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Change to costs and lengths of stay in the emergency department and the Brisbane Accelerated CHest pain (BACH) protocol: an observational study

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ABSTRACT

Objective: To compare health service cost and length of stay between a traditional and accelerated diagnostic approach to assess acute coronary syndromes (ACS) among patients who presented to the emergency department of a large tertiary hospital in Australia.

Design, setting and participants: This historically controlled trial analysed data collected from two independent patient cohorts presenting to the ED with potential ACS. Data from the first cohort of 938 patients were collected in 2008–2010, and these patients were assessed using the traditional diagnostic approach detailed in the national guideline. The second cohort of 921 patients was recruited in 2011–2013 and was assessed with the accelerated diagnostic approach named the Brisbane Accelerated CHest pain assessment (BACH) protocol. A decision tree model was used to compare the expected cost and length of stay in hospital between two approaches. Probabilistic sensitivity analysis was used to account for model uncertainty.

Results: Compared with the traditional diagnostic approach, the BACH protocol was associated with reduced cost and length of stay. The BACH protocol allowed physicians to discharge a higher proportion of low and intermediate risk patients from ED within 4 hours (72% versus 51%). Results from sensitivity analysis suggest the BACH protocol has a high chance of being both cost- and time-saving.

Conclusion: This study provides some evidence of cost savings from a decision to adopt the BACH protocol. Benefits would arise for the hospital and for patients and their families.

Strengths and limitations of this study

- This study is the first to report the changes to length of stay and cost from adopting an accelerated diagnostic approach for unspecified chest pain in Australian emergency departments.
- It was a large study that prospectively collected data on costs and outcomes
- A decision tree model was developed to compare outcomes of the two approaches using realistic and clinically relevant patient pathways.
- Probabilistic sensitive analysis was used to account for uncertainties.
- This is an observational study and differences were found between the two cohorts

INTRODUCTION

Chest pain is a principal reason for adult emergency department (ED) visits[1] with the most common cause being acute coronary syndromes (ACS) including acute myocardial infarction (AMI) and unstable angina (UA). Yet after thorough investigation most patients have non-cardiac conditions such as musculoskeletal pain or gastrointestinal causes for chest discomfort. In 2007–2008 5.5 million people in the United States presented to emergency departments with chest pain and only 13% were diagnosed with ACS.[2]

Current management of patients with possible ACS in Australia arises from National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines.[3] Patients are stratified into low, intermediate and high risk categories based on clinical features, electrocardiography (ECG) and troponin test results over a minimum of six hours when using a sensitive troponin assay. Low risk patients can be safely discharged. High risk patients require admission to hospital and intensive management. Intermediate risk patients form the largest group and require objective diagnostic testing to identify coronary artery disease. The costs to health services and patient outcomes from these guidelines were described in a recent Australian study.[4]

The National Emergency Access Target (NEAT) was introduced in 2011 in Australia as part of the National Partnership Agreement on Improving Public Hospital Services.[5] It requires 90% of all presentations to the ED be discharged, admitted to hospital or transferred to another hospital for treatment within four hours. This target requires patients to be processed faster in the ED setting, and with the current guidelines requiring delayed troponin sampling, all patients with possible cardiac chest pain are steered towards admission to hospital.

Accelerated diagnostic protocols (ADP) that risk stratify individuals within 2–3 hours have recently been trialed.[6-10] A large proportion of patients can be classified as low risk and rapidly referred for objective testing.[6-8 11] A study reporting on the implementation of the accelerated protocol found that average ED length of stay was reduced in the group of patients deemed low risk and health outcomes were maintained.[9] Ongoing improvements in the assessment process of ED patients with chest pain have occurred, and are in clinical use.[12]

A novel method of assessment of ED patients with chest pain, the Brisbane Accelerated CHest

pain assessment (BACH) protocol, was derived at a large tertiary hospital in Australia. This study compares the cost of managing patients for ACS who present to the ED under two competing configurations of health services: the traditional guidelines based approach[3] and the BACH protocol. Detailed clinical outcomes of patients were not reported as this study focused on health economic outcomes of two diagnostic approaches.

METHODS

Data Collection

This was a historically controlled study. Data were collected from two independent patient cohorts presenting to the ED of a large tertiary hospital in Australia with ACS. Data from the first cohort of 938 patients were prospectively collected in 2008–2010, and these patients were assessed using the traditional diagnostic approach detailed in national guideline.[3] The second cohort of 921 patients was prospectively collected in 2011–2013 and was assessed with the BACH protocol.

Patients were recruited for both studies between 8am and 5pm and were included if they were aged ≥ 18 years, presented to the ED with at least five minutes of chest pain suggestive of ACS and were being investigated for ACS. In accordance with American Heart Association case definitions,[13] pain suggestive of ACS includes acute chest, epigastric, neck, jaw, or arm pain; or discomfort or pressure without an apparent non-cardiac source. Research staff identified all eligible patients using the emergency department admissions database and in collaboration with the treating clinicians. Patients were excluded if: there was a clear non-ACS cause for their symptoms; they were unwilling or unable to provide informed consent such as a language barrier; staff considered that recruitment was inappropriate, such as terminal illness; they were transferred from another hospital; they were pregnant; they were recruited to the study within the previous 45 days; or they were unable or unwilling to be contacted after discharge. Perceived high risk was not an exclusion criterion. Consecutive eligible cases were included.

Research nurses collected data on presentation date, admission date, discharge date, risk stratification and exercise stress test (EST) results. Total costs including the cost of the ED visit and any inpatient costs were extracted from a linked administrative database. Adverse events that occurred with 30 days after discharge from hospital also were recorded. Adverse events were adjudicated independently by local cardiologists using predefined standardised reporting guidelines.[14] Cardiologists had knowledge of the clinical record, ECG, troponin results and objective testing from standard care. A second cardiologist conducted a blind review of all ACS cases and 10% of non-ACS cases. In cases of disagreement, endpoints were agreed by consensus. This was achieved for all end points. For the intervention study, a single cardiologist completed endpoint adjudication. Diagnosis of AMI and UAP was based on accepted international standards as described previously.[15]

Decision Tree Model

The events and costs relevant to each alternative patient pathway were entered into a decision tree model. The traditional approach based on national guidelines [3] is shown by Figure 1. All non-high risk patients were initially stratified into intermediate and low risk categories based on clinical features, ECG findings and troponin results obtained on presentation. Ongoing clinical assessment and repeat ECG and troponin testing was performed six hours later. Low risk patients were discharged and costs arising from the index presentation were included. After serial troponin and ECG testing six hours after presentation were normal, patients in the intermediate risk group were referred for EST, however due to clinical reasons some intermediate risk patients did not have this test. If the EST result was positive, patients were further stratified to high risk and admitted to an inpatient bed. If negative, patients were considered low risk and discharged home. Patients with an equivocal EST and who were discharged within 24 hours were defined as low risk and those discharged greater than 24 hours were defined as high risk. Patients who did not have an EST were either directly admitted to an inpatient bed or discharged home after appropriate management in the ED and/or ED short stay unit. A small number of patients left against medical advice before treatment commenced.

A fundamental change in the new assessment process was the introduction of early serial troponin testing at 0 and 2 hours after presentation for low and intermediate risk patients, in comparison to the traditional 0 and 6 hour testing. The alternate BACH protocol is shown in Figure 2 and the management protocol used in the hospital is shown in Figure 3. High risk patients were initially identified and managed according to the traditional approach since the BACH protocol was designed for low and intermediate risk patients. All non-high risk patients were then assessed using the BACH protocol. Those under 40 years of age without diabetes or renal impairment were defined as BACH-low risk while the rest were classified as BACH-intermediate risk. Patients in the BACH-intermediate risk group were referred for EST. As this was a pragmatic trial design, some patients from the BACH-low risk group were also referred for EST based on individual patient characteristics. If the EST was positive, the patient was considered high risk and admitted to an inpatient bed. If negative, patients were discharged and any problems within 30 days were included. If equivocal and discharged within 24 hours, patients were defined as low risk. If they were admitted greater than 24 hours they were categorised as high risk. Patients who were not referred for an EST were either admitted to an inpatient bed or discharged home after appropriate management in the ED/ED short stay unit. Again, only a small number of patients left against medical advice.

The decision trees are designed to summarise expected costs and hospital length of stay under the traditional approach and BACH protocol. If there are differences in the number of deaths, this will also be shown quantitatively by the decision tree. Clinicians working in the ED validated the structure of the decision tree model prior to data analysis.

Data Analysis

Age, gender, risk factors and prior medical history were compared across the two cohorts. The

primary outcomes are health service cost and length of stay in hospital and were compared using the decision tree model. As the BACH protocol is for low to intermediate risk patients, all high-risk patients were managed according to the current National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines[3] and were excluded from the analysis. The proportion of patients discharged from ED within 4 hours was compared to show if the BACH protocol was associated with improved performance against the NEAT target.

This was a historically controlled trial without random assignment, hence there may have been differences between the two cohorts at baseline. To account for this we used iterative post-stratification to match the marginal distributions of the traditional approach cohort to the BACH protocol cohort. The variables matched were age (10 year bands), gender, prior MI, prior angina, prior CAD, prior arrhythmia, prior CHF, prior hypertension, prior dyslipidaemia and prior family CAD. We then calculated the percent discharged within 4 hours between the two cohorts using the post-stratification weights and compared this with an unweighted percent. We used the 'rake' function in the 'survey' library in R.[16]

Updating the decision tree with information

The probabilities associated with the events at each circular chance node in the decision trees were derived from the two patient cohorts. The estimated probabilities were the risk of patients having low or intermediate risk, undergoing EST, having positive, negative or equivocal EST results, being admitted to inpatient ward or being discharged. Prior beta distributions that can only take values between zero and one, were used to model the probabilities and the uncertainty.

The costs incurred for the ED and inpatient wards were retrieved from each patient's hospital administration record that had been linked to the primary patient data. ED costs that include a fixed cost and an activity-based component were based on triage categories of urgency. [4] Inpatient costs were derived from procedure-related Australian refined diagnosis-related group reimbursement codes used for activity-based funding. [4] These costs were summed for each individual. For patients who moved through a common pathway in the decision tree, the median costs values were calculated to inform the cost outcome of that path. A prior gamma distribution was fitted to these data to capture the inherent skew in costs data.[17] Costs from 2008 to 2012 were adjusted by an inflation rate of 3.4% per year to equal 2013 prices.[18] Lengths of stay in hospital were derived from dates of presentation and discharge, and were also fitted to Gamma distributions.

Expected costs and lengths of stay are based on the summation of the pathway cost and hours-in-hospital weighted by the pathway probabilities. By comparing the expected cost and length of stay of the two competing diagnostic approaches, we defined the costs and time spent in emergency department when the BACH protocol was used.

A probabilistic sensitivity analysis was used to account for uncertainty in the information used in the model. Resampling was done 10,000 times from the prior distributions using Monte

Carlo simulation with cost and length of stay varying simultaneously. The probability of an approach being optimal was derived by counting the number of times out of 10,000 the approach had lower costs or shorter length of hospital stay.

RESULTS

Patient characteristics

The baseline patient characteristics for both cohorts are shown in Table 1. Patients in traditional approach group were older and suffered more frequently from hypertension, dyslipidaemia and family history of coronary artery disease. Moreover, the proportion of patients having prior medical conditions was higher among the traditional approach group.

Table 1: Baseline characteristics by cohort

Variable	Traditional Approach (n=938)	BACH protocol (n=921)	p
Age, Mean (SD)	54.8 (15.1)	50.8 (12.9)	<0.01
Male sex	573 (61.1)	538 (58.4)	0.24
Risk Factors			
Hypertension	396 (42.2)	306 (33.2)	<0.01
Dyslipidaemia	391 (41.7)	320 (34.7)`	<0.01
Diabetes	115 (12.3)	105 (11.4)	0.57
Family history of CAD	434 (46.3)	352 (38.3)	<0.01
Current smoking	259 (27.6)	267 (29.0)	0.51
Prior Medical History			
Prior MI	158 (16.8)	115 (12.5)	<0.01
Prior angina	211 (22.5)	99 (10.7)	<0.01
Prior angioplasty	101 (10.8)	74 (8.0)	0.04
Prior CABG	58 (6.2)	31 (3.4)	<0.01
Prior Peripheral arterial disease	19 (2.0)	11 (1.2)	0.16
Prior CHF	43 (4.6)	12 (1.3)	<0.01
Prior arrhythmia	83 (8.9)	49 (5.3)	<0.03
Prior CAD	194 (20.7)	121 (13.14)	<0.01
Prior tachycardia	19 (1.9)	10 (1.1)	0.14

Data are number (%) except where otherwise specified. SD=standard deviation, CAD=coronary artery disease. MI=myocardial infarction, CABG=coronary artery bypass graft, CHF=congestive heart failure.

Cost and length of stay analysis

In the traditional approach (n=938) less than 1% (n=9) were allocated to the low risk category, 62% (n=585) were classed as intermediate risk, 36% (n=336) as high risk, and 0.8% (n=8) of patients left against medical advice (Table 2). None of the 9 low risk patients had EST and they spent fewer hours in hospital than intermediate and high risk patients. Among patients in the intermediate risk group, those who had an EST incurred lower costs than those who did not ($1,863 versus $2,974). The difference arose as 88% of patients having an EST were discharged from hospital following a negative EST result. In contrast 128 (56%) of 229 patients who did not perform an EST were admitted to the ward for further investigation, which incurred higher costs. Five patients died, with 3 having a cardiovascular cause of death during their hospital stay and 2 dying within 6 days of hospital discharge from non-cardiovascular causes.

Table 2: Summary statistics on cost and length of stay for the traditional approach

Risk stratification	Number of patients N=938 (%)	Cost (AUD) Median (25-75th perc.)	Hours in hospital Median (25-75th perc.)
Low	**9 (1.0%)**	**$1,636 ($1,155-$3,592)**	**11.5 (9.5-31.5)**
Intermediate	**585 (62.4%)**	**$1,961 ($1,466-$3,780)**	**24.6 (9.9-35.1)**
EST	356	$1,863 ($1,493-$2,528)	23.8 (10.2-28.7)
Negative	*312*	*$1,799 ($1,477-2,243)*	*20.4 (10.1-27.8)*
Equivocal	*26*	*$2,700 ($1,904-4,277)*	*29.7 (26.0-52.1)*
Positive	*18*	*$7,113 ($5,419-$10,348)*	*61.8 (34.5-130.5)*
No EST	229	$2,974 ($1,294-$7,163)	27.6 (8.5-76.7)
Send home	*101*	*$1,285 ($1,094-$1,626)*	*8.4 (6.2-10.4)*
Admit to ward	*128*	*$6,642 ($3,975-$9,085)*	*71.0 (34.2-126.7)*
High	**336 (35.8%)**	**$6,743 ($2,755-$12,509)**	**73.2 (27.5-143.7)**
Alive with treatment	*331*	*$6,705 ($2,755-$12,495)*	*72.3 (27.0-142.4)*
Died <30 days	*5*	*$9,340 ($3,177-$38,594)*	*146.4 (83.4-426.5)*
Left against medical advice	**8 (0.8%)**	**$1,461 ($1,057-$2,232)**	**14.1 (5.5-25.0)**

Of the 921 patients available for the BACH protocol 18% (n=169) were classed as 'BACH-low' risk, 55% (n=514) as 'BACH-intermediate' risk, 25% (n=230) as high risk, and 0.9% (n=8) of patients left against medical advice (Table 3). Overall 50% of patients managed by the BACH protocol performed an EST. In comparison, 38% of the cohort in traditional approach performed an EST. In the 'BACH-low' risk group, 39 of 169 patients

performed an EST, while 420 out of 514 in the 'BACH-intermediate' risk group had an EST. Patients in the 'BACH-low' risk group incurred fewer costs and spent fewer hours in hospital than those in the 'BACH-intermediate' risk group ($1,061 versus $1,485; 5.3 hours versus 7.9 hours). Patients who left against medical advice incurred the least cost. No one died within 30 days after discharge in this cohort.

Table 3: Summary statistics on cost and length of stay for the BACH protocol

Risk stratification	Number of patients N=921(%)	Cost (AUD) Median (25-75th perc.)	Hours in hospital Median (25-75th perc.)
BACH-low	**169 (18.3%)**	**$1,061 ($901-$1,374)**	**5.3 (4.3-7.0)**
EST	39	$1,563 ($1,042-$1,807)	7.7 (6.5-24.5)
Negative	*37*	*$1,515 ($1,028 -$1,706)*	*7.7 (6.4-10.4)*
Equivocal	*2*	*$3,897*	*28.9*
No EST	136	$1,009 ($820-$1,233)	4.8 (4.2-5.9)
Send home	*129*	*$989 ($818-$1,198)*	*4.8 (4.2-5.7)*
Admit to ward	*7*	*$2,858 ($1,028-$9,777)*	*23.0 (4.8-127.5)*
BACH-intermediate	**514 (55.8%)**	**$1,485 ($1,095-$2,086)**	**7.9 (6.3-15.2)**
EST	420	$1,449 ($1,085-$1,759)	7.7 (6.3-10.1)
Negative	*351*	*$1,366 ($1,063-$1,618)*	*7.3 (6.1-8.8)*
Equivocal	*47*	*$3,111 ($1,770- $5,492)*	*26.8(9.6-34.3)*
Positive	*22*	*$6,056 ($4,065-$6,765)*	*46.3 (28.9-52)*
No EST	94	$2,840 ($1,143-$7,838)	27.5 (6.2-53.4)
Send home	*42*	*$1,116 ($942-$1,436)*	*621 (4.7-8.5)*
Admit to ward	*52*	*$6,856 ($4,178-$11,238)*	*50.8 (29.5-80.0)*
High	**230 (25.0%)**	**$5,626 ($2,655-$9,545)**	**43.7 (24.4-74.8)**
Left against medical advice	**8 (0.9%)**	**$1,272 ($1,168-$1,737)**	**6.0 (5.2-7.3)**

In Table 4, costs and hospital length of stay according to admission category were compared between traditional approach group and the BACH protocol group. Nearly 83% of patients assessed by the BACH protocol were admitted to ED only and ED short stay unit compared with 66% in traditional approach group. Total hospital length of stay was shorter with the BACH protocol. Fewer patients in the BACH protocol group received inpatient care (17% versus 33%) and they had on shorter lengths of stay, 45 hours versus 52.5 hours. The median cost and length of stay when considering all patients were lower among members of the BACH cohort.

Table 4: Costs and hospital length of stay of ED patients with chest pain according to admission category (without high risk group as the BACH protocol targeted low/intermediate risk patients)

	Traditional approach			BACH protocol		
Admission category	**Number of patients (%)**	**Cost (AUD) Median (25-75th perc.)**	**Hours in hospital Median (25-75th perc.)**	**Number of patients (%)**	**Cost (AUD) Median (25-75th perc.)**	**Hours in hospital Median (25-75th perc.)**
ED only	28 (4.7%)	$882 ($865-$1,027)	5.6 (4.1-8.4)	78 (11.3%)	$976 ($919-$1,068)	4.7 (3.9-5.8)
ED Short Stay Unit	368 (61.1%)	$1,619 ($1,393-$2,024)	11.3 (9.3-25.5)	496 (71.8%)	$1,315 ($1,048-$1,605)	7.0 (5.8-8.6)
Inpatient ward	201 (33.4%)	$5,673 ($3,331-$8,301)	52.5 (30.8-116.3)	116 (16.8%)	$5,852 ($3,193-$8,467)	45.0 (28.5-74.0)
Transferred	5 (0.8%)	$1,071 ($999-$1,299)	44.8 (18.8-70.6)	1 (0.1%)	$1,028	4.1
All categories	602 (100%)	$1,959 ($1,455-$3,726)	24.3 (9.9-34.1)	691 (100%)	$1,363 ($1,037-$1,803)	7.2 (5.7-10.4)

Percentage of patients achieved NEAT

The percentage of patients who were discharged from ED within four hours is shown in Table 5, and we give the results before and after patient characteristics in the traditional approach were adjusted in an attempt to make the two cohorts more comparable. As the BACH protocol only further stratified low and intermediate risk groups, the proportion of patients discharged from ED in high-risk group were similar between two approaches. The BACH protocol enabled physicians to discharge a higher proportion of patients within 4 hours in low and intermediate risk groups than the traditional approach (72% versus 51%).

Table 5: Percentage of patients discharged from ED within 4 hours by risk stratification before and after baseline characteristics were adjusted

	Traditional approach (not adjusted)	Traditional approach (adjusted)	BACH protocol
High risk	26.0%	30.1%	30.2%
Low and intermediate risk	46.1%	50.6%	72.3%

Decision tree model outputs

The expected costs and length of stay in hospital of the two approaches from the decision tree model are shown in Table 6. The average patient managed by the BACH protocol cost $1,229 less, and 26 hours in hospital was saved compared to the traditional approach. These differences are shown by the probabilistic sensitivity analysis and are plotted in Figure 4.

Table 6: Expected costs and length of stay in hospital per patient for the traditional approach and BACH protocol (without high risk group as the BACH protocol targeted low/intermediate risk patients)

	Expected cost (95%CI)	Expected length of stay (95% CI)	Incremental cost (95% CI)	Incremental length of stay (95% CI)
Traditional approach	$3,454 ($1,438-$7,159)	42hrs (8hrs-153hrs)		
BACH protocol	$2,225 ($1,282-$3,609)	16hrs (7hrs-32hrs)	-$1,229 (-$5,122- $1,266)	-26hrs (-136hrs-14hrs)

Figure 5 provides the proportion of the 10,000 resamples where the BACH protocol resulted in a lower cost or shorter stays for the average patient. When only cost is taken into consideration, the BACH protocol has a 78% probability of incurring fewer costs. When shorter length of stay is the decision criteria, there was a 79% probability the BACH protocol is optimal.

DISCUSSION

We report the first study of the potential health services gain of adopting an ADP into routine practice in the Australian healthcare setting. Some advantages of ADP for assessing patients presenting to ED with chest pain have previously been demonstrated.[6-8] This analysis used data collected over two different periods, and included it in a decision tree model to compare cost and length of stay between traditional assessment approach and the BACH protocol. We demonstrated the economic benefits of applying BACH protocol in a hospital setting.

The BACH protocol for the assessment of emergency patients with possible cardiac chest pain may have considerable benefits to patients with early notification about the underlying cause of their symptoms, and early discharge of those without a cardiac diagnosis. Adopting a BACH protocol could also assist in meeting NEAT targets. Seventy percent of non-high risk patients could be assessed rapidly for ACS and discharged from ED within 4 hours under the BACH protocol. In the hospital the average ED length of stay fell from 289 minutes between 2008–2010 to 243 minutes between 2011–2014, the period when the BACH protocol was implemented. Whether this observed saving of 45 minutes per patient was caused by the BACH protocol cannot be known for certain due to the study design used. The overall capacity released for the hospital was substantial, with a reduction in the expected assessment period from 42 hours to 16 hours for all non-high risk patients. The reduction in need for lengthy admission supported same day discharge for many patients. The economics of this in terms of time missed from work, family and social activities is hard to quantify, however early discharge home for patients is likely to have had a positive effect on patient satisfaction.

The BACH protocol identified a large proportion of patients as low risk. This is a significant increase by comparison to the current National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines risk stratification process, and is an equivalent sized low risk cohort in comparison to other risk scores such as TIMI and GRACE scores when used for ED patient assessment. The true reduction in need for EST testing in this cohort, may have larger systems effects in terms of improving access for other patients requiring this cardiac investigation. This was not assessed in the study. Compared to other ADP approaches, the BACH protocol has its strength that it incorporates both AMI and UA. There are other approaches used to identify those at risk of AMI alone,[19 20] but these ignore the increased short to medium term risk of recurrent ischemic events in those with underlying coronary artery disease and UA.

Other economic analysis of applying ADP to assess chest pain patients also shows evidence for reduced hospitalisation stay and lower costs. Asher et al. [21] in Israel examined the clinical outcomes and cost-effectiveness of an ADP using contemporary technology versus routine care and found that an ADP could save time and resources. There was a slight decrease in total costs when patients were treated ADP, but the difference was not significant. Compared with their comparative prospective study, our study has strengths in that we combined comparative study with an economic decision model. By taking account of the probability of being classified as low or intermediate risk and the probability of having an EST, the decision

tree model demonstrates the expected cost and length of stay for a patient who presents to ED with chest pain. In addition, we conducted probabilistic sensitivity analysis to account for parameter uncertainty surrounding cost and length of stay. The BACH protocol has shown a high probability of being optimal compared to traditional approach.

The limitations of this analysis should be acknowledged. Ideally a pragmatic parallel multi-centre randomised controlled trial would be done, but this would cost millions of dollars and will take time to organise. With the observational design we cannot be sure that the BACH protocol contributed to the differences in the outcomes. The results of the adjustment (Table 5) provide some evidence of an effect arising from the BACH protocol. When the two cohorts were adjusted for the baseline variables the proportion patients discharged from ED within 4 hours did change, but not dramatically. Despite these limitations the improvement in cost and length of stay outcomes are plausible, and the purpose of this study is to provide data that contribute to a decision being made, rather than perfectly estimtaing the size of an effect. As this study is focused on the health economic outcomes of the BACH protocol, this study does not report the detailed clinical outcomes of patients managed according to the traditional diagnostic approach and BACH protocol.

CONCLUSION

The Brisbane Accelerated CHest pain (BACH) protocol may be a cost saving change to services for the assessment of ED patients with possible ACS. Patients and the emergency departments that manage them might benefit from this system of care.

Contributors

LC, JHG, WAP, NG, AGB and KM led the design of the study. Data analysis was undertaken by QC, JHG, AGB and KM. All authors critically reviewed each draft of the manuscript. The final version was approved by all authors.

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Competing interests

None declared.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

No additional data are available.

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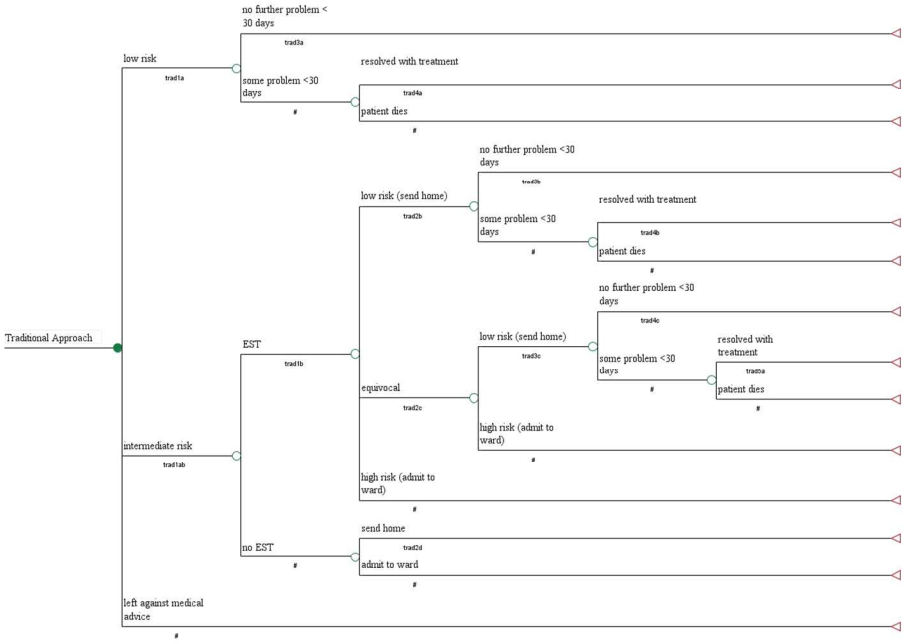

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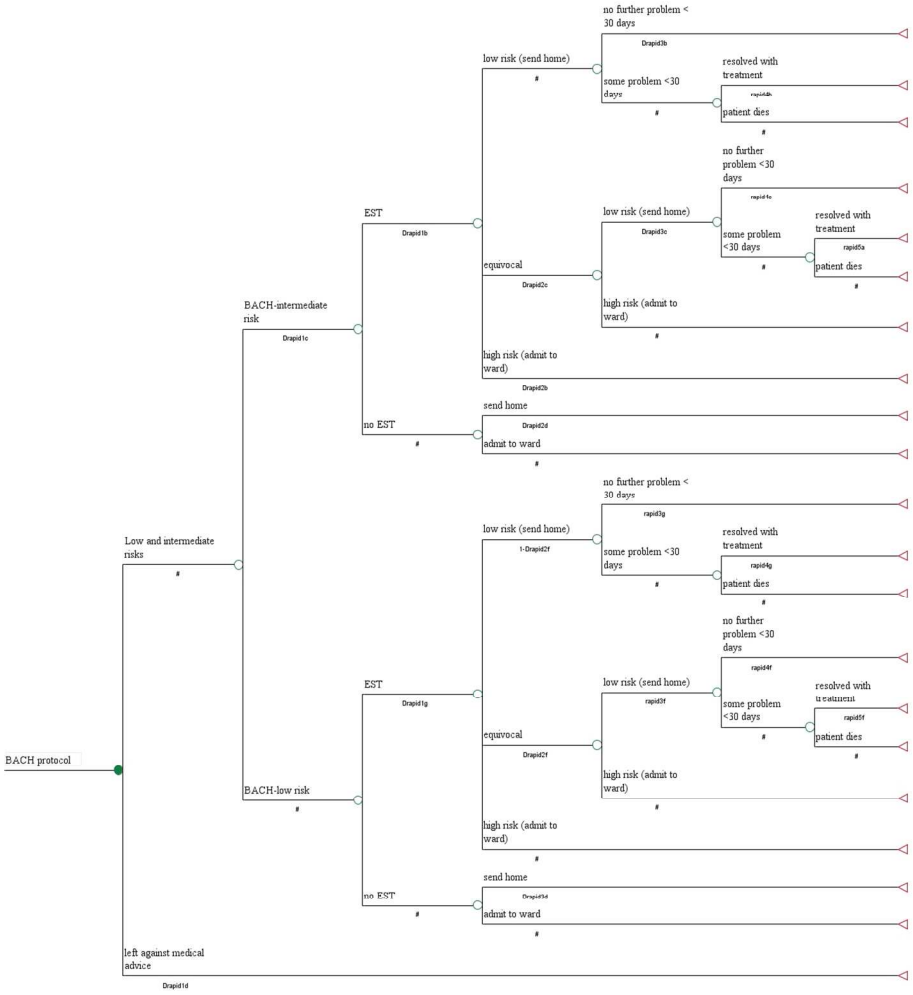

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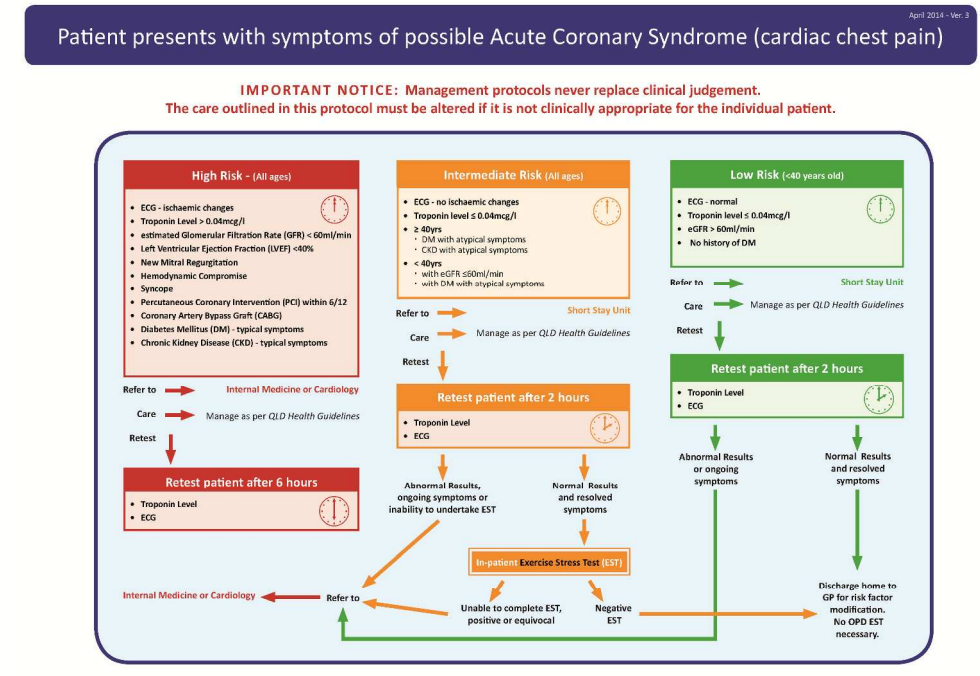

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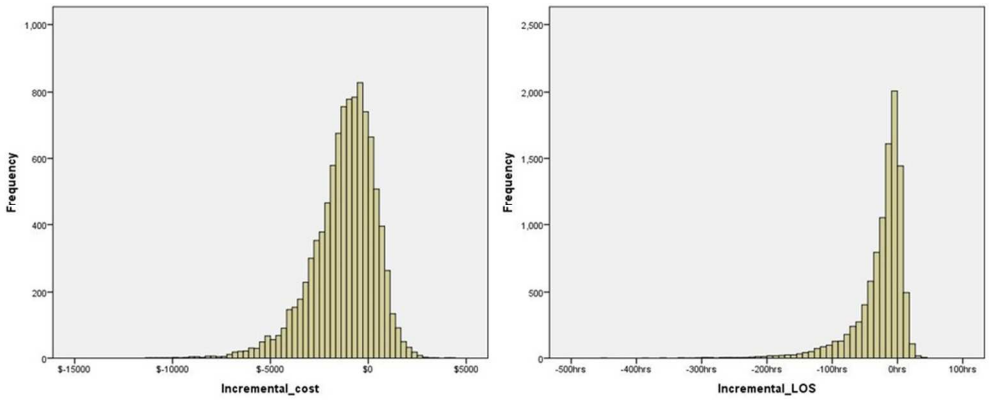

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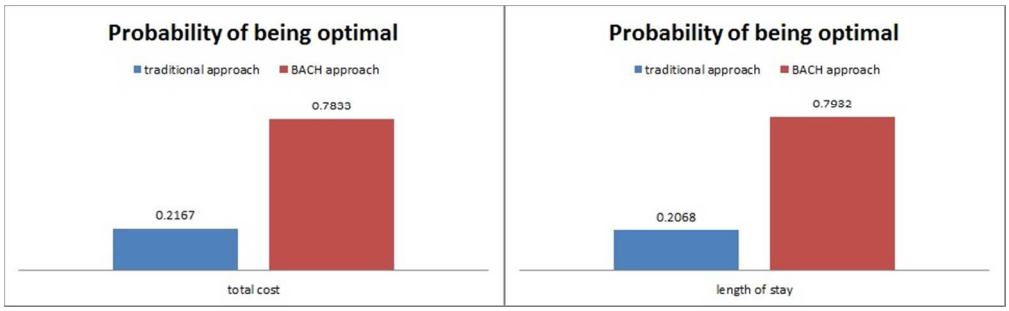

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	*Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	✓
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	✓
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	✓

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	✓
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	✓
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	✓
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	✓
		(*b*) Report category boundaries when continuous variables were categorized	✓
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	✓
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Change to costs and lengths of stay in the emergency department and the Brisbane protocol: an observational study

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Change to costs and lengths of stay in the emergency department and the Brisbane protocol: an observational study

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ABSTRACT

Objective: To compare health service cost and length of stay between a traditional and accelerated diagnostic approach to assess acute coronary syndromes (ACS) among patients who presented to the emergency department (ED) of a large tertiary hospital in Australia.

Design, setting and participants: This historically controlled trial analysed data collected from two independent patient cohorts presenting to the ED with potential ACS. The first cohort of 938 patients was recruited in 2008–2010, and these patients were assessed using the traditional diagnostic approach detailed in the national guideline. The second cohort of 921 patients was recruited in 2011–2013 and was assessed with the accelerated diagnostic approach named the Brisbane protocol. The Brisbane protocol applied early serial troponin testing for patients at 0 and 2 hours after presentation to ED, in comparison to 0 and 6 hour testing in traditional assessment process. The Brisbane protocol also defined a low-risk group of patients in whom no objective testing was performed. A decision tree model was used to compare the expected cost and length of stay in hospital between two approaches. Probabilistic sensitivity analysis was used to account for model uncertainty.

Results: Compared with the traditional diagnostic approach, the Brisbane protocol was associated with reduced expected cost of $1,229 (95% CI: -$1,266 to $5,122) and reduced expected length of stay of 26 hours (95% CI: -14 hours to 136 hours). The Brisbane protocol allowed physicians to discharge a higher proportion of low and intermediate risk patients from ED within 4 hours (72% versus 51%). Results from sensitivity analysis suggested the Brisbane protocol had a high chance of being both cost- and time-saving.

Conclusion: This study provides some evidence of cost savings from a decision to adopt the Brisbane protocol. Benefits would arise for the hospital and for patients and their families.

Strengths and limitations of this study

- This study is the first to report the changes to length of stay and cost from adopting an accelerated diagnostic approach for unspecified chest pain in Australian emergency departments.
- It was a large study that prospectively collected data on costs and outcomes
- A decision tree model was developed to compare outcomes of the two approaches using realistic and clinically relevant patient pathways.
- Probabilistic sensitive analysis was used to account for uncertainties.
- This is an observational study and differences were found between the two cohorts

INTRODUCTION

Chest pain is a principal reason for adult emergency department (ED) visits[1] with the most common cause being acute coronary syndromes (ACS) including acute myocardial infarction (AMI) and unstable angina pectoris (UAP) . Yet after thorough investigation most patients have non-cardiac conditions such as musculoskeletal pain or gastrointestinal causes for chest discomfort. In 2007–2008 5.5 million people in the United States presented to emergency departments with chest pain and only 13% were diagnosed with ACS.[2]

Current management of patients with possible ACS in Australia arises from National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines.[3] Patients are stratified into low, intermediate and high risk categories based on clinical features, electrocardiography (ECG) and troponin test results over a minimum of six hours when using a sensitive troponin assay. Low risk patients can be safely discharged. High risk patients require admission to hospital and intensive management. Intermediate risk patients form the largest group and further objective diagnostic testing to identify coronary artery disease (CAD) is required. The costs to health services and patient outcomes from these guidelines were described in a recent Australian study.[4]

The National Emergency Access Target (NEAT) was introduced in 2011 in Australia as part of the National Partnership Agreement on Improving Public Hospital Services.[5] It requires 90% of all presentations to the ED be discharged, admitted to hospital or transferred to another hospital for treatment within four hours. This target requires patients to be processed faster in the ED setting, and with the current guidelines requiring delayed troponin sampling, all patients with possible cardiac chest pain are steered towards admission to hospital.

Accelerated diagnostic protocols (ADP) that risk stratify individuals within 2–3 hours have recently been trialed.[6-10] A large proportion of patients can be classified as low risk and rapidly referred for objective testing.[6-8 11] A study reporting on the implementation of the accelerated protocol found that average ED length of stay was reduced in the group of patients deemed low risk and health outcomes were maintained.[9] Ongoing improvements in the assessment process of ED patients with chest pain have occurred, and are in clinical use.[12]

A novel method of assessment of ED patients with chest pain, the Brisbane protocol, was derived at a large tertiary hospital in Australia. This study compares the cost of managing patients for ACS who present to the ED under two competing configurations of health

services: the traditional guidelines based approach[3] and the Brisbane protocol. Detailed clinical outcomes of patients were not reported as this study focused on health economic outcomes of two diagnostic approaches.

METHODS

Data Collection

This was a historically controlled study. Two separate prospective trials were conducted and have been included in this study. Data were prospectively collected from two independent patient cohorts presenting to the ED of a large tertiary hospital in Australia with ACS. The first trial was a prospective observational trial, whereby 938 consenting patients were recruited in 2008–2010, and these patients were assessed using the traditional diagnostic approach detailed in national guideline.[3] The second study was a prospective intervention trial as outlined in this study, whereby 921 patients was recruited and assessed with the Brisbane protocol in 2011–2013.

Patients were recruited for both trials between 8am and 5pm and were included if they were aged ≥ 18 years, presented to the ED with at least five minutes of chest pain suggestive of ACS and were being investigated for ACS. In accordance with American Heart Association case definitions,[13] pain suggestive of ACS includes acute chest, epigastric, neck, jaw, or arm pain; or discomfort or pressure without an apparent non-cardiac source. Research staff identified all eligible patients using the emergency department admissions database and in collaboration with the treating clinicians. Patients were excluded if: there was a clear non-ACS cause for their symptoms; they were unwilling or unable to provide informed consent such as a language barrier; staff considered that recruitment was inappropriate, such as terminal illness; they were transferred from another hospital; they were pregnant; they were recruited to the study within the previous 45 days; or they were unable or unwilling to be contacted after discharge. Perceived high risk was not an exclusion criterion. Consecutive eligible cases were included. The number of patients approached and the number of patients excluded for each reason in the first trial have been published. [4] In the second trial, 1,438 patients were approached. Excluded patients are as follows: 289 declined or were unable to consent; 72 were identified > 2 hours after presentation; 39 were interhospital transfers; 17 were pregnant; 100 did not have matching cost data.

Research nurses collected data on presentation date, admission date, discharge date, risk stratification and exercise stress test (EST) results. Total costs including the cost of the ED visit and any inpatient costs were extracted from a linked administrative database. Thirty days after initial attendance, research nurses conducted telephone follow-up and medical record review for the diagnosis of ACS. Information was obtained from the patient and from hospital databases about whether there had been any cardiac events or investigations, or contact with any health care providers, during the 30-day period. All follow-up information was verified through contact with the health care provider, and original copies of medical records and

cardiac investigation results were obtained. Relevant investigations included EST, stress echocardiography, myocardial perfusion scanning, coronary computed tomography angiography, or coronary angiography. The 30-day clinical outcomes were adjudicated independently by at least one of two local cardiologists using predefined standardised reporting guidelines.[14] Cardiologists had knowledge of all clinical information collected within a 30-day period. For both cohorts, this included all hospital medical records, public and private investigations, details provided by general practitioners and specialists seen within 30 days after discharge and by telephone contact with patients. In the first trial a second cardiologist conducted a blind review of all ACS cases and a random sample of 10% of non-ACS cases. In cases of disagreement, endpoints were agreed by consensus. This was achieved for all end points. For the second trial, a single cardiologist completed endpoint adjudication as the second adjudication of the outcomes has not occurred at this point in time. The clinical outcomes will be fully reported once this second adjudication has occurred. Diagnosis of AMI and UAP was based on accepted international standards as described previously.[15]

Decision Tree Model

The events and costs relevant to each alternative patient pathway were entered into a decision tree model. The traditional approach based on national guidelines [3] is shown by **Figure 1**. All non-high risk patients were initially stratified into intermediate and low risk categories based on clinical features, ECG findings and troponin results obtained on presentation. Ongoing clinical assessment and repeat ECG and troponin testing was performed six hours later. Low risk patients were discharged and costs arising from the index presentation were included. After serial troponin and ECG testing six hours after presentation were normal, patients in the intermediate risk group were referred for EST, however due to clinical reasons some intermediate risk patients did not have this test. If the EST result was positive, patients were further stratified to high risk and admitted to an inpatient bed. If negative, patients were considered low risk and discharged home. Patients with an equivocal EST and who were discharged within 24 hours were defined as low risk and those discharged greater than 24 hours were defined as high risk. Patients who did not have an EST were either directly admitted to an inpatient bed or discharged home after appropriate management in the ED and/or ED short stay unit. A small number of patients left against medical advice before treatment commenced.

Figure 1: Traditional approach pathways

A fundamental change in the new assessment process was the introduction of early serial troponin testing at 0 and 2 hours after presentation for low and intermediate risk patients, in comparison to the traditional 0 and 6 hour testing. The alternate Brisbane protocol is shown in **Figure 2** and the management protocol used in the hospital is shown in **Figure 3**. High risk patients were initially identified and managed according to the traditional approach since the Brisbane protocol was designed for low and intermediate risk patients. All non-high risk patients were then assessed using the Brisbane protocol. Those under 40 years of age without diabetes or renal impairment were defined as Brisbane protocol-low risk while the rest were

classified as Brisbane protocol-intermediate risk. Patients in the Brisbane protocol-intermediate risk group were referred for EST. As this was a pragmatic trial design, some patients from the Brisbane protocol-low risk group were also referred for EST based on individual patient characteristics. If the EST was positive, the patient was considered high risk and admitted to an inpatient bed. If negative, patients were discharged and any problems within 30 days were included. If equivocal and discharged within 24 hours, patients were defined as low risk. If they were admitted greater than 24 hours they were categorised as high risk. Patients who were not referred for an EST were either admitted to an inpatient bed or discharged home after appropriate management in the ED/ED short stay unit. Again, only a small number of patients left against medical advice.

The decision trees are designed to summarise expected costs and hospital length of stay under the traditional approach and Brisbane protocol. If there are differences in the number of deaths, this is also be shown quantitatively by the decision tree. Clinicians working in the ED validated the structure of the decision tree model prior to data analysis.

Figure 2: Brisbane protocol pathways

Figure 3: Management protocol of patients presenting with symptoms of possible ACS

Data Analysis

Age, gender, risk factors and prior medical history were compared across the two cohorts. The primary outcomes are health service cost and length of stay in hospital and were compared using the decision tree model. As the Brisbane protocol is for low to intermediate risk patients, all high-risk patients were managed according to the current National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines[3] and were excluded from the analysis. The proportion of patients discharged from ED within 4 hours was compared to show if the Brisbane protocol was associated with improved performance against the NEAT target.

This was a historically controlled trial without random assignment, hence there may have been differences between the two cohorts at baseline. We used multiple variable regression models to test if baseline characteristics were associated with risk stratification, cost, length of stay in hospital and proportion of patients discharged from ED within 4 hours (in IBM SPSS Statistics 21). To test whether more patients were risk stratified to low risk was due to baseline characteristics or the Brisbane protocol, we used binary logistic regression models as the new stratification only works on low and intermediate risk patients. The results suggest that it was the Brisbane protocol that was mainly responsible for the change in risk stratification so any difference in baseline characteristics should not have greatly impacted on risk stratification. We have also run linear regression models to test if baseline characteristics had any impact on cost and length of stay for patients who moved through the same pathway in the decision tree model (e.g. patients who were classed as intermediate risk, had EST and had negative EST outcome). The results suggested little impact from baseline characteristics on total costs and length of stay in hospital. This is probably because patients who moved

through the same pathway in the decision tree were relatively homogeneous. Thus, baseline differences between patients had less potential to influence costs and length of stay. Therefore, we did not adjust decision tree model inputs (risk stratification, costs and length of stay) by baseline characteristics.

However, we found that differences between two cohorts at baseline did influence the proportion of patients discharged from ED within 4 hours. To account for this we used iterative post-stratification to match the marginal distributions of the traditional approach cohort to the Brisbane protocol cohort. The variables matched were age (10 year bands), gender, prior MI (myocardial infarction), prior angina, prior CAD, prior arrhythmia, prior CHF (congestive heart failure), prior hypertension, prior dyslipidaemia and prior family CAD. We then calculated the percent discharged within 4 hours between the two cohorts using the post-stratification weights and compared this with an unweighted percent. We used the 'rake' function in the 'survey' library in R.[16]

Updating the decision tree with information

The probabilities associated with the events at each circular chance node in the decision trees were derived from the two patient cohorts. The estimated probabilities were the risk of patients having low or intermediate risk, undergoing EST, having positive, negative or equivocal EST results, being admitted to inpatient ward or being discharged. Prior beta distributions that can only take values between zero and one, were used to model the probabilities and the uncertainty.

The costs incurred for the ED and inpatient wards were retrieved from each patient's hospital administration record that had been linked to the primary patient data. ED costs that include a fixed cost and an activity-based component were based on triage categories of clinical urgency. [4] Inpatient costs were derived from procedure-related Australian refined diagnosis-related group reimbursement codes used for activity-based funding. [4] These costs were summed for each individual. For patients who moved through a common pathway in the decision tree, the median costs values were calculated to inform the cost outcome of that path. A prior gamma distribution was fitted to these data to capture the inherent skew in costs data.[17] Costs from 2008 to 2012 were adjusted by an inflation rate of 3.4% per year to equal 2013 prices.[18] Lengths of stay in hospital were derived from dates of presentation and discharge, and were also fitted to gamma distributions.

Expected costs and lengths of stay are based on the summation of the pathway cost and hours-in-hospital weighted by the pathway probabilities. By comparing the expected cost and length of stay of the two competing diagnostic approaches, we defined the costs and time spent in emergency department when the Brisbane protocol was used.

A probabilistic sensitivity analysis was used to account for uncertainty in the information used in the model. Resampling was done 10,000 times from the prior distributions using Monte Carlo simulation with cost and length of stay varying simultaneously. The probability of an approach being optimal was derived by counting the number of times out of 10,000 the

approach had lower costs or shorter length of hospital stay.

RESULTS

Patient characteristics

The baseline patient characteristics for both cohorts are shown in **Table 1**. Patients in traditional approach group were older and suffered more frequently from hypertension, dyslipidaemia and family history of CAD. Moreover, the proportion of patients having prior medical conditions was higher among the traditional approach group.

Table 1: Baseline characteristics by cohort

Variable	Traditional Approach (n=938)	Brisbane protocol (n=921)	p
Age, Mean (SD)	54.8 (15.1)	50.8 (12.9)	<0.01
Male sex	573 (61.1)	538 (58.4)	0.24
Risk Factors			
Hypertension	396 (42.2)	306 (33.2)	<0.01
Dyslipidaemia	391 (41.7)	320 (34.7)`	<0.01
Diabetes	115 (12.3)	105 (11.4)	0.57
Family history of CAD	434 (46.3)	352 (38.3)	<0.01
Current smoking	259 (27.6)	267 (29.0)	0.51
Prior Medical History			
Prior MI	158 (16.8)	115 (12.5)	<0.01
Prior angina	211 (22.5)	99 (10.7)	<0.01
Prior angioplasty	101 (10.8)	74 (8.0)	0.04
Prior CABG	58 (6.2)	31 (3.4)	<0.01
Prior Peripheral arterial disease	19 (2.0)	11 (1.2)	0.16
Prior CHF	43 (4.6)	12 (1.3)	<0.01
Prior arrhythmia	83 (8.9)	49 (5.3)	<0.03
Prior CAD	194 (20.7)	121 (13.14)	<0.01
Prior tachycardia	19 (1.9)	10 (1.1)	0.14

Data are number (%) except where otherwise specified. SD=standard deviation, CAD=coronary artery disease. MI=myocardial infarction, CABG=coronary artery bypass graft, CHF=congestive heart failure.

Cost and length of stay analysis

In the traditional approach (n=938) less than 1% (n=9) were allocated to the low risk category, 62% (n=585) were classed as intermediate risk, 36% (n=336) as high risk, and 0.8% (n=8) of patients left against medical advice (**Table 2**). None of the 9 low risk patients had EST and they spent fewer hours in hospital than intermediate and high risk patients. Among patients in the intermediate risk group, those who had an EST incurred lower costs than those who did not ($1,863 versus $2,974). The difference arose as 88% of patients having an EST were discharged from hospital following a negative EST result. In contrast 128 (56%) of 229 patients who did not perform an EST were admitted to the ward for further investigation, which incurred higher costs. Five patients died, with 3 having a cardiovascular cause of death during their hospital stay and 2 dying within 6 days of hospital discharge from non-cardiovascular causes.

Table 2: Summary statistics on cost and length of stay for the traditional approach

Risk stratification	Number of patients N=938 (%)	Cost (AUD) Median (25-75th perc.)	Hours in hospital Median (25-75th perc.)
Low	**9 (1.0%)**	**$1,636 ($1,155-$3,592)**	**11.5 (9.5-31.5)**
Intermediate	**585 (62.4%)**	**$1,961 ($1,466-$3,780)**	**24.6 (9.9-35.1)**
EST	356	$1,863 ($1,493-$2,528)	23.8 (10.2-28.7)
Negative	*312*	*$1,799 ($1,477-2,243)*	*20.4 (10.1-27.8)*
Equivocal	*26*	*$2,700 ($1,904-4,277)*	*29.7 (26.0-52.1)*
Positive	*18*	*$7,113 ($5,419-$10,348)*	*61.8 (34.5-130.5)*
No EST	229	$2,974 ($1,294-$7,163)	27.6 (8.5-76.7)
Send home	*101*	*$1,285 ($1,094-$1,626)*	*8.4 (6.2-10.4)*
Admit to ward	*128*	*$6,642 ($3,975-$9,085)*	*71.0 (34.2-126.7)*
High	**336 (35.8%)**	**$6,743 ($2,755-$12,509)**	**73.2 (27.5-143.7)**
Alive with treatment	*331*	*$6,705 ($2,755-$12,495)*	*72.3 (27.0-142.4)*
Died <30 days	*5*	*$9,340 ($3,177-$38,594)*	*146.4 (83.4-426.5)*
Left against medical advice	**8 (0.8%)**	**$1,461 ($1,057-$2,232)**	**14.1 (5.5-25.0)**

Of the 921 patients available for the Brisbane protocol 18% (n=169) were classed as 'Brisbane protocol-low' risk, 55% (n=514) as 'Brisbane protocol-intermediate' risk, 25% (n=230) as high risk, and 0.9% (n=8) of patients left against medical advice (**Table 3**). Overall 50% of patients managed by the Brisbane protocol performed an EST. In comparison, 38% of the cohort in traditional approach performed an EST. In the 'Brisbane protocol-low' risk group, 39 of 169 patients performed an EST, while 420 out of 514 in the 'Brisbane protocol-intermediate' risk group had an EST. Patients in the 'Brisbane protocol-low' risk

group incurred fewer costs and spent fewer hours in hospital than those in the 'Brisbane protocol-intermediate' risk group ($1,061 versus $1,485; 5.3 hours versus 7.9 hours). Patients who left against medical advice incurred the least cost. No one died within 30 days after discharge in this cohort.

Table 3: Summary statistics on cost and length of stay for the Brisbane protocol

Risk stratification	Number of patients N=921(%)	Cost (AUD) Median (25-75th perc.)	Hours in hospital Median (25-75th perc.)
Brisbane protocol-low	**169 (18.3%)**	**$1,061 ($901-$1,374)**	**5.3 (4.3-7.0)**
EST	39	$1,563 ($1,042-$1,807)	7.7 (6.5-24.5)
Negative	*37*	*$1,515 ($1,028 -$1,706)*	*7.7 (6.4-10.4)*
Equivocal	*2*	*$3,897*	*28.9*
No EST	136	$1,009 ($820-$1,233)	4.8 (4.2-5.9)
Send home	*129*	*$989 ($818-$1,198)*	*4.8 (4.2-5.7)*
Admit to ward	*7*	*$2,858 ($1,028-$9,777)*	*23.0 (4.8-127.5)*
Brisbane protocol-intermediate	**514 (55.8%)**	**$1,485 ($1,095-$2,086)**	**7.9 (6.3-15.2)**
EST	420	$1,449 ($1,085-$1,759)	7.7 (6.3-10.1)
Negative	*351*	*$1,366 ($1,063-$1,618)*	*7.3 (6.1-8.8)*
Equivocal	*47*	*$3,111 ($1,770- $5,492)*	*26.8(9.6-34.3)*
Positive	*22*	*$6,056 ($4,065-$6,765)*	*46.3 (28.9-52)*
No EST	94	$2,840 ($1,143-$7,838)	27.5 (6.2-53.4)
Send home	*42*	*$1,116 ($942-$1,436)*	*621 (4.7-8.5)*
Admit to ward	*52*	*$6,856 ($4,178-$11,238)*	*50.8 (29.5-80.0)*
High	**230 (25.0%)**	**$5,626 ($2,655-$9,545)**	**43.7 (24.4-74.8)**
Left against medical advice	**8 (0.9%)**	**$1,272 ($1,168-$1,737)**	**6.0 (5.2-7.3)**

In **Table 4**, costs and hospital length of stay according to admission category were compared between traditional approach group and the Brisbane protocol group. Nearly 83% of patients assessed by the Brisbane protocol were admitted to ED only and ED short stay unit compared with 66% in traditional approach group. Total hospital length of stay was shorter with the Brisbane protocol. Fewer patients in the Brisbane protocol group received inpatient care (17% versus 33%) and they had on shorter lengths of stay, 45 hours versus 52.5 hours. The median cost and length of stay when considering all patients were lower among members of the Brisbane protocol cohort.

Table 4: Costs and hospital length of stay of ED patients with chest pain according to admission category (without high risk group as the Brisbane protocol targeted low/intermediate risk patients)

	Traditional approach			Brisbane protocol		
Admission category	**Number of patients (%)**	**Cost (AUD) Median (25-75th perc.)**	**Hours in hospital Median (25-75th perc.)**	**Number of patients (%)**	**Cost (AUD) Median (25-75th perc.)**	**Hours in hospital Median (25-75th perc.)**
ED only	28 (4.7%)	$882 ($865-$1,027)	5.6 (4.1-8.4)	78 (11.3%)	$976 ($919-$1,068)	4.7 (3.9-5.8)
ED Short Stay Unit	368 (61.1%)	$1,619 ($1,393-$2,024)	11.3 (9.3-25.5)	496 (71.8%)	$1,315 ($1,048-$1,605)	7.0 (5.8-8.6)
Inpatient ward	201 (33.4%)	$5,673 ($3,331-$8,301)	52.5 (30.8-116.3)	116 (16.8%)	$5,852 ($3,193-$8,467)	45.0 (28.5-74.0)
Transferred	5 (0.8%)	$1,071 ($999-$1,299)	44.8 (18.8-70.6)	1 (0.1%)	$1,028	4.1
All categories	602 (100%)	$1,959 ($1,455-$3,726)	24.3 (9.9-34.1)	691 (100%)	$1,363 ($1,037-$1,803)	7.2 (5.7-10.4)

Percentage of patients discharged within 4 hours from ED

The percentage of patients who were discharged from ED within four hours by risk stratification is shown in **Table 5**, and we give the results before and after patient characteristics in the traditional approach were adjusted in an attempt to make the two cohorts more comparable. As the Brisbane protocol only further stratified low and intermediate risk groups, the proportion of patients discharged from ED in high-risk group were similar between two approaches. Although the Brisbane protocol failed to achieve NEAT and discharged, admitted or transferred 62% of ED patients from all risk groups within 4 hours, it enabled physicians to discharge a higher proportion of patients within 4 hours in low and intermediate risk groups than the traditional approach (72% versus 51%).

Table 5: Percentage of patients discharged from ED within 4 hours by risk stratification before and after baseline characteristics were adjusted

	Traditional approach (not adjusted)	Traditional approach (adjusted)	Brisbane protocol
High risk	26.0%	30.1%	30.2%
Low and intermediate risk	46.1%	50.6%	72.3%

Decision tree model outputs

The expected costs and length of stay in hospital of the two approaches from the decision tree model are shown in **Table 6**. The average patient managed by the Brisbane protocol cost $1,229 less, and 26 hours in hospital was saved compared to the traditional approach. These differences are shown by the probabilistic sensitivity analysis and are plotted in **Figure 4**.

Table 6: Expected costs and length of stay in hospital per patient for the traditional approach and Brisbane protocol (without high risk group as the Brisbane protocol targeted low/intermediate risk patients)

	Expected cost (95%CI)	Expected length of stay (95% CI)	Incremental cost (95% CI)	Incremental length of stay (95% CI)
Traditional approach	$3,454 ($1,438-$7,159)	42hrs (8hrs-153hrs)		
Brisbane protocol	$2,225 ($1,282-$3,609)	16hrs (7hrs-32hrs)	-$1,229 (-$5,122- $1,266)	-26hrs (-136hrs-14hrs)

Figure 4: Distributions of incremental cost (AUD) and length of stay for the Brisbane protocol with the traditional approach as the reference from the 10,000 probabilistic sensitivity analyses

Figure 5 provides the proportion of the 10,000 resamples where the Brisbane protocol resulted in a lower cost or shorter stays for the average patient. When only cost was taken into consideration, the Brisbane protocol had a 78% probability of incurring fewer costs. When shorter length of stay was the decision criteria, there was a 79% probability the Brisbane protocol is optimal.

Figure 5: probability of an approach being optimal in terms of cost and length of stay from the 10,000 probabilistic sensitivity analyses

DISCUSSION

We report the first study of the potential health services gain of adopting an ADP into routine practice in the Australian healthcare setting. Some advantages of ADP for assessing patients presenting to ED with chest pain have previously been demonstrated.[6-8] This analysis used data collected over two different periods, and included it in a decision tree model to compare cost and length of stay between traditional assessment approach and the Brisbane protocol. We demonstrated the economic benefits of applying Brisbane protocol in a hospital setting.

The Brisbane protocol for the assessment of emergency patients with possible cardiac chest pain may have considerable benefits to patients with early notification about the underlying cause of their symptoms, and early discharge of those without a cardiac diagnosis. Adopting a Brisbane protocol could also assist in meeting NEAT targets. Seventy percent of non-high risk patients could be assessed rapidly for ACS and discharged from ED within 4 hours under the Brisbane protocol. In the hospital the average ED length of stay fell from 289 minutes between 2008–2010 to 243 minutes between 2011–2014, the period when the Brisbane protocol was implemented. Whether this observed saving of 45 minutes per patient was caused by the Brisbane protocol cannot be known for certain due to the study design used. The overall capacity released for the hospital was substantial, with a reduction in the expected assessment period from 42 hours to 16 hours for all non-high risk patients. The reduction in need for lengthy admission supported same day discharge for many patients. The economics of this in terms of time missed from work, family and social activities is hard to quantify, however early discharge home for patients is likely to have had a positive effect on patient satisfaction.

The Brisbane protocol identified a large proportion of patients as low risk. This is a significant increase by comparison to the current National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines risk stratification process, and is an equivalent sized low risk cohort in comparison to other risk scores such as TIMI and GRACE scores when used for ED patient assessment. The true reduction in need for EST testing in this cohort, may have larger systems effects in terms of improving access for other patients requiring this cardiac investigation. This was not assessed in the study. Compared to other ADP approaches, the Brisbane protocol has its strength that it incorporates both AMI and UAP. There are other approaches used to identify those at risk of AMI alone,[19 20] but these ignore the increased short to medium term risk of recurrent ischemic events in those with underlying CAD and UAP.

Other economic analysis of applying ADP to assess chest pain patients also shows evidence for reduced hospitalisation stay and lower costs. Asher et al. [21] in Israel examined the clinical outcomes and cost-effectiveness of an ADP using contemporary technology versus routine care and found that an ADP could save time and resources. There was a slight decrease in total costs when patients were treated ADP, but the difference was not significant. Compared with their comparative prospective study, our study has strengths in that we combined comparative study with an economic decision model. By taking account of the probability of

being classified as low or intermediate risk and the probability of having an EST, the decision tree model demonstrates the expected cost and length of stay for a patient who presents to ED with chest pain. In addition, we conducted probabilistic sensitivity analysis to account for parameter uncertainty surrounding cost and length of stay. The Brisbane protocol has shown a high probability of being optimal compared to traditional approach.

The limitations of this analysis should be acknowledged. First, in both trials, patients were recruited between 8am and 5pm due to the significant cost of out-of-hours recruitment. The potential impact of enrolling patients for a portion of the day is not known as we are unable to quantify any possible effect without data from out-of-hours patients. However, we do not believe the impact of predominantly in-hours recruitment will have a significant impact on the findings. One of our previous studies examined whether in-hour recruitment biased the findings.[22] We found that individuals recruited outside work hours did not differ from those recruited within work hours in terms of demographics and medical history. Second, ideally a pragmatic parallel multi-centre randomised controlled trial would be done, but this would cost millions of dollars and will take time to organise. With the observational design we cannot be sure that the Brisbane protocol contributed to the differences in the outcomes. The results of the adjustment (**Table 5**) provide some evidence of an effect arising from the Brisbane protocol. When the two cohorts were adjusted for the baseline variables the proportion patients discharged from ED within 4 hours did change, but not dramatically. Despite these limitations the improvement in cost and length of stay outcomes are plausible, and the purpose of this study is to provide data that contribute to a decision being made, rather than perfectly estimtaing the size of an effect. As this study is focused on the health economic outcomes of the Brisbane protocol, this study does not report the detailed clinical outcomes of patients managed according to the traditional diagnostic approach and Brisbane protocol.

CONCLUSION

The Brisbane protocol may be a cost saving change to services for the assessment of ED patients with possible ACS. Patients and the emergency departments that manage them might benefit from this system of care.

Contributors

LC, JHG, WAP, WFP, NG, AGB and KM led the design of the study. Data analysis was undertaken by QC, JHG, AGB and KM. All authors critically reviewed each draft of the manuscript. The final version was approved by all authors.

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No additional data are available.

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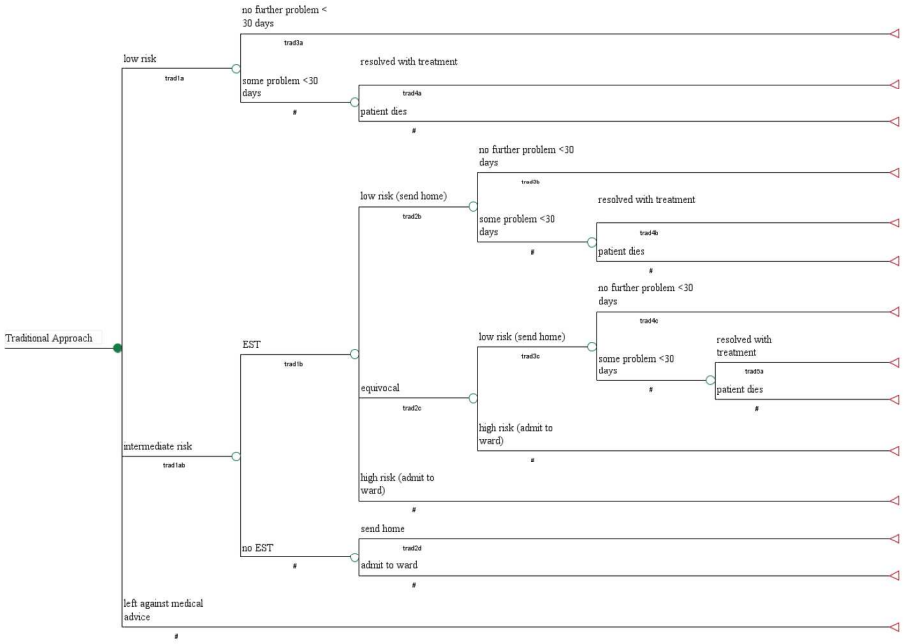

Figure 1: Traditional approach pathways
377x245mm (300 x 300 DPI)

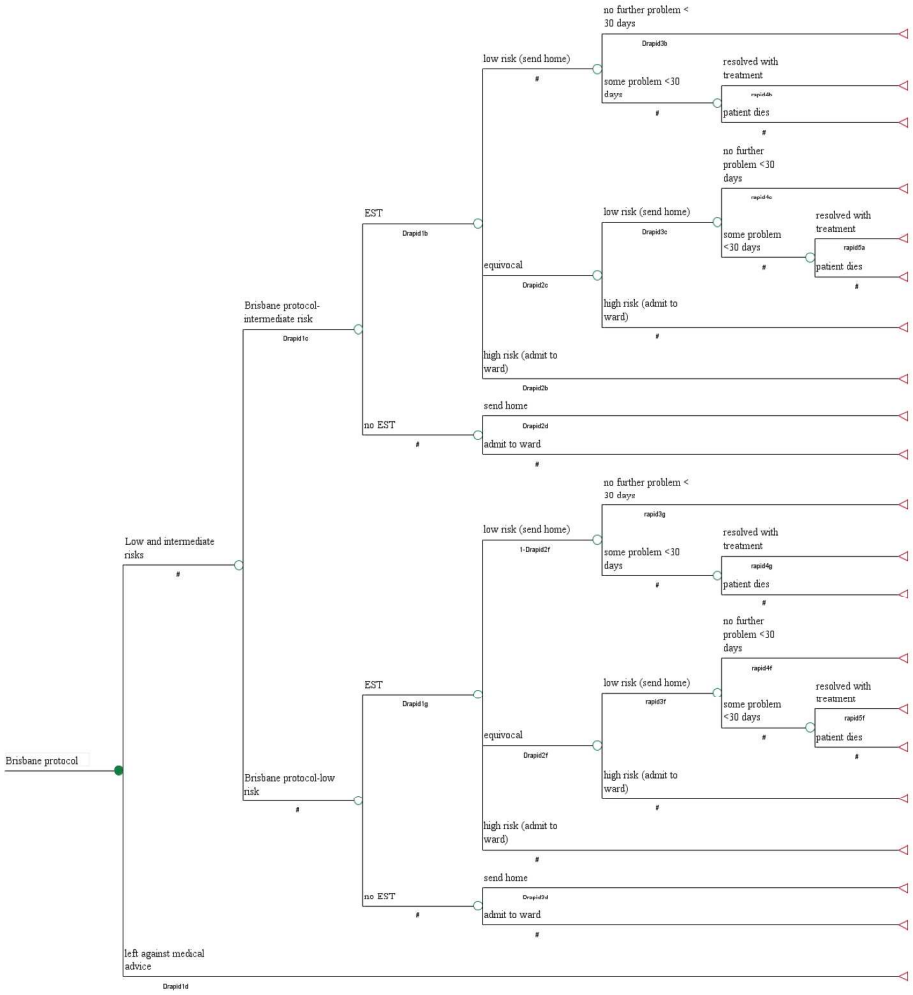

Figure 2: Brisbane protocol pathways
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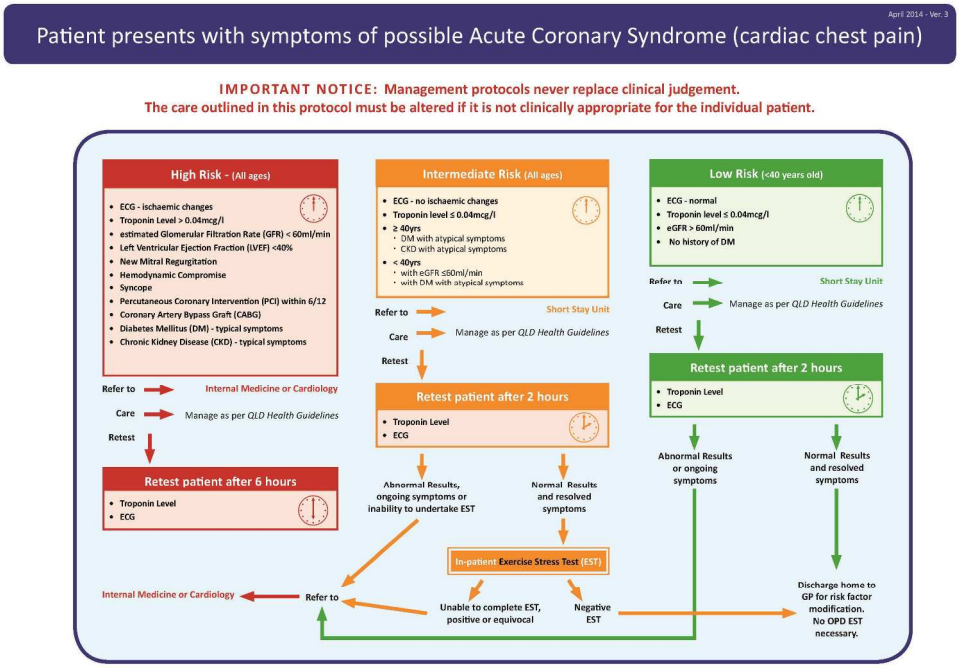

Figure 3: Management protocol of patients presenting with symptoms of possible ACS
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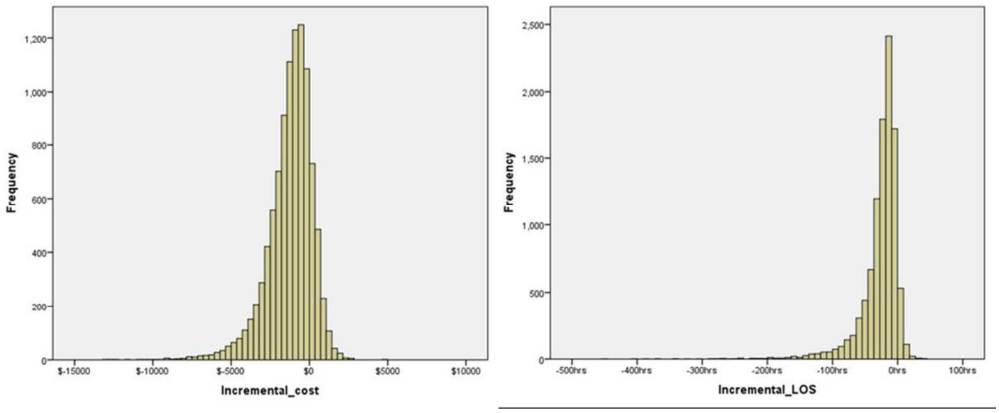

Figure 4: Distributions of incremental cost (AUD) and length of stay for the Brisbane protocol with the traditional approach as the reference from the 10,000 probabilistic sensitivity analyses
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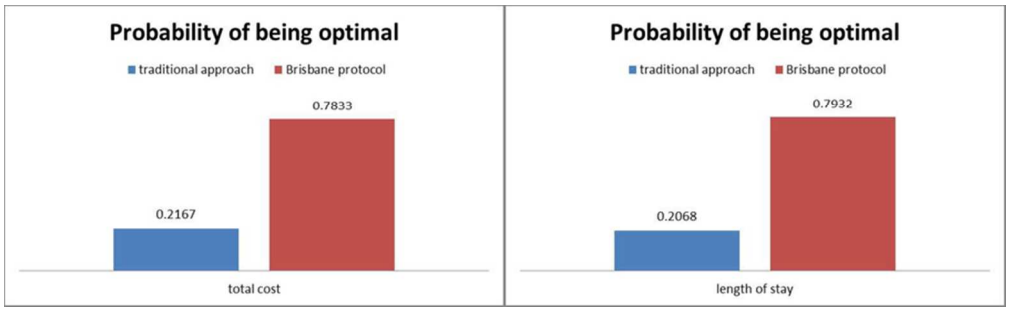

Figure 5: probability of an approach being optimal in terms of cost and length of stay from the 10,000 probabilistic sensitivity analyses
76x23mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	*Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	✓
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	✓
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	✓

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	✓
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	✓
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	✓
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	✓
		(*b*) Report category boundaries when continuous variables were categorized	✓
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	✓
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Change to costs and lengths of stay in the emergency department and the Brisbane protocol: an observational study

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Change to costs and lengths of stay in the emergency department and the Brisbane protocol: an observational study

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Key Words: emergency department, chest pain, acute coronary syndrome, accelerated diagnostic approach, cost analysis

Word count: 4263

ABSTRACT

Objective: To compare health service cost and length of stay between a traditional and accelerated diagnostic approach to assess acute coronary syndromes (ACS) among patients who presented to the emergency department (ED) of a large tertiary hospital in Australia.

Design, setting and participants: This historically controlled study analysed data collected from two independent patient cohorts presenting to the ED with potential ACS. The first cohort of 938 patients was recruited in 2008–2010, and these patients were assessed using the traditional diagnostic approach detailed in the national guideline. The second cohort of 921 patients was recruited in 2011–2013 and was assessed with the accelerated diagnostic approach named the Brisbane protocol. The Brisbane protocol applied early serial troponin testing for patients at 0 and 2 hours after presentation to ED, in comparison with 0 and 6 hour testing in traditional assessment process. The Brisbane protocol also defined a low-risk group of patients in whom no objective testing was performed. A decision tree model was used to compare the expected cost and length of stay in hospital between two approaches. Probabilistic sensitivity analysis was used to account for model uncertainty.

Results: Compared with the traditional diagnostic approach, the Brisbane protocol was associated with reduced expected cost of $1,229 (95% CI: –$1,266 to $5,122) and reduced expected length of stay of 26 hours (95% CI: –14 hours to 136 hours). The Brisbane protocol allowed physicians to discharge a higher proportion of low and intermediate risk patients from ED within 4 hours (72% versus 51%). Results from sensitivity analysis suggested the Brisbane protocol had a high chance of being both cost- and time-saving.

Conclusion: This study provides some evidence of cost savings from a decision to adopt the Brisbane protocol. Benefits would arise for the hospital and for patients and their families.

Strengths and limitations of this study

- This is the first study to report the changes to length of stay and cost from adopting an accelerated diagnostic approach for unspecified chest pain in Australian emergency departments.
- It was a large study that prospectively collected data on costs and outcomes.
- A decision tree model was developed to compare outcomes of the two approaches using realistic and clinically relevant patient pathways.
- Probabilistic sensitive analysis was used to account for uncertainties.
- This is an observational study and differences were found between the two cohorts that may confound differences due to the two approaches.

INTRODUCTION

Chest pain is a principal reason for adult emergency department (ED) visits[1] with the most common cause being acute coronary syndromes (ACS) including acute myocardial infarction (AMI) and unstable angina pectoris (UAP) . Yet after thorough investigation most patients have non-cardiac conditions such as musculoskeletal pain or gastrointestinal causes for chest discomfort. In 2007–2008 5.5 million people in the United States presented to emergency departments with chest pain and only 13% were diagnosed with ACS.[2]

Current management of patients with possible ACS in Australia arises from National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines.[3] Patients are stratified into low, intermediate and high risk categories based on clinical features, electrocardiography (ECG) and troponin test results over a minimum of six hours when using a sensitive troponin assay. Low risk patients can be safely discharged. High risk patients require admission to hospital and intensive management. Intermediate risk patients form the largest group and further objective diagnostic testing to identify coronary artery disease (CAD) is required. The costs to health services and patient outcomes from these guidelines were described in a recent Australian study.[4]

The National Emergency Access Target (NEAT) was introduced in 2011 in Australia as part of the National Partnership Agreement on Improving Public Hospital Services.[5] It requires 90% of all presentations to the ED to be discharged, admitted to hospital or transferred to another hospital for treatment within four hours. This target requires patients to be processed faster in the ED setting, and with the current guidelines requiring delayed troponin sampling, all patients with possible cardiac chest pain are steered towards admission to hospital.

Accelerated diagnostic protocols (ADP) that risk stratify individuals within 2–3 hours have recently been trialed.[6-10] A large proportion of patients can be classified as low risk and rapidly referred for objective testing.[6-8 11] A study reporting on the implementation of the accelerated protocol found that average ED length of stay was reduced in the group of patients deemed low risk and health outcomes were maintained.[9] Ongoing improvements in

the assessment process of ED patients with chest pain have occurred, and are in clinical use.[12]

A novel method of assessment of ED patients with chest pain, the Brisbane protocol, was developed prior to the advent of NEAT in Australia. It was a clinician-led initiative in response to our improved clinical understanding of the impact of improvements in biomarker (troponin) assays and the unnecessary delays in testing during patient assessment. We believed that we could safely accelerate the assessment process, and therefore designed the Brisbane protocol. This study compares the cost of managing patients for ACS who present to the ED under two competing configurations of health services: the traditional guidelines based approach[3] and the Brisbane protocol. Detailed clinical outcomes of patients were not reported as this study focused on health economic outcomes of two diagnostic approaches.

METHODS

Data Collection

This was an observational study that analysed data from two separate prospective patient cohorts presenting to the ED of a large tertiary hospital in Australia with possible ACS. The first patient cohort of 938 consenting patients were recruited in 2008–2010, and these patients were assessed using the traditional diagnostic approach detailed in the national guidelines.[3] The main reason for recruiting the first cohort was to report on costs to health services and patient outcomes from applying the national guidelines.[4] In this study, the first patient cohort was a baseline comparison group to assess the changes in the ED after the Brisbane protocol was designed and implemented. The second patient cohort (n=921) was recruited and assessed with the Brisbane protocol in 2011–2013. Process of care for patients managed by the traditional approach and Brisbane protocol is shown in **Figure 1**.

Figure 1: Process of care for patients with possible acute coronary syndromes under the traditional approach and Brisbane protocol

Patients were recruited for both cohorts between 8am and 5pm and were included if they were aged ≥ 18 years, presented to the ED with at least five minutes of chest pain suggestive of ACS and were being investigated for ACS. In accordance with American Heart Association case definitions,[13] pain suggestive of ACS includes acute chest, epigastric, neck, jaw, or arm pain; or discomfort or pressure without an apparent non-cardiac source. Research staff identified all eligible patients using the emergency department admissions database and in collaboration with the treating clinicians. Patients were excluded if: there was a clear non-ACS cause for their symptoms; they were unwilling or unable to provide informed consent such as a language barrier; staff considered that recruitment was inappropriate, such as terminal illness; they were transferred from another hospital; they were pregnant; they were recruited to the study within the previous 45 days; or they were unable or unwilling to be contacted after discharge. Perceived high risk was not an exclusion criterion. Consecutive eligible cases were included. The number of patients approached and the number of patients

excluded for each reason in the first cohort have been published. [4] In the second cohort, 1,438 patients were approached. Excluded patients are as follows: 289 declined or were unable to consent; 72 were identified > 2 hours after presentation; 39 were interhospital transfers; 17 were pregnant; 100 did not have cost data. Patients who were not eligible, who refused consent, and who presented outside of recruitment periods were managed according to the historical guideline-based process of assessment.

Research nurses collected data on presentation date, admission date, discharge date, risk stratification and exercise stress test (EST) results. Total costs including the cost of the ED visit and any inpatient costs were extracted from a linked administrative database. Thirty days after initial attendance, research nurses conducted telephone follow-up and medical record review for the diagnosis of ACS. Information was obtained from the patient and from hospital databases about whether there had been any cardiac events or investigations, or contact with any health care providers, during the 30-day period. All follow-up information was verified through contact with the health care provider, and original copies of medical records and cardiac investigation results were obtained. Relevant investigations included EST, stress echocardiography, myocardial perfusion scanning, coronary computed tomography angiography, or coronary angiography. The 30-day clinical outcomes were adjudicated independently by at least one of two local cardiologists using predefined standardised reporting guidelines.[14] Cardiologists had knowledge of all clinical information collected within a 30-day period. For both cohorts, this included all hospital medical records, public and private investigations, details provided by general practitioners and specialists seen within 30 days after discharge and by telephone contact with patients. In the first trial a second cardiologist conducted a blind review of all ACS cases and a random sample of 10% of non-ACS cases. In cases of disagreement, endpoints were agreed by consensus. This was achieved for all end points. For the second trial, a single cardiologist completed endpoint adjudication as the second adjudication of the outcomes has not occurred at this point in time. The clinical outcomes will be fully reported once this second adjudication has occurred. Diagnosis of AMI and UAP was based on accepted international standards as described previously.[15]

Decision Tree Model

A decision tree model was developed to compare costs and health outcomes of the two approaches using realistic and clinically relevant patient pathways. The model enabled the change to costs and health outcomes to be clearly presented, and the uncertainties in the data to be included. The purpose of the model was to inform a decision between the Brisbane Protocol and the traditional approach. The traditional approach based on national guidelines [3] is shown by **Figure 2**. All non-high risk patients were initially stratified into intermediate and low risk categories based on clinical features, ECG findings and troponin results obtained on presentation. Ongoing clinical assessment and repeat ECG and troponin testing was performed six hours later. Low risk patients were discharged and costs arising from the index presentation were included. After serial troponin and ECG testing six hours after presentation were normal, patients in the intermediate risk group were referred for EST, however due to clinical reasons some intermediate risk patients did not have this test. If the EST result was

positive, patients were further stratified to high risk and admitted to an inpatient bed. If negative, patients were considered low risk and discharged home. Patients with an equivocal EST and who were discharged within 24 hours were defined as low risk and those discharged greater than 24 hours were defined as high risk. Patients who did not have an EST were either directly admitted to an inpatient bed or discharged home after appropriate management in the ED and/or ED short stay unit. A small number of patients left against medical advice before treatment commenced.

Figure 2: Traditional approach pathways

A fundamental change in the new assessment process was the introduction of early serial troponin testing at 0 and 2 hours after presentation for low and intermediate risk patients, in comparison to the traditional 0 and 6 hour testing. The alternate Brisbane protocol is shown in **Figure 3**. High risk patients were initially identified and managed according to the traditional approach since the Brisbane protocol was designed for low and intermediate risk patients. All non-high risk patients were then assessed using the Brisbane protocol. Those under 40 years of age without diabetes or renal impairment were defined as Brisbane protocol-low risk while the rest were classified as Brisbane protocol-intermediate risk. Patients in the Brisbane protocol-intermediate risk group were referred for EST. As this was a pragmatic study design, some patients from the Brisbane protocol-low risk group were also referred for EST based on individual patient characteristics. If the EST was positive, the patient was considered high risk and admitted to an inpatient bed. If negative, patients were discharged and any problems within 30 days were included. If equivocal and discharged within 24 hours, patients were defined as low risk. If they were admitted greater than 24 hours they were categorised as high risk. Patients who were not referred for an EST were either admitted to an inpatient bed or discharged home after appropriate management in the ED/ED short stay unit. Again, only a small number of patients left against medical advice.

The decision trees are designed to summarise expected costs and hospital length of stay under the traditional approach and Brisbane protocol to give a system-level picture of the costs and benefits that would be useful to a high level decision maker. If there are differences in the number of deaths, this is also be shown quantitatively by the decision tree. Clinicians working in the ED validated the structure of the decision tree model prior to data analysis.

Figure 3: Brisbane protocol pathways

Data Analysis

Age, gender, risk factors and prior medical history were compared across the two cohorts. The primary outcomes are health service cost and length of stay in hospital and were compared using the decision tree model. As the Brisbane protocol is for low to intermediate risk patients, all high-risk patients were managed according to the current National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines[3] and were excluded from the analysis. The proportion of patients discharged from ED within 4 hours was compared to show if the Brisbane protocol was associated with improved performance against the NEAT

target.

This was a historically controlled study without random assignment, hence there may have been differences between the two cohorts at baseline. We used multiple variable regression models to test if baseline characteristics were associated with risk stratification, cost, length of stay in hospital and proportion of patients discharged from ED within 4 hours (in IBM SPSS Statistics 21). Results of regression analysis are provided in the supplementary file. To test whether more patients were risk stratified to low risk was due to baseline characteristics or the Brisbane protocol, we used binary logistic regression as the new stratification only works on low and intermediate risk patients. The results suggest that it was the Brisbane protocol that was mainly responsible for the change in risk stratification so any difference in baseline characteristics should not have greatly impacted on risk stratification. We also used linear regression to test if baseline characteristics had any impact on cost and length of stay for patients who moved through the same pathway in the decision tree model (e.g. patients who were classed as intermediate risk, had EST and had negative EST outcome). The results suggested little impact from baseline characteristics on total costs and length of stay in hospital. This is probably because patients who moved through the same pathway in the decision tree were relatively homogeneous. Thus, baseline differences between patients had less potential to influence costs and length of stay. Therefore, we did not adjust decision tree model inputs by baseline characteristics.

Differences between two cohorts at baseline did influence the proportion of patients discharged from ED within 4 hours. To account for this we used iterative post-stratification to match the marginal distributions of the traditional approach cohort to the Brisbane protocol cohort. The variables matched were age (10 year bands), gender, prior MI (myocardial infarction), prior angina, prior CAD, prior arrhythmia, prior CHF (congestive heart failure), prior hypertension, prior dyslipidaemia and prior family CAD. We then calculated the percent discharged within 4 hours between the two cohorts using the post-stratification weights and compared this with an unweighted percent. We used the ‘rake’ function in the ‘survey’ library in R.[16]

Updating the decision tree with information

The probabilities associated with the events at each circular chance node in the decision trees were derived from the two patient cohorts. The estimated probabilities were the risk of patients having low or intermediate risk, undergoing EST, having positive, negative or equivocal EST results, being admitted to inpatient ward or being discharged. Prior beta distributions that can only take values between zero and one, were used to model the probabilities and the uncertainty.

The costs incurred for the ED and inpatient wards were retrieved from each patient’s hospital administration record that had been linked to the primary patient data. ED costs that include a fixed cost and an activity-based component were based on triage categories of clinical urgency. [4] Inpatient costs were derived from procedure-related Australian refined diagnosis-related group reimbursement codes used for activity-based funding. [4] These costs

were summed for each individual. For patients who moved through a common pathway in the decision tree, the median costs values were calculated to inform the cost outcome of that path. The costs of adverse events that might occur after discharge were not included. A prior gamma distribution was fitted to these data to capture the inherent skew in cost data.[17] Costs from 2008 to 2012 were adjusted by an inflation rate of 3.4% per year to equal 2013 prices.[18] Lengths of stay in hospital were derived from dates of presentation and discharge, and were also fitted to gamma distributions.

Expected costs and lengths of stay are based on the summation of the pathway cost and hours-in-hospital weighted by the pathway probabilities. By comparing the expected cost and length of stay of the two competing diagnostic approaches, we defined the costs and time spent in emergency department when the Brisbane protocol was used.

A probabilistic sensitivity analysis was used to account for uncertainty in the information used in the model. Resampling was done 10,000 times from the prior distributions using Monte Carlo simulation with cost and length of stay varying simultaneously. The probability of an approach being optimal was derived by counting the number of times out of 10,000 the approach had lower costs or shorter length of hospital stay.

RESULTS

Patient characteristics

The baseline patient characteristics for both cohorts are shown in **Table 1**. Patients in traditional approach group were older and suffered more frequently from hypertension, dyslipidaemia and family history of CAD. Moreover, the proportion of patients having prior medical conditions was higher among the traditional approach group.

Table 1: Baseline characteristics by cohort

Variable	Traditional Approach (n=938)	Brisbane protocol (n=921)	p
Age, Mean (SD)	54.8 (15.1)	50.8 (12.9)	<0.01
Male sex, n (%)	573 (61.1)	538 (58.4)	0.24
Risk Factors n (%)			
Hypertension	396 (42.2)	306 (33.2)	<0.01
Dyslipidaemia	391 (41.7)	320 (34.7)`	<0.01
Diabetes	115 (12.3)	105 (11.4)	0.57
Family history of CAD	434 (46.3)	352 (38.3)	<0.01
Current smoking	259 (27.6)	267 (29.0)	0.51
Prior Medical History n (%)			
Prior MI	158 (16.8)	115 (12.5)	<0.01
Prior angina	211 (22.5)	99 (10.7)	<0.01
Prior angioplasty	101 (10.8)	74 (8.0)	0.04
Prior CABG	58 (6.2)	31 (3.4)	<0.01
Prior Peripheral arterial disease	19 (2.0)	11 (1.2)	0.16
Prior CHF	43 (4.6)	12 (1.3)	<0.01
Prior arrhythmia	83 (8.9)	49 (5.3)	<0.03
Prior CAD	194 (20.7)	121 (13.14)	<0.01
Prior tachycardia	19 (1.9)	10 (1.1)	0.14

Data are number (%) except where otherwise specified. SD=standard deviation, CAD=coronary artery disease. MI=myocardial infarction, CABG=coronary artery bypass graft, CHF=congestive heart failure.

Cost and length of stay analysis

In the traditional approach (n=938) less than 1% (n=9) were allocated to the low risk category, 62% (n=585) were classed as intermediate risk, 36% (n=336) as high risk, and 0.8% (n=8) of patients left against medical advice (**Table 2**). None of the 9 low risk patients had EST and they spent fewer hours in hospital than intermediate and high risk patients. Among patients in the intermediate risk group, those who had an EST incurred lower costs than those who did not ($1,863 versus $2,974). The difference arose as 88% of patients having an EST were discharged from hospital following a negative EST result. In contrast 128 (56%) of 229 patients who did not perform an EST were admitted to the ward for further investigation, which incurred higher costs. Five patients died, with 3 having a cardiovascular cause of death during their hospital stay and 2 dying within 6 days of hospital discharge from non-cardiovascular causes.

Table 2: Summary statistics on cost and length of stay for the traditional approach

Risk stratification	Number of patients N=938 (%)	Cost (AUD) Median (25-75th perc.)	Hours in hospital Median (25-75th perc.)
Low	**9 (1.0%)**	**$1,636 ($1,155-$3,592)**	**11.5 (9.5-31.5)**
Intermediate	**585 (62.4%)**	**$1,961 ($1,466-$3,780)**	**24.6 (9.9-35.1)**
EST	356	$1,863 ($1,493-$2,528)	23.8 (10.2-28.7)
Negative	*312*	*$1,799 ($1,477-2,243)*	*20.4 (10.1-27.8)*
Equivocal	*26*	*$2,700 ($1,904-4,277)*	*29.7 (26.0-52.1)*
Positive	*18*	*$7,113 ($5,419-$10,348)*	*61.8 (34.5-130.5)*
No EST	229	$2,974 ($1,294-$7,163)	27.6 (8.5-76.7)
Send home	*101*	*$1,285 ($1,094-$1,626)*	*8.4 (6.2-10.4)*
Admit to ward	*128*	*$6,642 ($3,975-$9,085)*	*71.0 (34.2-126.7)*
High	**336 (35.8%)**	**$6,743 ($2,755-$12,509)**	**73.2 (27.5-143.7)**
Alive with treatment	*331*	*$6,705 ($2,755-$12,495)*	*72.3 (27.0-142.4)*
Died <30 days	*5*	*$9,340 ($3,177-$38,594)*	*146.4 (83.4-426.5)*
Left against medical advice	**8 (0.8%)**	**$1,461 ($1,057-$2,232)**	**14.1 (5.5-25.0)**

Of the 921 patients available for the Brisbane protocol 18% (n=169) were classed as 'Brisbane protocol-low' risk, 55% (n=514) as 'Brisbane protocol-intermediate' risk, 25% (n=230) as high risk, and 0.9% (n=8) of patients left against medical advice (**Table 3**). Overall 50% of patients managed by the Brisbane protocol performed an EST. In comparison, 38% of the cohort in traditional approach performed an EST. In the 'Brisbane protocol-low' risk group, 39 of 169 patients performed an EST, while 420 out of 514 in the 'Brisbane protocol-intermediate' risk group had an EST. Patients in the 'Brisbane protocol-low' risk group incurred fewer costs and spent fewer hours in hospital than those in the 'Brisbane protocol-intermediate' risk group ($1,061 versus $1,485; 5.3 hours versus 7.9 hours). Patients who left against medical advice incurred the least cost. No one died within 30 days after discharge in the Brisbane protocol cohort.

Table 3: Summary statistics on cost and length of stay for the Brisbane protocol

Risk stratification	Number of patients N=921(%)	Cost (AUD) Median (25-75th perc.)	Hours in hospital Median (25-75th perc.)
Brisbane protocol-low	**169 (18.3%)**	**$1,061 ($901-$1,374)**	**5.3 (4.3-7.0)**
EST	39	$1,563 ($1,042-$1,807)	7.7 (6.5-24.5)
Negative	*37*	*$1,515 ($1,028 -$1,706)*	*7.7 (6.4-10.4)*
Equivocal	*2*	*$3,897*	*28.9*
No EST	136	$1,009 ($820-$1,233)	4.8 (4.2-5.9)
Send home	*129*	*$989 ($818-$1,198)*	*4.8 (4.2-5.7)*
Admit to ward	*7*	*$2,858 ($1,028-$9,777)*	*23.0 (4.8-127.5)*
Brisbane protocol-intermediate	**514 (55.8%)**	**$1,485 ($1,095-$2,086)**	**7.9 (6.3-15.2)**
EST	420	$1,449 ($1,085-$1,759)	7.7 (6.3-10.1)
Negative	*351*	*$1,366 ($1,063-$1,618)*	*7.3 (6.1-8.8)*
Equivocal	*47*	*$3,111 ($1,770- $5,492)*	*26.8(9.6-34.3)*
Positive	*22*	*$6,056 ($4,065-$6,765)*	*46.3 (28.9-52)*
No EST	94	$2,840 ($1,143-$7,838)	27.5 (6.2-53.4)
Send home	*42*	*$1,116 ($942-$1,436)*	*621 (4.7-8.5)*
Admit to ward	*52*	*$6,856 ($4,178-$11,238)*	*50.8 (29.5-80.0)*
High	**230 (25.0%)**	**$5,626 ($2,655-$9,545)**	**43.7 (24.4-74.8)**
Left against medical advice	**8 (0.9%)**	**$1,272 ($1,168-$1,737)**	**6.0 (5.2-7.3)**

In **Table 4**, costs and hospital length of stay according to admission category were compared between traditional approach group and the Brisbane protocol group. Nearly 83% of patients assessed by the Brisbane protocol were admitted to ED only and ED short stay unit compared with 66% in traditional approach group. Total hospital length of stay was shorter with the Brisbane protocol. Fewer patients in the Brisbane protocol group received inpatient care (17% versus 33%) and they had generally shorter lengths of stay, median 45 hours versus 52.5 hours. The median cost and length of stay when considering all patients were lower in the Brisbane protocol cohort.

Table 4: Costs and hospital length of stay of ED patients with chest pain according to admission category (without high risk group as the Brisbane protocol targeted low/intermediate risk patients)

	Traditional approach			Brisbane protocol		
Admission category	**Number of patients (%)**	**Cost (AUD) Median (25-75th perc.)**	**Hours in hospital Median (25-75th perc.)**	**Number of patients (%)**	**Cost (AUD) Median (25-75th perc.)**	**Hours in hospital Median (25-75th perc.)**
ED only	28 (4.7%)	$882 ($865-$1,027)	5.6 (4.1-8.4)	78 (11.3%)	$976 ($919-$1,068)	4.7 (3.9-5.8)
ED Short Stay Unit	368 (61.1%)	$1,619 ($1,393-$2,024)	11.3 (9.3-25.5)	496 (71.8%)	$1,315 ($1,048-$1,605)	7.0 (5.8-8.6)
Inpatient ward	201 (33.4%)	$5,673 ($3,331-$8,301)	52.5 (30.8-116.3)	116 (16.8%)	$5,852 ($3,193-$8,467)	45.0 (28.5-74.0)
Transferred	5 (0.8%)	$1,071 ($999-$1,299)	44.8 (18.8-70.6)	1 (0.1%)	$1,028	4.1
All categories	602 (100%)	$1,959 ($1,455-$3,726)	24.3 (9.9-34.1)	691 (100%)	$1,363 ($1,037-$1,803)	7.2 (5.7-10.4)

Percentage of patients discharged within 4 hours from ED

The percentage of patients who were discharged from ED within four hours by risk stratification is shown in **Table 5**, and we give the results before and after patient characteristics in the traditional approach were adjusted in an attempt to make the two cohorts more comparable. As the Brisbane protocol only further stratified low and intermediate risk groups, the proportion of patients discharged from ED in high-risk group were similar between two approaches. Although the Brisbane protocol failed to achieve NEAT and discharged, admitted or transferred 62% of ED patients from all risk groups within 4 hours, it enabled physicians to discharge a higher proportion of patients within 4 hours in low and intermediate risk groups than the traditional approach (72% versus 51%).

Table 5: Percentage of patients discharged from ED within 4 hours by risk stratification before and after baseline characteristics were adjusted

	Traditional approach (not adjusted)	Traditional approach (adjusted)	Brisbane protocol
High risk	26.0%	30.1%	30.2%
Low and intermediate risk	46.1%	50.6%	72.3%

Decision tree model outputs

The expected costs and length of stay in hospital of the two approaches from the decision tree model are shown in **Table 6**. The average patient managed by the Brisbane protocol cost $1,229 less, and 26 hours in hospital was saved compared to the traditional approach. These differences are shown by the probabilistic sensitivity analysis and are plotted in **Figure 4**.

Table 6: Expected costs and length of stay in hospital per patient for the traditional approach and Brisbane protocol (without high risk group as the Brisbane protocol targeted low/intermediate risk patients)

	Expected cost (95%CI)	Expected length of stay (95% CI)	Incremental cost (95% CI)	Incremental length of stay (95% CI)
Traditional approach	$3,454 ($1,438 to $7,159)	42hrs (8hrs to 153hrs)		
Brisbane protocol	$2,225 ($1,282 to $3,609)	16hrs (7hrs to 32hrs)	–$1,229 (–$5,122 to $1,266)	–26hrs (–136hrs to 14hrs)

Figure 4: Distributions of incremental cost (AUD) and length of stay for the Brisbane protocol with the traditional approach as the reference from the 10,000 probabilistic sensitivity analyses

Figure 5 provides the proportion of the 10,000 resamples where the Brisbane protocol resulted in a lower cost or shorter stays for the average patient. When only cost was taken into consideration, the Brisbane protocol had a 78% probability of incurring fewer costs. When shorter length of stay was the decision criteria, there was a 79% probability the Brisbane protocol is optimal.

Figure 5: probability of an approach being optimal in terms of cost and length of stay from the 10,000 probabilistic sensitivity analyses

DISCUSSION

We report the first study of the potential health services gain of adopting an ADP into routine practice in the Australian healthcare setting. Some advantages of ADP for assessing patients presenting to ED with chest pain have previously been demonstrated.[6-8] This analysis used data collected over two different periods, and included it in a decision tree model to compare cost and length of stay between traditional assessment approach and the Brisbane protocol. We demonstrated the economic benefits of applying Brisbane protocol in a hospital setting.

The Brisbane protocol for the assessment of emergency patients with possible cardiac chest pain may have considerable benefits to patients with early notification about the underlying cause of their symptoms, and early discharge of those without a cardiac diagnosis. Adopting a Brisbane protocol could also assist in meeting NEAT targets. Seventy percent of non-high risk patients could be assessed rapidly for ACS and discharged from ED within 4 hours under the Brisbane protocol. In the hospital the average ED length of stay fell from 289 minutes between 2008–2010 to 243 minutes between 2011–2014, the period when the Brisbane protocol was implemented. Whether this observed saving of 45 minutes per patient was caused by the Brisbane protocol cannot be known for certain due to the non-randomised study design. The overall capacity released for the hospital was substantial, with a reduction in the expected assessment period from 42 hours to 16 hours for all non-high risk patients. The reduction in need for lengthy admission supported same day discharge for many patients. The economics of this in terms of time missed from work, family and social activities is hard to quantify, however early discharge home for patients is likely to have had a positive effect on patient satisfaction.

The Brisbane protocol identified a large proportion of patients as low risk. This is a significant increase by comparison to the current National Heart Foundation and Cardiac Society of Australia and New Zealand Guidelines risk stratification process, and is an equivalent sized low risk cohort in comparison to other risk scores such as TIMI and GRACE scores when used for ED patient assessment. The true reduction in need for EST testing in this cohort, may have larger systems effects in terms of improving access for other patients requiring this cardiac investigation. This was not assessed in the study. Compared to other ADP approaches, the Brisbane protocol has its strength that it incorporates both AMI and UAP. There are other approaches used to identify those at risk of AMI alone,[19 20] but these ignore the increased short to medium term risk of recurrent ischemic events in those with underlying CAD and UAP. Moreover, the tools required for implementation of Brisbane protocol do not differ from what is currently widely available. Troponin assays and ECGs will continue to be performed, and the risk stratification process can be easily adopted in other hospitals. We believe that the uptake of this strategy into clinical practice will be rapid.

Other economic analysis of applying ADP to assess chest pain patients also shows evidence for reduced hospitalisation stay and lower costs. Asher et al. [21] in Israel examined the clinical outcomes and cost-effectiveness of an ADP using contemporary technology versus routine care and found that an ADP could save time and resources. There was a slight decrease in

total costs when patients were treated ADP, but the difference was not significant. Compared with their comparative prospective study, our study has strengths in that we combined comparative study with an economic decision model. By taking account of the probability of being classified as low or intermediate risk and the probability of having an EST, the decision tree model demonstrates the expected cost and length of stay for a patient who presents to ED with chest pain. In addition, we conducted probabilistic sensitivity analysis to account for parameter uncertainty surrounding cost and length of stay. The Brisbane protocol has shown a high probability of being optimal compared to traditional approach.

The limitations of this analysis should be acknowledged. First, in both cohorts, patients were recruited between 8am and 5pm due to the significant cost of out-of-hours recruitment. The potential impact of enrolling patients for a portion of the day is not known as we are unable to quantify any possible effect without data from out-of-hours patients. However, we do not believe the impact of predominantly in-hours recruitment will have a significant impact on the findings. One of our previous studies examined whether in-hour recruitment biased the findings.[22] We found that individuals recruited outside work hours did not differ from those recruited within work hours in terms of demographics and medical history. Second, ideally a pragmatic parallel multi-centre randomised controlled trial would be done, but this would cost millions of dollars and will take time to organise. With the observational design we cannot be sure that the Brisbane protocol contributed to the differences in the outcomes. The results of the adjustment (**Table 5**) provide some evidence of an effect arising from the Brisbane protocol. When the two cohorts were adjusted for the baseline variables the proportion patients discharged from ED within 4 hours did change, but not dramatically. Despite these limitations the improvement in cost and length of stay outcomes are plausible, and the purpose of this study is to provide data that contribute to a decision being made, rather than perfectly estimtaing the size of an effect. As this study is focused on the health economic outcomes of the Brisbane protocol, this study does not report the detailed clinical outcomes of patients managed according to the traditional diagnostic approach and Brisbane protocol.

CONCLUSION

The Brisbane protocol may be a cost saving change to services for the assessment of ED patients with possible ACS. Patients and the emergency departments that manage them might benefit from this system of care.

Contributors

LC, JHG, WAP, WFP, NG, AGB and KM led the design of the study. Data analysis was undertaken by QC, JHG, AGB and KM. All authors critically reviewed each draft of the manuscript. The final version was approved by all authors.

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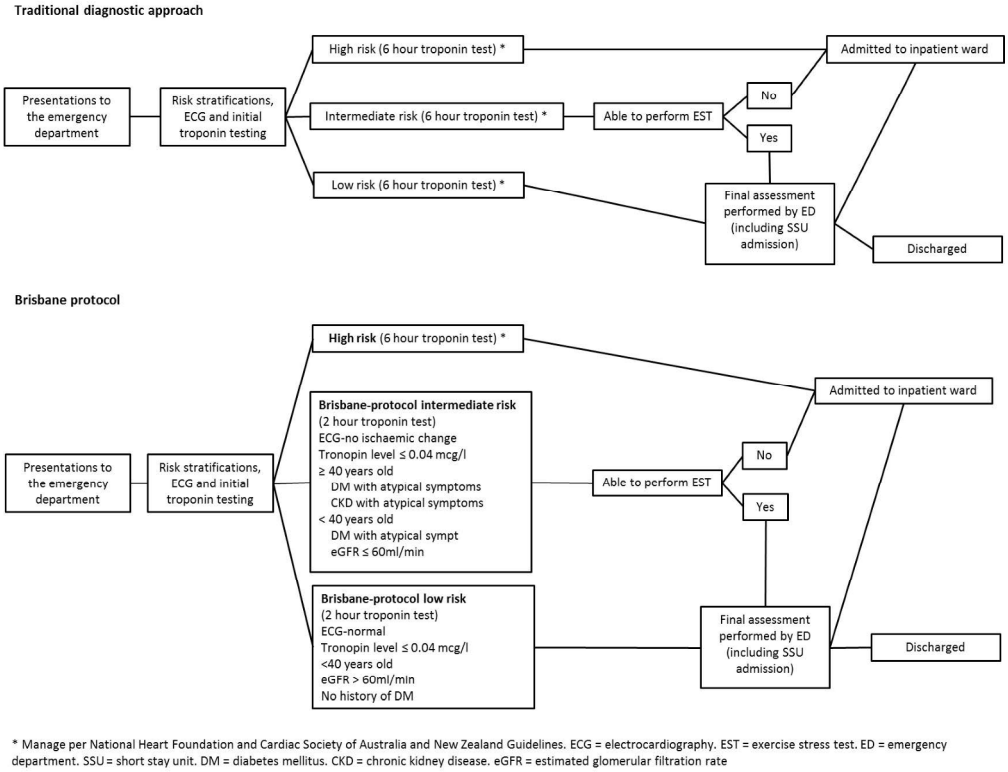

Figure 1: Process of care for patients with possible acute coronary syndromes under the traditional approach and Brisbane protocol
292x226mm (300 x 300 DPI)

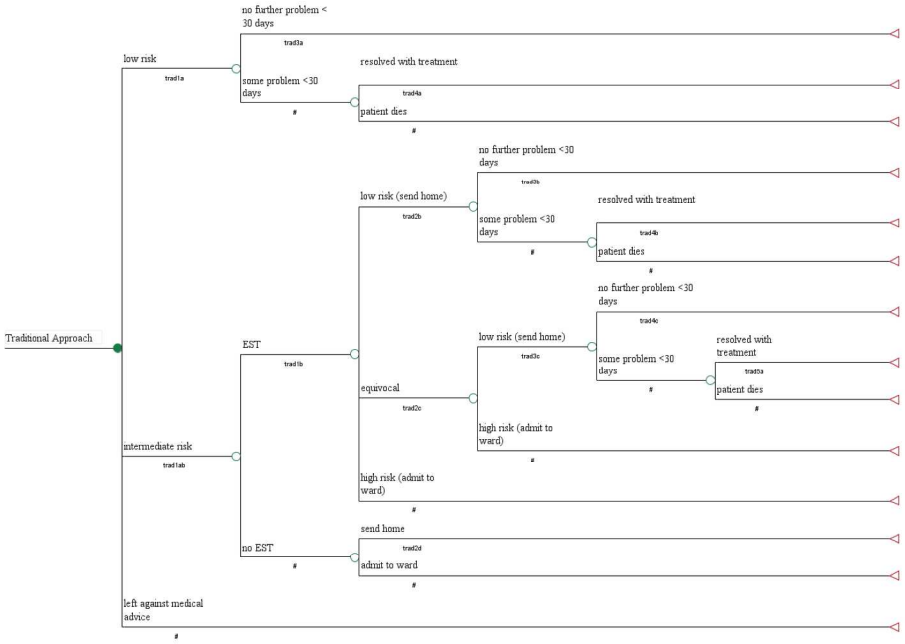

Figure 2: Traditional approach pathways
377x245mm (300 x 300 DPI)

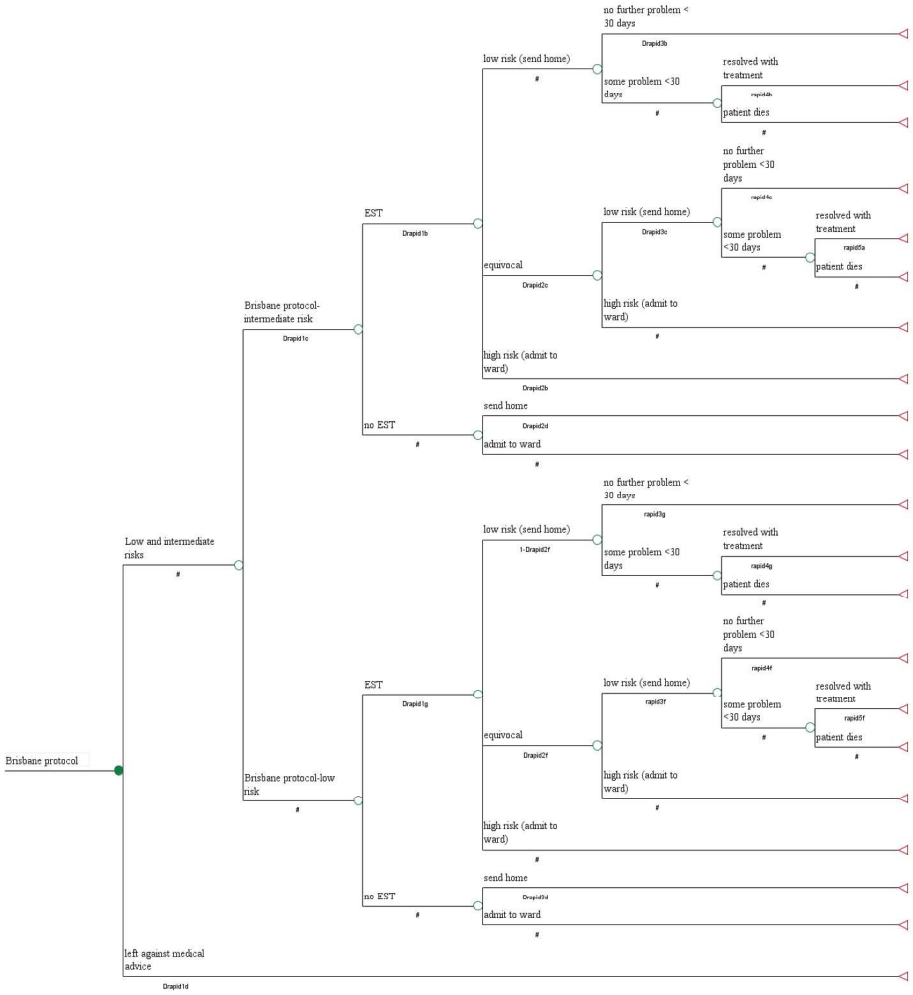

Figure 3: Brisbane protocol pathways
377x377mm (300 x 300 DPI)

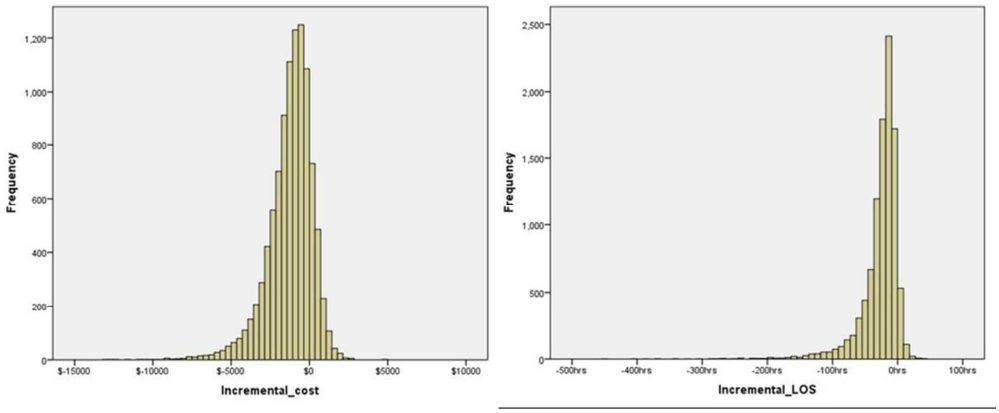

Figure 4: Distributions of incremental cost (AUD) and length of stay for the Brisbane protocol with the traditional approach as the reference from the 10,000 probabilistic sensitivity analyses
82x33mm (300 x 300 DPI)

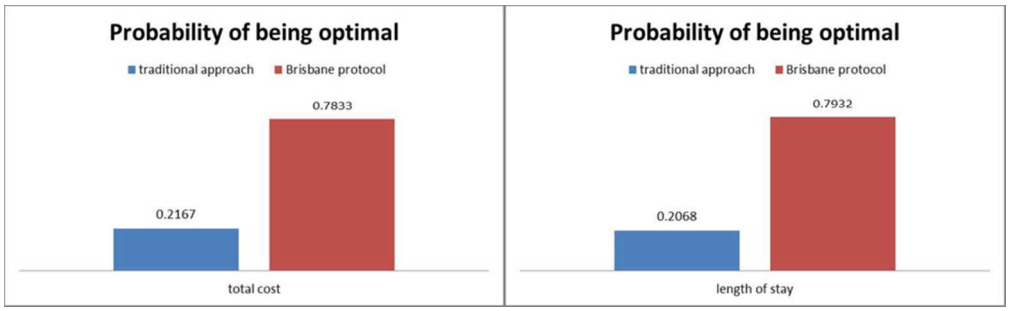

Figure 5: probability of an approach being optimal in terms of cost and length of stay from the 10,000 probabilistic sensitivity analyses
76x23mm (300 x 300 DPI)

Results of Regression Analysis (supplement)

Linear regression

Dependent variable: Total cost, Hours in hospital

Independent variables:

study	0=accelerated approach, 1=traditional approach
Gender	1=Male, 2=Female
MI	1=have prior MI, 0= no prior MI
angina	1=have prior angina, 0= no prior angina
tachycardia	1=have prior tachycardia, 0= no prior tachycardia
CAD	1=have prior CAD, 0= no prior CAD
arrhythmia	1=have prior arrhythmia, 0= no prior arrhythmia
CHF	1=have prior CHF, 0= no prior CHF
stroke	1=have prior stroke, 0= no prior stroke
PAD	1=have prior PAD, 0= no prior PAD
angioplasty	1=have prior angioplasty, 0= no prior angioplasty
hypertension	1=have hypertension, 0= no hypertension
diabetes	1=have diabetes, 0= no diabetes
dyslipidaemia	1=have dyslipidaemia, 0= no dyslipidaemia
family_CAD	1=have family history of CAD, 0= no family history of CAD
smoking	1=current smoker, 0= non-smoker
Age	

Low risk

	Mean age	N
Accelerated approach	50.6 years	169
Traditional approach	57.3 years	9

Total cost

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.305[a]	.093	-.003	$1,361.07188

a. Predictors: (Constant), smoking, study, PAD, arrhythmia, Stroke, family_CAD, Gender, dyslipidaemia, tachycardia, angioplasty, diabetes, Age, hypertension, CHF, Angina, MI, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	648.393	568.931		1.140	.256
	study	675.962	526.534	.109	1.284	.201
	Age	11.001	9.703	.106	1.134	.259
	Gender	264.102	219.621	.094	1.203	.231
	MI	-279.255	562.581	-.075	-.496	.620
	Angina	-28.800	478.708	-.007	-.060	.952
	tachycardia	-173.778	719.321	-.021	-.242	.809
	CAD	-4.209	581.405	-.001	-.007	.994
	arrhythmia	941.069	476.978	.167	1.973	.050
	CHF	-937.393	818.306	-.114	-1.146	.254
	Stroke	-276.133	582.297	-.042	-.474	.636
	PAD	1048.684	1658.932	.058	.632	.528
	angioplasty	253.993	558.805	.049	.455	.650
	hypertension	-286.193	264.632	-.099	-1.081	.281
	diabetes	-274.363	361.634	-.067	-.759	.449
	dyslipidaemia	-15.014	247.233	-.005	-.061	.952
	family_CAD	3.639	219.633	.001	.017	.987
	smoking	-54.392	247.112	-.017	-.220	.826

a. Dependent Variable: total_costs

Length of stay

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.354[a]	.125	.032	16.55283

a. Predictors: (Constant), smoking, study, PAD, arrhythmia, Stroke, family_CAD, Gender, dyslipidaemia, tachycardia, angioplasty, diabetes, Age, hypertension, CHF, Angina, MI, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	1.107	6.919		.160	.873
	study	9.461	6.403	.124	1.477	.142
	Age	.100	.118	.078	.846	.399
	Gender	3.587	2.671	.103	1.343	.181
	MI	-4.605	6.842	-.100	-.673	.502
	Angina	-.749	5.822	-.015	-.129	.898
	tachycardia	.251	8.748	.002	.029	.977
	CAD	.904	7.071	.020	.128	.898
	arrhythmia	16.016	5.801	.230	2.761	.006
	CHF	-11.837	9.952	-.117	-1.189	.236
	Stroke	-.610	7.082	-.008	-.086	.931
	PAD	14.284	20.175	.064	.708	.480
	angioplasty	3.574	6.796	.055	.526	.600
	hypertension	-4.682	3.218	-.131	-1.455	.148
	diabetes	-3.055	4.398	-.060	-.695	.488
	dyslipidaemia	-.217	3.007	-.006	-.072	.943
	family_CAD	.446	2.671	.013	.167	.868
	smoking	-1.404	3.005	-.036	-.467	.641

a. Dependent Variable: Hours_Hospital

Intermediate risk - have EST – Negative outcome

	Mean age	N
Accelerated approach	51.0 years	351
Traditional approach	47.7 years	312

Total cost

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.375[a]	.141	.118	$953.96739

a. Predictors: (Constant), smoking, MI, Gender, tachycardia, Stroke, family_CAD, arrhythmia, CHF, dyslipidaemia, study, PAD, diabetes, hypertension, age, Angina, angioplasty, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	1468.558	210.118		6.989	.000
	study	661.453	78.682	.325	8.407	.000
	Gender	-99.939	77.426	-.049	-1.291	.197
	age	2.184	3.599	.026	.607	.544
	MI	40.563	308.617	.010	.131	.895
	Angina	-14.921	213.520	-.004	-.070	.944
	tachycardia	-314.725	444.062	-.027	-.709	.479
	CAD	68.635	321.001	.018	.214	.831
	arrhythmia	-196.548	211.511	-.035	-.929	.353
	CHF	1719.377	444.670	.147	3.867	.000
	Stroke	-275.547	237.475	-.044	-1.160	.246
	PAD	-279.236	449.146	-.024	-.622	.534
	angioplasty	489.456	297.948	.095	1.643	.101
	hypertension	68.112	91.882	.031	.741	.459
	diabetes	139.958	156.626	.036	.894	.372
	dyslipidaemia	-63.185	88.642	-.029	-.713	.476
	family_CAD	-106.729	76.985	-.052	-1.386	.166
	smoking	104.928	86.679	.046	1.211	.227

a. Dependent Variable: Total_costs

Length of stay

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.411[a]	.169	.147	16.248

a. Predictors: (Constant), smoking, MI, Gender, tachycardia, Stroke, family_CAD, arrhythmia, CHF, dyslipidaemia, study, PAD, diabetes, hypertension, age, Angina, angioplasty, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	6.245	3.579		1.745	.081
	study	13.786	1.340	.391	10.287	.000
	Gender	-.096	1.319	-.003	-.073	.942
	age	.033	.061	.023	.543	.587
	MI	2.355	5.256	.033	.448	.654
	Angina	-2.085	3.637	-.031	-.573	.567
	tachycardia	-3.833	7.563	-.019	-.507	.613
	CAD	-.966	5.467	-.014	-.177	.860
	arrhythmia	-1.794	3.603	-.019	-.498	.619
	CHF	24.859	7.574	.122	3.282	.001
	Stroke	-3.607	4.045	-.033	-.892	.373
	PAD	-4.345	7.650	-.021	-.568	.570
	angioplasty	5.696	5.075	.064	1.122	.262
	hypertension	1.708	1.565	.045	1.091	.275
	diabetes	.727	2.668	.011	.272	.785
	dyslipidaemia	.751	1.510	.020	.498	.619
	family_CAD	-.456	1.311	-.013	-.348	.728
	smoking	1.636	1.476	.041	1.108	.268

a. Dependent Variable: Hours_hospital

Intermediate risk – have EST – Equivocal outcome

	Mean age	N
Accelerated approach	49.8 years	47
Traditional approach	50.7 years	26

Total cost

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.495[a]	.245	.029	$2,530.91250

a. Predictors: (Constant), smoking, Stroke, diabetes, Gender, tachycardia, family_CAD, angioplasty, dyslipidaemia, study, CHF, hypertension, Age, Angina, arrhythmia, MI, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	1357.160	2051.442		.662	.511
	study	530.054	737.743	.100	.718	.475
	Age	70.166	36.881	.316	1.902	.062
	Gender	-830.245	643.083	-.158	-1.291	.202
	MI	-77.304	2615.929	-.008	-.030	.977
	Angina	-1178.929	2235.993	-.105	-.527	.600
	tachycardia	-5403.139	4274.559	-.246	-1.264	.211
	CAD	3628.954	2602.856	.444	1.394	.169
	arrhythmia	2211.990	2003.910	.197	1.104	.274
	CHF	902.497	4269.768	.041	.211	.833
	Stroke	-773.900	1462.804	-.083	-.529	.599
	angioplasty	-3716.798	2437.241	-.332	-1.525	.133
	hypertension	-840.308	869.950	-.149	-.966	.338
	diabetes	-1079.138	1246.054	-.125	-.866	.390
	dyslipidaemia	493.760	731.497	.093	.675	.502
	family_CAD	318.244	661.766	.062	.481	.632
	smoking	-193.293	723.896	-.036	-.267	.790

a. Dependent Variable: total_costs

Length of stay

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.461[a]	.212	-.013	31.39997

a. Predictors: (Constant), smoking, Stroke, diabetes, Gender, tachycardia, family_CAD, angioplasty, dyslipidaemia, study, CHF, hypertension, Age, Angina, arrhythmia, MI, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-5.559	25.451		-.218	.828
	study	20.923	9.153	.323	2.286	.026
	Age	.763	.458	.283	1.667	.101
	Gender	-2.578	7.978	-.040	-.323	.748
	MI	15.152	32.455	.124	.467	.642
	Angina	-11.091	27.741	-.081	-.400	.691
	tachycardia	-24.259	53.033	-.091	-.457	.649
	CAD	14.396	32.293	.145	.446	.657
	arrhythmia	19.774	24.862	.145	.795	.430
	CHF	29.981	52.973	.112	.566	.574
	Stroke	-12.028	18.148	-.107	-.663	.510
	angioplasty	-29.804	30.238	-.219	-.986	.329
	hypertension	-12.163	10.793	-.178	-1.127	.265
	diabetes	-9.240	15.459	-.088	-.598	.552
	dyslipidaemia	5.072	9.075	.078	.559	.578
	family_CAD	3.330	8.210	.053	.406	.687
	smoking	.707	8.981	.011	.079	.938

a. Dependent Variable: Hours_Hospital

Intermediate – have EST – Positive outcome

	Mean age	N
Accelerated approach	53.5 years	22
Traditional approach	58.4 years	18

Total cost

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.470[a]	.221	-.266	$3,417.94795

a. Predictors: (Constant), smoking, Study_no, Stroke, family_CAD, tachycardia, angioplasty, Age, arrhythmia, Gender, hypertension, MI, dyslipidaemia, diabetes, Angina, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	7836.668	3468.273		2.260	.033
	Study	1039.286	1258.454	.172	.826	.417
	Age	-21.742	71.908	-.077	-.302	.765
	Gender	-113.623	1478.845	-.019	-.077	.939
	MI	3241.752	3451.198	.386	.939	.357
	Angina	-3244.754	3269.428	-.386	-.992	.331
	tachycardia	-887.129	3937.584	-.046	-.225	.824
	CAD	-3290.257	6778.701	-.329	-.485	.632
	arrhythmia	-5836.089	3858.058	-.424	-1.513	.143
	Stroke	4441.228	5384.162	.323	.825	.418
	angioplasty	709.351	7177.138	.062	.099	.922
	hypertension	-740.147	1560.760	-.121	-.474	.640
	diabetes	-1934.467	2907.085	-.193	-.665	.512
	dyslipidaemia	1370.218	1691.820	.228	.810	.426
	family_CAD	-544.764	1297.630	-.090	-.420	.678
	smoking	-89.941	1465.007	-.013	-.061	.952

a. Dependent Variable: total_costs

Length of stay

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.574[a]	.329	-.090	47.29760

a. Predictors: (Constant), smoking, Study_no, Stroke, family_CAD, tachycardia, angioplasty, Age, arrhythmia, Gender, hypertension, MI, dyslipidaemia, diabetes, Angina, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	100.664	47.994		2.097	.047
	Study_no	32.037	17.414	.356	1.840	.078
	Age	-.814	.995	-.194	-.818	.422
	Gender	7.114	20.464	.079	.348	.731
	MI	32.927	47.758	.263	.689	.497
	Angina	-30.011	45.242	-.240	-.663	.513
	tachycardia	-35.983	54.488	-.126	-.660	.515
	CAD	26.290	93.804	.176	.280	.782
	arrhythmia	-50.314	53.388	-.245	-.942	.355
	Stroke	-5.382	74.506	-.026	-.072	.943
	angioplasty	-67.026	99.317	-.395	-.675	.506
	hypertension	-17.065	21.598	-.187	-.790	.437
	diabetes	-38.281	40.228	-.257	-.952	.351
	dyslipidaemia	18.166	23.411	.203	.776	.445
	family_CAD	-11.400	17.957	-.127	-.635	.532
	smoking	-15.871	20.273	-.158	-.783	.441

a. Dependent Variable: Hours_Hospital

Intermediate – No EST – Sent Home

	Mean age	N
Accelerated approach	49.7 years	42
Traditional approach	47.1 years	101

Total cost

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.672[a]	.451	.376	$505.14122

a. Predictors: (Constant), smoking, arrhythmia, CHF, family_CAD, PAD, Gender, study, Stroke, angioplasty, diabetes, tachycardia, dyslipidaemia, hypertension, Angina, age, MI, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	1258.012	252.367		4.985	.000
	study	105.510	98.585	.075	1.070	.287
	age	-2.939	3.940	-.062	-.746	.457
	Gender	73.919	90.045	.058	.821	.413
	MI	218.484	242.761	.087	.900	.370
	Angina	26.572	169.423	.014	.157	.876
	tachycardia	4528.504	573.650	.592	7.894	.000
	CAD	199.513	285.008	.093	.700	.485
	arrhythmia	-245.397	235.735	-.088	-1.041	.300
	CHF	163.239	338.012	.037	.483	.630
	Stroke	258.300	194.245	.103	1.330	.186
	PAD	1989.521	606.870	.260	3.278	.001
	angioplasty	-408.735	293.664	-.129	-1.392	.166
	hypertension	25.279	109.822	.019	.230	.818
	diabetes	125.050	184.733	.052	.677	.500
	dyslipidaemia	-120.254	111.946	-.088	-1.074	.285
	family_CAD	121.578	91.165	.095	1.334	.185
	smoking	-20.258	100.343	-.015	-.202	.840

a. Dependent Variable: Total_costs

Length of stay

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.386[a]	.149	.033	5.224

a. Predictors: (Constant), smoking, arrhythmia, CHF, family_CAD, PAD, Gender, study, Stroke, angioplasty, diabetes, tachycardia, dyslipidaemia, hypertension, Angina, age, MI, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	8.451	2.610		3.238	.002
	study	1.111	1.020	.096	1.090	.278
	age	-.028	.041	-.072	-.693	.490
	Gender	.392	.931	.037	.421	.675
	MI	-3.452	2.511	-.166	-1.375	.172
	Angina	2.291	1.752	.147	1.308	.193
	tachycardia	5.951	5.933	.094	1.003	.318
	CAD	1.514	2.948	.085	.514	.608
	arrhythmia	-2.675	2.438	-.116	-1.097	.275
	CHF	2.533	3.496	.069	.725	.470
	Stroke	2.124	2.009	.102	1.057	.292
	PAD	14.513	6.276	.228	2.312	.022
	angioplasty	.865	3.037	.033	.285	.776
	hypertension	-.054	1.136	-.005	-.048	.962
	diabetes	-.736	1.911	-.037	-.385	.701
	dyslipidaemia	-.504	1.158	-.044	-.435	.664
	family_CAD	1.567	.943	.147	1.662	.099
	smoking	-1.044	1.038	-.096	-1.006	.316

a. Dependent Variable: Hours_hospital

Intermediate – No EST – Admitted to ward

	Mean age	N
Accelerated approach	50.4 years	52
Traditional approach	58.2 years	128

Total cost

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.320[a]	.103	.008	$5,910.57595

a. Predictors: (Constant), smoking, study, PAD, tachycardia, dyslipidaemia, CHF, family_CAD, Gender, diabetes, Stroke, arrhythmia, angioplasty, hypertension, Angina, age, MI, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	3326.388	2479.039		1.342	.182
	study	-782.632	1051.278	-.060	-.744	.458
	age	103.585	36.719	.260	2.821	.005
	Gender	-993.437	965.099	-.084	-1.029	.305
	MI	581.249	1571.096	.038	.370	.712
	Angina	-913.058	1303.903	-.066	-.700	.485
	tachycardia	6457.081	6163.645	.081	1.048	.296
	CAD	-646.869	1734.300	-.047	-.373	.710
	arrhythmia	371.569	1484.404	.020	.250	.803
	CHF	-3760.423	3616.827	-.082	-1.040	.300
	Stroke	2401.351	1643.401	.122	1.461	.146
	PAD	-3123.403	3851.185	-.068	-.811	.419
	angioplasty	-94.987	1828.757	-.006	-.052	.959
	hypertension	-146.856	1039.214	-.012	-.141	.888
	diabetes	-606.393	1729.221	-.028	-.351	.726
	dyslipidaemia	-128.998	1030.942	-.011	-.125	.901
	family_CAD	1198.192	943.064	.101	1.271	.206
	smoking	1806.990	1035.114	.139	1.746	.083

a. Dependent Variable: Total_costs

Length of stay

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.454[a]	.206	.122	138.481

a. Predictors: (Constant), smoking, study, PAD, tachycardia, dyslipidaemia, CHF, family_CAD, Gender, diabetes, Stroke, arrhythmia, angioplasty, hypertension, Angina, age, MI, CAD

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-40.193	58.082		-.692	.490
	study	26.974	24.631	.083	1.095	.275
	age	1.924	.860	.194	2.236	.027
	Gender	7.898	22.612	.027	.349	.727
	MI	-2.566	36.810	-.007	-.070	.945
	Angina	38.155	30.550	.111	1.249	.213
	tachycardia	52.996	144.410	.027	.367	.714
	CAD	-63.302	40.634	-.185	-1.558	.121
	arrhythmia	-12.369	34.779	-.027	-.356	.723
	CHF	-29.102	84.740	-.025	-.343	.732
	Stroke	146.647	38.504	.299	3.809	.000
	PAD	-63.624	90.231	-.055	-.705	.482
	angioplasty	5.344	42.847	.014	.125	.901
	hypertension	-51.173	24.348	-.173	-2.102	.037
	diabetes	-16.965	40.515	-.031	-.419	.676
	dyslipidaemia	41.521	24.154	.137	1.719	.088
	family_CAD	-6.851	22.095	-.023	-.310	.757
	smoking	17.289	24.252	.054	.713	.477

a. Dependent Variable: Hours_hospital

Binary logistic regression

Dependent variable: risk stratification (0=low risk, 1= intermediate risk)

Independent variables:

study	0=accelerated approach, 1=traditional approach
Gender	1=Male, 2=Female
MI	1=have prior MI, 0= no prior MI
angina	1=have prior angina, 0= no prior angina
tachycardia	1=have prior tachycardia, 0= no prior tachycardia
CAD	1=have prior CAD, 0= no prior CAD
arrhythmia	1=have prior arrhythmia, 0= no prior arrhythmia
CHF	1=have prior CHF, 0= no prior CHF
stroke	1=have prior stroke, 0= no prior stroke
PAD	1=have prior PAD, 0= no prior PAD
angioplasty	1=have prior angioplasty, 0= no prior angioplasty
hypertension	1=have hypertension, 0= no hypertension
diabetes	1=have diabetes, 0= no diabetes
dyslipidaemia	1=have dyslipidaemia, 0= no dyslipidaemia
family_CAD	1=have family history of CAD, 0= no family history of CAD
smoking	1=current smoker, 0= non-smoker
Age	

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	610.648[a]	.248	.371

a. Estimation terminated at iteration number 6 because parameter estimates changed by less than .001.

Classification Table[a]

			Predicted		
			risk_stratification		Percentage Correct
			Low	Intermediate	
Step 1	risk_stratification	Low	541	29	94.9
		Intermediate	131	48	26.8
	Overall Percentage				78.6

a. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	study	-3.552	.399	79.405	1	.000	.029
	age	-.005	.008	.357	1	.550	.995
	Gender	.523	.214	5.983	1	.014	1.687
	MI	.027	.516	.003	1	.959	1.027
	Angina	.192	.417	.211	1	.646	1.211
	tachycardia	1.477	.745	3.934	1	.047	4.379
	CAD	.205	.520	.155	1	.694	1.227
	arrhythmia	-.024	.428	.003	1	.955	.976
	CHF	.469	.641	.537	1	.464	1.599
	Stroke	.228	.529	.186	1	.666	1.256
	PAD	-1.829	1.180	2.404	1	.121	.161
	angioplasty	-.810	.463	3.067	1	.080	.445
	hypertension	-.291	.246	1.402	1	.236	.747
	diabetes	.119	.329	.130	1	.718	1.126
	dyslipidaemia	.215	.244	.778	1	.378	1.240
	family_CAD	-.094	.208	.204	1	.651	.910
	smoking	-.414	.234	3.139	1	.076	.661
	Constant	-.573	.516	1.230	1	.267	.564

a. Variable(s) entered on step 1: study, age, Gender, MI, Angina, tachycardia, CAD, arrhythmia, CHF, Stroke, PAD, angioplasty, hypertension, diabetes, dyslipidaemia, family_CAD, smoking.

Binary logistic regression

Dependent variable: Discharged within 4 hours (0=No, 1= Yes)

Independent variables:

study	0=accelerated approach, 1=traditional approach
Gender	1=Male, 2=Female
MI	1=have prior MI, 0= no prior MI
angina	1=have prior angina, 0= no prior angina
tachycardia	1=have prior tachycardia, 0= no prior tachycardia
CAD	1=have prior CAD, 0= no prior CAD
arrhythmia	1=have prior arrhythmia, 0= no prior arrhythmia
CHF	1=have prior CHF, 0= no prior CHF
stroke	1=have prior stroke, 0= no prior stroke
PAD	1=have prior PAD, 0= no prior PAD
angioplasty	1=have prior angioplasty, 0= no prior angioplasty
hypertension	1=have hypertension, 0= no hypertension
diabetes	1=have diabetes, 0= no diabetes
dyslipidaemia	1=have dyslipidaemia, 0= no dyslipidaemia
family_CAD	1=have family history of CAD, 0= no family history of CAD
smoking	1=current smoker, 0= non-smoker
Age	

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	2229.426[a]	.161	.215

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.

Classification Table[a]

	Observed		Predicted		
			Discharged_4hrs		Percentage Correct
			no	yes	
Step 1	Discharged_4hrs	no	571	348	62.1
		yes	250	673	72.9
	Overall Percentage				67.5

a. The cut value is .500

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	study	-.807	.103	61.075	1	.000	.446
	age	-.025	.004	30.349	1	.000	.976
	Gender	-.015	.105	.022	1	.882	.985
	MI	-.085	.256	.110	1	.740	.919
	Angina	-.195	.204	.909	1	.340	.823
	tachycardia	-.910	.503	3.271	1	.071	.402
	CAD	-.828	.270	9.417	1	.002	.437
	arrhythmia	-.306	.231	1.750	1	.186	.736
	CHF	-.691	.463	2.224	1	.136	.501
	Stroke	-.034	.246	.019	1	.890	.967
	PAD	-.130	.543	.057	1	.811	.878
	angioplasty	.069	.275	.062	1	.803	1.071
	hypertension	-.223	.119	3.489	1	.062	.800
	diabetes	-.673	.179	14.186	1	.000	.510
	dyslipidaemia	-.051	.119	.185	1	.667	.950
	family_CAD	-.077	.105	.537	1	.464	.926
	smoking	-.261	.116	5.021	1	.025	.770
	Constant	2.210	.275	64.646	1	.000	9.115

a. Variable(s) entered on step 1: study, age, Gender, MI, Angina, tachycardia, CAD, arrhythmia, CHF, Stroke, PAD, angioplasty, hypertension, diabetes, dyslipidaemia, family_CAD, smoking.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	*Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	✓
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	✓
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	✓
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	✓

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	✓
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	✓
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	✓
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	✓
		(*b*) Report category boundaries when continuous variables were categorized	✓
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	✓
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.