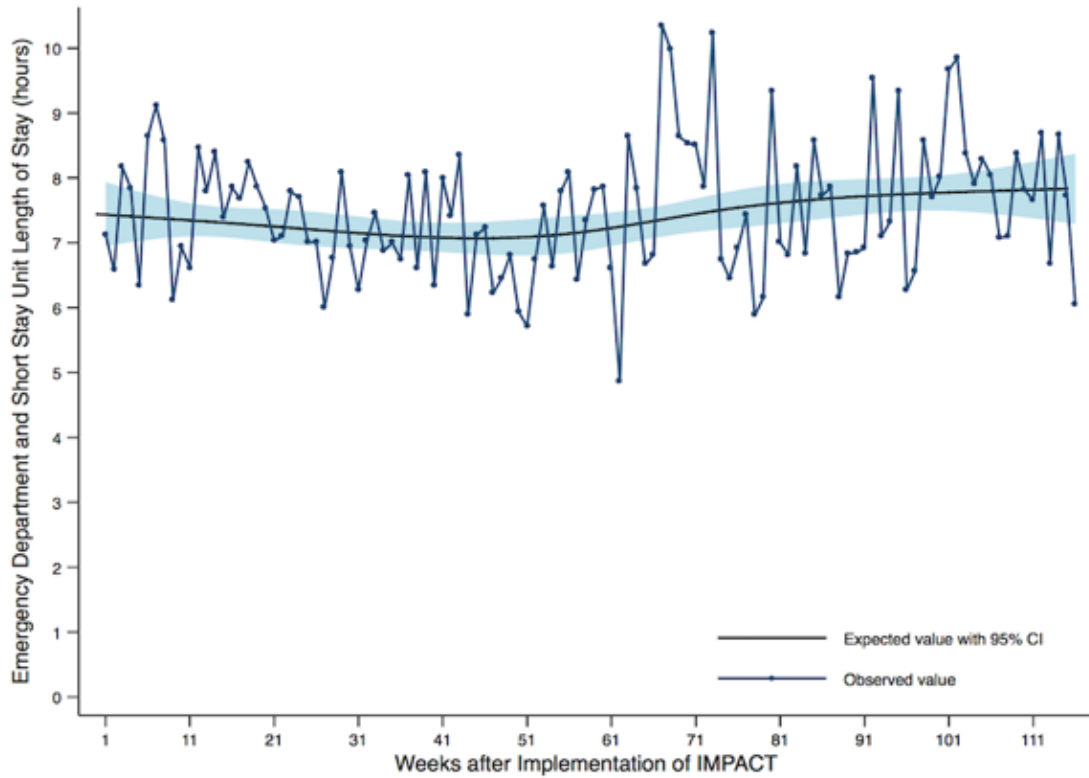
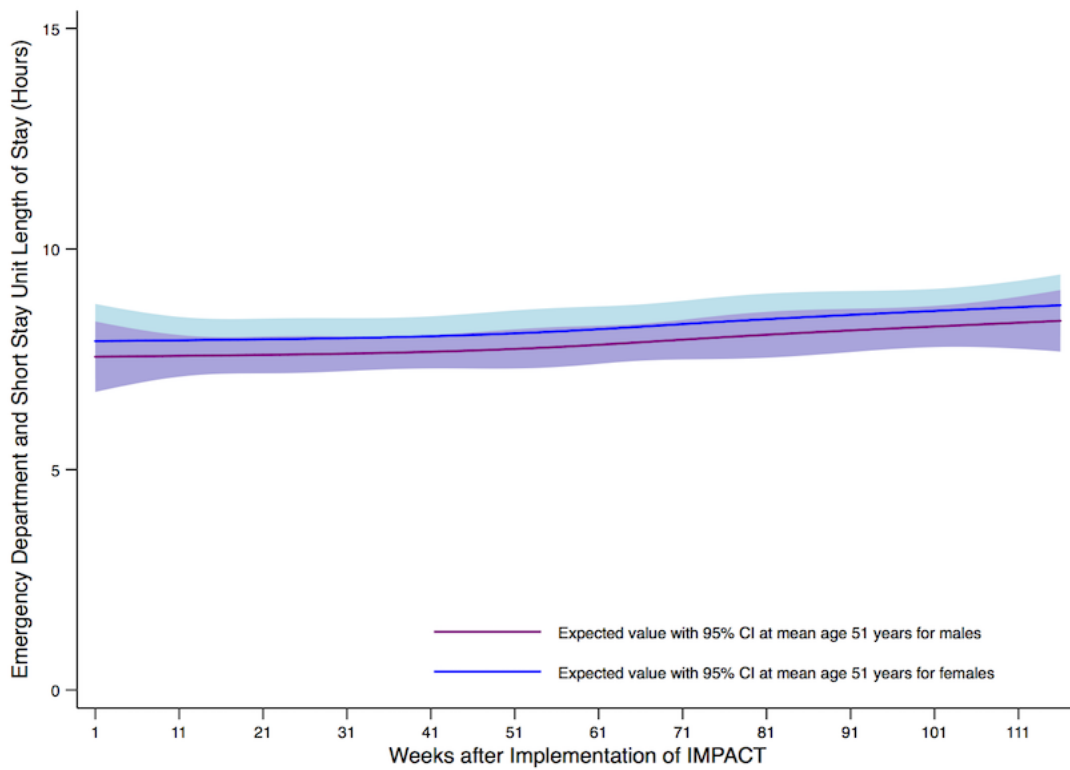Figure 7. Median ED and SSU length of stay by time

Figure 8. ED and SSU length of stay by time for accelerated patients. Data presented for an

average age of 51 years.

Discussion

This evaluation of the implementation of the IMPACT protocol demonstrated that after the conclusion of the original IMPACT study period, there was uptake of the IMPACT protocol in a clinical setting. There was an initial increase in proportion of patients being accelerated before plateauing before the end of the study period. The secondary outcomes of ED and SSU length of stay and admission rates for accelerated patients remained unchanged throughout this study period, suggesting consistency in the use of the IMPACT protocol at the RBWH ED.

The overall proportion of patients who underwent accelerated assessment during this study period was 49.2%, lower than the 75.6% reported by the IMPACT study. A lower proportion was expected in a transition from a research setting, where dedicated research nurses facilitated the use of the IMPACT protocol, to real world conditions. It was also partially attributed to the nature of the original IMPACT study where some high-risk patients may not have been recruited. For example, if a patient was too unwell or was unable to consent, the patient may not be able to be enrolled in the IMPACT study. In this observational study, patients were not required to be enrolled and were automatically included based on the troponin testing inclusion criteria, hence there may be a higher capture rate of high-risk patients, leading to the proportion of accelerated patients to appear lower when compared to the IMPACT study.

As this study's cohort was older than that of the IMPACT study's (58 years in this study vs 51 years in the IMPACT study), the proportion of patients being accelerated was adjusted for sex and age (to the average age of 51 years) to allow for comparison between the two studies and evaluate the IMPACT protocol's uptake. After adjustment, the predicted proportion of patients being accelerated reached 66.7% for males and 72.7% for females by the end of the study period. The proportion of patients being accelerated increased over this study period,

suggesting increasing acceptance of the IMPACT protocol over time. The proportion of patients accelerated were achieved due to multiple factors. Firstly, the protocol had been implemented in a trial at the RBWH ED for a period of time prior to this study, with research staff previously ensuring that troponin ordering practices were in accordance with the IMPACT protocol. There was consistent leadership engagement to ensure correct use of the protocol. Secondly, the IMPACT protocol was resource efficient and thus clinicians were likely inclined to use it. The IMPACT protocol has previously been shown in a study by Cullen et al. to allow accelerated patients to be discharged earlier while maintaining safety;[1] the median hospital length of stay for accelerated patients was 9.8 hours, shorter than the median hospital length of stay of 23.9 hours for all patients. Taking into account that the latter group included high risk patients, the shorter hospital length of stay in the accelerated group may have been contributed to not only by the second troponin test being ordered earlier, but also potentially by allowing further investigations to be performed on the same day during working hours (for example, exercise stress test). This was consistent with the median hospital length of stay for accelerated patients being shorter if they presented during working hours (8.0 hours) than if presenting outside of working hours (11.6 hours). Likewise, the median ED and SSU length of stay for accelerated patients increased from 6.7 hours during working hours to 8.1 hours outside of working hours.

The median ED and SSU length of stay was 7.2 hours for accelerated patients. The SSU is an area within the ED that is separate from the ED acute assessment area, and is designated for short term observations, treatment, assessment and reassessment of patients. It is designed for short term stays no longer than 24 hours. The median ED and SSU length of stay for accelerated patients did not change across this study period, indicating that the accelerated assessment using the IMPACT protocol persisted throughout this post-implementation period.

The median hospital length of stay for accelerated patients in this study was 9.8 hours, while the IMPACT study's median hospital length of stay was 5.1 hours for low risk patients and 7.7 hours for intermediate risk patients. The longer length of stay in this study was attributed to the transition from a research setting, where dedicated research nurses ensured patient flow, to real world conditions. In addition, the IMPACT study included only presentations during working hours, whereas this study included presentations at all hours, potentially contributing to a longer length of stay as some services were only available during working hours (for example, exercise stress tests).

The hospital admission rate for the overall cohort decreased over the first six months post-implementation, in line with the proportion of accelerated patients increasing over the same period, suggesting gradual increasing uptake of the IMPACT protocol. The hospital admission rate for accelerated patients remained unchanged across this study period, indicating sustainability in the use of the IMPACT protocol and its consistent effect on this secondary outcome. Adjusted for age and sex, the accelerated cohort's admission rate was 19.1% for females and 21.1% for males, comparable to the 17% admission rate for low- and intermediate-risk patients in the IMPACT study.

Increased age was associated with decreased odds of being accelerated and increased admission rates. This was likely due to age (over 40 years old) being an exclusion criterion for the low risk group, and increasing age being associated with multiple co-morbidities that would place the patient in the high-risk group. ED and SSU length of stay increased with age but decreased after the age of 60, possibly reflective of the decision to admit older patients at an earlier stage of their assessment.

Given that the proportion of accelerated patients plateaued by the end of this study period, along with the secondary outcomes of ED and SSU length of stay and admission rates for accelerated patients, the IMPACT protocol was shown to be sustainable under real world conditions.

Limitations

This study was conducted at the single centre that was responsible for the development of the IMPACT protocol that was used in this study. The clinicians were exposed to the IMPACT protocol during the original trial period. This likely increased acceptability, and thus eased its adaptation as the standard protocol during the post-implementation period. To assess generalisability, further study would need to be performed to ascertain whether translation would be similarly successful in other centres that were not involved with the development of the IMPACT protocol.

In addition, this observation period immediately succeeded the trial period; while data was available in the period prior to the implementation of IMPACT protocol as standard care, the data would be reflective of that during the trial period. Therefore, no data prior to the utilisation of the IMPACT protocol was available for comparison.

Patients were included based on troponin testing being performed. At RBWH, samples for troponin testing were routinely taken on presentation for chest pain suspected of ACS. Raised cardiac troponin indicated damage to the myocardium and was therefore specifically used in the assessment of cardiac complaints. Also, troponin measurement was a core component of

the guidelines for the management of ACS. As such, we believed that including patients based on the presence of troponin testing would identify the group of patients being investigated for ACS with a high degree of accuracy. While this method may miss patients, we believed this was likely to be a small number as troponin testing would be required for the diagnosis of ACS. Inclusion based on troponin testing also created inclusion bias as the primary outcome of this study was the proportion of patients receiving zero- and two-hour troponin testing. However, alternative methods of identifying patients from the databases, such as using a presenting complaint or discharge diagnosis, were likely to be less sensitive and specific than troponin testing given the length of time required to assign an accurate diagnosis and that ACS could have a broad range of potential presentations.

Patients were excluded if they only had a single troponin test performed. The guideline used for comparison to the IMPACT study and hence this study was the 2006 NHFA/CSANZ guideline, which recommended that "a repeat serum troponin measurement (unless already positive) should be performed at least eight hours after the last episode of pain or other symptoms of coronary insufficiency".[9] We acknowledge that a single troponin test may be used at a clinician's discretion in the investigation of ACS, and hence the exclusion of patients with only one troponin test performed may miss cases of chest pain being investigated for possible ACS; however, given that at the time of the study, there were no firm recommendations on when a single troponin should be used, it would not be possible to determine which of the patients receiving a single troponin test were being investigated for ACS.

It was difficult to assess the degree of fidelity achieved. It had been assumed that the ordering of a zero-hour troponin test followed by a two-hour troponin test equated to the patient being stratified onto the accelerated pathway. However, as clinicians ordered investigations at their

own discretion, the ordering of troponin testing may not correspond to the timing that had been recommended by the IMPACT protocol. For example, the age-adjusted figures of 66.7% of females and 72.7% of males being accelerated may be deceptively high if patients with high-risk characteristics received zero- and two-hour troponins. On the other hand, accelerated patients may be incorrectly grouped into the high-risk group if their second troponin test was delayed due to workflow issues (for example, no available staff to take the blood sample for troponin testing at two hours). However, given the number of patients included in this study, it was likely that any effect caused by discrepancy in troponin ordering would be insignificant.

The IMPACT protocol utilised the high-risk criteria from the 2006 NHFA/CSANZ guidelines,[9] which were current at the time of the study. Updated guidelines were released in 2016, with minor changes to the high-risk group.[2] However, these changes were unlikely to have caused significant changes to the results, especially in the comparison between the IMPACT trial period and post-implementation period as both utilised the 2006 guidelines.

Conclusion

This study demonstrated that the IMPACT protocol was being adopted and utilised in a clinical setting following conclusion of the original trial. The initial increase in proportion of patients being accelerated, followed by a plateau before the end of the study period, indicated acceptability, adoption and sustainability of the IMPACT protocol. The secondary outcomes of ED and SSU length of stay and admission rates remained unchanged for accelerated patients across the post-implementation period, demonstrating sustainability and consistency in the use of the IMPACT protocol at the RBWH ED.

References

1. Cullen L, Greenslade JH, Hawkins T, et al. Improved Assessment of Chest pain Trial (IMPACT): assessing patients with possible acute coronary syndromes. *Med J Aust*. 2017;207(5):195-200.

2. Chew DP, Scott IA, Cullen L, et al. National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016. *Heart Lung Circ*. 2016;25(9):895-951.

3. Australian Institute of Health and Welfare. Cardiovascular disease, diabetes and chronic kidney disease – Australian facts: Prevalence and incidence. https://www.aihw.gov.au/getmedia/0ce5f234-0abf-41b9-a392-be5dd1e94c54/17034.pdf.aspx?inline=true. Published October 2014. Accessed January 7, 2019.

4. Cullen L, Greenslade J, Merollini K, et al. Cost and outcomes of assessing patients with chest pain in an Australian emergency department. *Med J Aust*. 2015;202(8):427-432.

5. Thygesen K, Alpert JS, White HD, et al. Universal definition of myocardial infarction. *Circulation*. 2007;116(22):2634-2653.

6. Mahajan VS, Jarolim P. How to interpret elevated cardiac troponin levels. *Circulation*. 2011;124(21):2350-2354.

7. Fox WR, Diercks DB. Troponin assay use in the emergency department for management of patients with potential acute coronary syndrome: current use and future directions. *Clin Exp Emerg Med*. 2016;3(1):1-8.

8. Mythili S, Malathi N. Diagnostic markers of acute myocardial infarction. *Biomed Rep*. 2015;3(6):743-748.

9. Acute Coronary Syndrome Guidelines Working Group. Guidelines for the management of acute coronary syndromes 2006. *Med J Aust.* 2006;184(8 Suppl):S1-32.

10. Chew DP, Aroney CN, Aylward PE, et al. 2011 Addendum to the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand Guidelines for the management of acute coronary syndromes (ACS) 2006. *Heart Lung Circ.* 2011;20(8):487-502.

11. Richardson DB. Increase in patient mortality at 10 days associated with emergency department overcrowding. *Med J Aust.* 2006;184(5):213-216.

12. Forero R, Hillman KM, McCarthy S, Fatovich DM, Joseph AP, Richardson DB. Access block and ED overcrowding. *Emerg Med Australas.* 2010;22(2):119-135.

13. Maumill L, Zic M, Esson AA, et al. The National Emergency Access Target (NEAT): can quality go with timeliness? *Med J Aust.* 2013;198(3):153-157.

14. Cheng Q, Greenslade JH, Parsonage WA, et al. Change to costs and lengths of stay in the emergency department and the Brisbane protocol: an observational study. *BMJ open.* 2016;6(2):e009746.

15. Morris ZS, Wooding S, Grant J. The answer is 17 years, what is the question: understanding time lags in translational research. *J R Soc Med.* 2011;104(12):510-520.

16. Brieger D, Kelly AM, Aroney C, et al. Acute coronary syndromes: consensus recommendations for translating knowledge into action. *Med J Aust.* 2009;191(6):334-338.

17. Than M, Aldous S, Lord SJ, et al. A 2-hour diagnostic protocol for possible cardiac chest pain in the emergency department: a randomized clinical trial. *JAMA Intern Med.* 2014;174(1):51-58.

18. George T, Ashover S, Cullen L, et al. Introduction of an accelerated diagnostic protocol in the assessment of emergency department patients with possible acute coronary syndrome: the Nambour Short Low-Intermediate Chest pain project. *Emerg Med Australas*. 2013;25(4):340-344.

19. Mahler SA, Riley RF, Hiestand BC, et al. The HEART Pathway randomized trial: identifying emergency department patients with acute chest pain for early discharge. *Circ Cardiovasc Qual Outcomes*. 2015;8(2):195-203.

20. Ebell M. AHRQ White Paper: Use of clinical decision rules for point-of-care decision support. *Med Decis Making.* 2010;30(6):712-721.

21. Stiell IG, Bennett C. Implementation of clinical decision rules in the emergency department. *Acad Emerg Med*. 2007;14(11):955-959.

22. Stiell I, Wells G, Laupacis A, et al. Multicentre trial to introduce the Ottawa ankle rules for use of radiography in acute ankle injuries. Multicentre Ankle Rule Study Group. *BMJ*. 1995;311(7005):594-597.

23. Sullivan CM, Staib A, Flores J, et al. Aiming to be NEAT: safely improving and sustaining access to emergency care in a tertiary referral hospital. *Aust Health Rev*. 2014;38(5):564-574.

24. Graham ID, Stiell IG, Laupacis A, O'Connor AM, Wells GA. Emergency physicians' attitudes toward and use of clinical decision rules for radiography. *Acad Emerg Med*. 1998;5(2):134-140.

25. Stiell IG, McKnight RD, Greenberg GH, et al. Implementation of the Ottawa ankle rules. *JAMA*. 1994;271(11):827-832.

26. Than MP, Pickering JW, Aldous SJ, et al. Effectiveness of EDACS Versus ADAPT Accelerated Diagnostic Pathways for Chest Pain: A Pragmatic Randomized Controlled Trial Embedded Within Practice. *Ann Emerg Med*. 2016;68(1):93-102.e1.
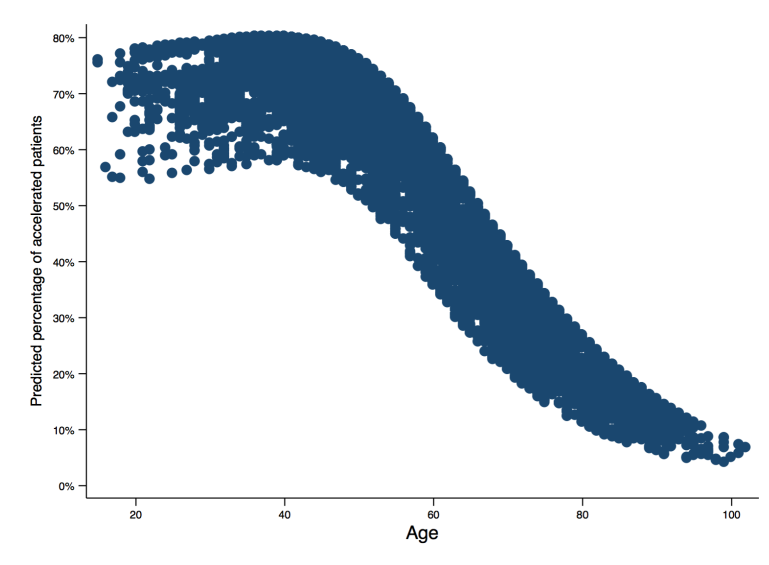
27. Graham ID, Stiell IG, Laupacis A, et al. Awareness and use of the Ottawa ankle and knee rules in 5 countries: can publication alone be enough to change practice? *Ann Emerg Med*. 2001;37(3):259-266.

28. Davis D, Galbraith R. Continuing medical education effect on practice performance: effectiveness of continuing medical education: American College of Chest Physicians Evidence-Based Educational Guidelines. *Chest*. 2009;135(3 Suppl):42s-48s.

29. Raja AS, Ip IK, Prevedello LM, et al. Effect of computerized clinical decision support on the use and yield of CT pulmonary angiography in the emergency department. *Radiology*. 2012;262(2):468-474.

30. Rajan A, Sullivan R, Bakker S, van Harten WH. Critical appraisal of translational research models for suitability in performance assessment of cancer centers. *Oncologist*. 2012;17(12):e48-57.

31. Trochim W, Kane C, Graham MJ, Pincus HA. Evaluating translational research: a process marker model. *Clin Transl Sci*. 2011;4(3):153-162.

32. Contopoulos-Ioannidis DG, Alexiou GA, Gouvias TC, Ioannidis JP. Medicine. Life cycle of translational research for medical interventions. *Science*. 2008;321(5894):1298-1299.

33. Ioannidis JP. Materializing research promises: opportunities, priorities and conflicts in translational medicine. *J Transl Med*. 2004;2(1):5.

34. Green LW, Ottoson JM, Garcia C, Hiatt RA. Diffusion theory and knowledge dissemination, utilization, and integration in public health. *Annu Rev Public Health*. 2009;30:151-174.

35. Contopoulos-Ioannidis DG, Ntzani E, Ioannidis JP. Translation of highly promising basic science research into clinical applications. *Am J Med*. 2003;114(6):477-484.

36. Hanney SR, Castle-Clarke S, Grant J, et al. How long does biomedical research take? Studying the time taken between biomedical and health research and its translation into products, policy, and practice. *Health Res Policy Syst*. 2015;13:1.

37. Chalmers I, Bracken MB, Djulbegovic B, et al. How to increase value and reduce waste when research priorities are set. *Lancet*. 2014;383(9912):156-165.

38. Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. *Adm Policy Ment Health*. 2011;38(2):65-76.

39. Parsonage WA, Milburn T, Ashover S, et al. Implementing change: evaluating the Accelerated Chest pain Risk Evaluation (ACRE) project. *Med J Aust*. 2017;207(5):201-205.

40. Skoien W, Page K, Parsonage W, Ashover S, Milburn T, Cullen L. Use of the Theoretical Domains Framework to evaluate factors driving successful implementation of the Accelerated Chest pain Risk Evaluation (ACRE) project. *Implement Sci*. 2016;11(1):136.

41. Harrell F. *Regression modeling strategies: With applications to linear models, logistic and ordinal regression, and survival analysis.* 2nd ed. Cham, Switzerland: Springer International Publishing; 2015.
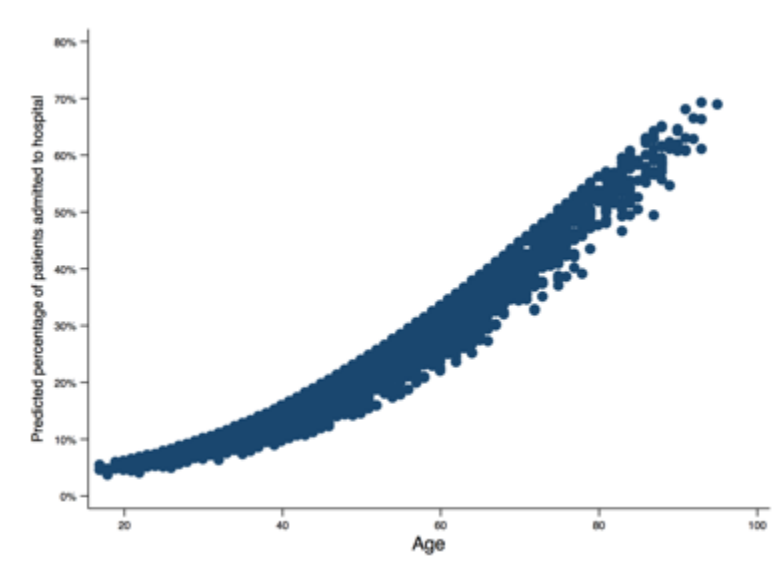
Supplementary Appendix

Supplementary Table 1: Comparison of risk stratification criteria from the 2006 National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand (NHFA/CSANZ) guideline and IMPACT protocol
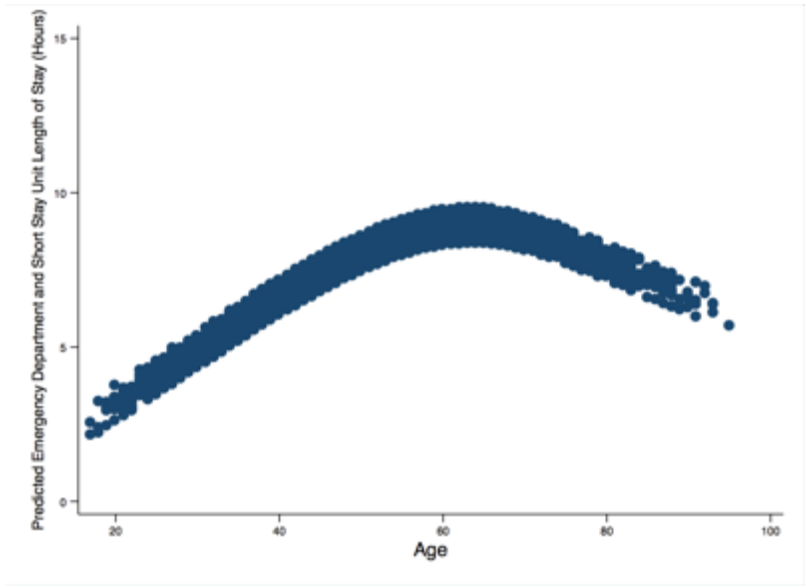
2006 NHFA/CSANZ guidelines	IMPACT protocol
High risk	
Presentation with clinical features consistent with ACS and any of the following: • Repetitive or prolonged (>10 min) chest pain or discomfort • Elevation of at least one cardiac biomarker (troponin or CK-MB) • Persistent or dynamic ST-segment depression ≥0.5mm, or new T-wave inversion ≥2mm • Transient ST-segment elevation (≥0.5mm) in more than two contiguous leads • Haemodynamic compromise – systolic blood pressure <90mmHg, cool peripheries, diaphoresis, Kilip class >1, and/or new onset mitral regurgitation • Sustained ventricular tachycardia • Syncope • Left ventricular systolic dysfunction (LVEF fraction <40%) • Prior percutaneous coronary intervention within six months or prior coronary artery bypass surgery • Diabetes (with typical symptoms of ACS) • Chronic kidney disease, eGFR <60mL/min/1.73m^2 (with typical symptoms of ACS)	Same as 2006 NHFA/CSANZ guidelines
Intermediate risk	
Presentation with clinical features consistent with ACS, with no high risk features, and any of: • Chest pain or discomfort within the past 48 hours that occurred at rest, or was repetitive or prolonged (but currently resolved) • Age >65 years • Known coronary heart disease – prior myocardial infarction with LVEF ≥40%, or known coronary lesion more than 50% stenosed • No high-risk changes on ECG (as listed above) • Two or more of the following risk factors: known hypertension, family history, active smoking or hyperlipidaemia • Presence of known diabetes (with atypical symptoms of ACS) • Chronic kidney disease, eGFR <60 mL/min/1.73m^2 (with atypical symptoms of ACS) • Prior aspirin use	No high risk features, and any of • Age ≥40 years • Chronic kidney disease, eGFR <60mL/min/1.73m^2 (with atypical symptoms of ACS) • Diabetes (with atypical symptoms of ACS)
Low risk	
Presentation with clinical features consistent with an ACS with no intermediate or high risk features	No intermediate or high risk features, and • No history of diabetes

Supplementary Figure 1. Proportion of patients accelerated by age

Supplementary Figure 2. Proportion of patients admitted by age

Supplementary Figure 3. ED and SSU length of stay by age