COMMERCIAL IN CONFIDENCE

FINAL REPORT

Cost effectiveness evaluation

The use of Ultrasound in the diagnosis of older, non-trauma patients who present to the Emergency Department with dyspnoea

Prepared for
Ipswich Hospital Foundation

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Summary

The aim of this report is to answer the question 'If we implemented basic lung ultrasound to detect heart failure in Queensland Emergency Departments, would it be worthwhile?'

This cost-effectiveness analysis compares the expected economic outcomes associated with using lung ultrasound (the intervention) to the diagnostic workup of older, non-trauma patients who present to the Emergency Department (ED) with dyspnoea. The study comparator is the use of chest x-ray, pathology and electrocardiography (ECG), as well as examination and history taking (the control).

It is based on data collected between May 2014 and October 2016 at three hospitals in Queensland — the Princess Alexandra Hospital (PAH), Ipswich Hospital and The Prince Charles Hospital (TPCH). A total of 439 older patients who presented to the ED with complaints of dyspnoea were included in the analysis, with an average patient age of 75 years. The outcomes considered include diagnostic accuracy, length of stay, rate of ED presentation, rate of hospital re-admission, cost per ED visit, cost per admitted person and patient mortality.

Overall it was found that the intervention improved diagnostic accuracy, and that an incorrect diagnosis (without lung ultrasound) may be more costly than a correct diagnosis (with lung ultrasound).

Key findings

Across the three hospitals, the use of lung ultrasound in the diagnosis of dyspnoea resulted in an average 3.9 per cent improvement in diagnostic accuracy, although results were mixed across settings, with:

- an *increase* in diagnostic accuracy at the TPCH of 6.8 per cent, from 87.0 per cent in the control group to 93.8 per cent in the intervention group
- an *increase* in diagnostic accuracy at the Ipswich hospital of 13.7 per cent, from 78.1 per cent in the control group to 91.8 per cent in the intervention group, and
- a *reduction* in diagnostic accuracy at the PAH of 8.1 per cent, from 90.9 per cent in the control group to 82.8 per cent in the intervention group.

Improved diagnostic accuracy is beneficial for patients, and to the average cost of care. This study found that:

- average length of stay for patients at any of the 3 hospitals with an incorrect diagnosis is longer than those with a correct diagnosis, although there is notable variation by hospital, with an extended length of stay most evident at PAH
- across all 3 hospitals, average hourly ED costs were 8 per cent lower for an incorrect diagnosis compared to a correct one, although the reverse was true for hospital costs, where average costs per day were 4 per cent higher for an incorrect diagnosis
- the rate of in hospital mortality trended upwards in patients with an incorrect diagnosis compared to those with a correct diagnosis (3.5 per cent compared to 2.4 per cent respectively), and
- the literature indicates that improved diagnostic accuracy would not be expected to impact on the hospital rate of admission.

Somewhat surprisingly, rates of ED representation and readmission were higher amongst those with a correct diagnosis compared to those with an incorrect diagnosis (47 per cent versus 25 per cent and 42 per cent verses 26 per cent for ED representation and readmission, respectively) indicating that incorrect diagnosis was not necessarily a precursor to representation/readmission.

Comparisons in costs between the intervention and control group showed mixed, nondefinitive results, including that:

- rates of ED representation and readmission were similar between the intervention and control groups
- average ED costs per person were the same for the intervention and control group, however, the cost of a correct diagnosis under the intervention was non-significantly higher than a correct diagnosis under the control ($969 versus $935 respectively)
- total average costs (ED and hospital) per person presenting to the ED were highest for patients in the control group with an incorrect diagnosis ($8 145) followed by those with a correct diagnosis in the intervention group ($7 437), those in the intervention group with an incorrect diagnosis ($7 011) and those in the control group with a correct diagnosis ($6 830) — however, average costs per patient are considered to be a poor indicator of the impact of the intervention and its diagnostic accuracy
- differences in ALOS between the comparator and control group for a correct diagnosis were marginal (half a day longer for the control group).

Given the importance of LOS on costs, costs per day (hospital) and per hour (ED) were calculated to assess the impacts of the intervention. It was found that:

- the intervention was associated with reduced hourly costs in the ED per patient presenting at the PAH(-19 per cent) and TPCH (-5 per cent), but not at Ipswich (+3 per cent), with an average reduction across all hospitals of 8 per cent per hour per presenting patient
- the intervention had a minor impact on total admission costs per day (+1 per cent), with minimal hospital variation (ranging from -1 per cent to +3 per cent).

Conclusion

This study confirms that an incorrect diagnosis is more expensive than a correct one when total hospital costs are considered. It also indicates that the intervention (ultrasound protocol) is likely to achieve a higher diagnostic accuracy. However, given hospital variation and the many factors that drive hospital costs, the results of this study are inconclusive and nondefinitive as to the impact of the ultrasound protocol on hospital costs.

1 Understanding the intervention and study design

This study estimates the expected economic outcomes associated with adding lung ultrasound (the intervention) into the diagnostic process when older, non-trauma patients present to the Emergency Department (ED) with dyspnoea.

The study comparator is the usual process of history taking, examination, and use of chest x-ray, pathology and electrocardiography (ECG).

The outcomes considered in the analysis include diagnostic accuracy, hospital length of stay, rate of ED presentation, rate of hospital re-admission, cost per ED visit, cost per admitted person, and patient mortality.

This study was based on data collected between May 2014 and October 2016 at three hospitals in Queensland (Princess Alexandra Hospital, Ipswich Hospital and The Prince Charles Hospital). A total of 439 older patients who presented to the ED with complaints of dyspnoea were included in the analysis. The average age of patients was 75 years. Nine patients were excluded due to cost-data inconsistencies.

Usual Care for elderly patients presenting with breathlessness

The conventional treatment pathway or 'Usual Care' for a patient presenting to the Emergency Department with breathlessness (dyspnoea or dyspnea) in the elderly has been set out in *LUS+ 2014 Trial Booklet Version 6, protocol* V2 (see chart 1.1). It provides a series of interventions (costs) against which the Study Path (intervention) costs and outcomes will be evaluated.

Important features of the Usual Care pathway include the following.

- **A *junior* medical officer makes the diagnosis and administers treatment, with the assistance of senior doctors when available and depending on the severity of the patient's condition**. This provides a 'control' for the assessment of the ability of junior doctors to undertake and interpret an ultrasound performed in the Study Path, however there may be varying levels of senior medical officer input (uncontrolled). Senior medical supervision is uncontrolled and varies but is generally more consistent in larger hospitals.
- **The use of a general ultrasound is not standard practice in all Emergency Departments**. While the benchmark or standard is for a review of patients by a senior medical officer, and for a 'focussed' ultrasound[1] to be incorporated in this review, this does not always occur. Not all Senior Medical Officers are competent in ultrasound

[1] A 'focussed' ultrasound may be used to exclude pneumothorax, examine heart contractility and visualise inferior vena cava (IVC) as a marker of fluid status.

for the exclusion of pneumothorax and contractility or visualising the inferior vena cava.

1.1 Usual care – Clinical pathway for patients presenting with breathlessness

Setting	Step	Description
IN EMERGENCY DEPARTMENT	1.	Elderly patient arrives, reporting dyspnoea
	2	Placed in cubicle – category 1, 2, and 3
	3	Nurse performs observations, applies comprehensive monitoring, inserts IV line, draws blood and performs ECG
	4	Junior doctor, occasionally senior, takes history, reviews ECG, arranges blood tests, examines patient and orders chest x-ray in almost all cases.
	5	If available, a senior doctor is consulted and may question/examine the patient. If competent, they use focussed point of care ultrasound of heart, lung and IVC to assist diagnosis[a]
	6	Junior doctor makes diagnosis (of Wet/Dry) and commences treatment or consults with senior doctor and then commences treatment
	7	Adjust patient management based on the response to the initial treatment and/or as test results become available
	8	Patient is referred to: a. medical registrar (hospital) for ongoing treatment (x%) b. transferred to another hospital (y%) c. discharged if care has provided significant improvement (uncommon, %)
IN HOSPITAL	9.	We assume no differences to the Study Path

[a] Only where the Senior Medical Officer is competent in identifying pneumothorax and inferior vena cava as a marker of fluid status will those tests be performed. The review by a SMO is a benchmark that is often not met in practice, although this may vary from hospital to hospital and may be more closely followed in tertiary centres.

Data source: CIE using LUS+ 2014 Trial Booklet, Version 6, protocol V2 and input from Dr Kylie Baker.

- **A chest x-ray is standard in the Usual Care pathway.** Nearly all older patients presenting with breathlessness receive a chest x-ray, unless the patient has had recent chest x-rays or where anxiety is suspected. Those without a chest x-ray comprise of less than a dozen individuals in the Usual Care group. Those chest x-rays are then reviewed by the junior medical officer, and potentially supported by the senior medical officer, to contribute to the diagnosis. In tertiary hospitals, a specialist radiologist report may be available during hours, on request.
- **A delayed chest x-ray report is also provided in the Usual Care pathway, however its use in the initial Wet/Dry diagnosis is limited by the delay.** Typically, chest x-ray reports provided by radiologists/cardiologists are not available at the time of the diagnosis. The delay is estimated to be one day in larger hospitals such as Princess Alexandra and Prince Charles, compared to one week in a regional hospital, such as

Ipswich Hospital. In Princess Alexandra Hospital, it is possible to ask for an immediate urgent report as they have a 24/7 radiology registrar, although this is rare.

  – The 'gold standard' with regard to diagnostic accuracy is the echocardiogram with a CT scan at the time of presentation to the ED. Chest x-ray, even with expert report, is not considered an adequate reference standard as it has a significant error rate when diagnosing heart failure.

- **The use of echocardiology is more widespread in the larger hospitals.** While the larger hospitals (such as PAH) may offer an 'echo' during admission, smaller hospitals had echo only part of the time (estimated to be 60 per cent). There is a current shortfall of Echocardiologists as they require extensive training.
- **As with the intervention (as per the Study Pathway), the diagnosis of 'Wet' versus 'Dry' condition in the lungs is the major dichotomy affecting the treatment of patients. The treatments are diametrically opposed.** It has been shown that harm occurs from providing the wrong treatment.[2]
- **The extent of experience/seniority and resources varies significantly depending on the hospital.** The junior medical officers implementing either the standard or Study Path protocol have varying years of experience. Typically, the more regional hospitals such as Ipswich Hospital have less experienced junior medical officers and have lesser senior medical officer supervision than larger hospitals such as Princess Alexandra Hospital.

Alternative use of lung ultrasound

Chart 1.2 summarises the clinical pathways associated with the Study Path (the intervention). The intervention is shown in step 5, which is to include a 'trial-credentialed clinician marks impression of 'wet or dry or other' with specification if relevant'. The additional in-hospital steps are of an administrative nature and do not affect patient care.

Several considerations for the intervention are:

- **The 'trial-credentialed clinician' that performs the intervention ultrasound scan was usually the junior doctor.**
- **The Study Path includes the cardiac scan producing cardiac views, however it was not well mastered.** The cardiac views are difficult compared to the lung views and, while all study path patients should have received a cardiac scan, retrospective analysis suggests that less than one third of the cardiac views were potentially useful, indicating that novice cardiac views may be a poor diagnostic adjunct.
- **All Study Path patients received the ultrasound scan by an inexperienced or junior clinician.** In addition, approximately 16 of the Usual Care patient cohort received a

2 Management of 'Wet' or waterlogged lungs involves drying them out, such as through provision of diuretics, decreasing the immediate fluid load on the heart (using 'vasodilator' medications to open peripheral blood vessels), or by blowing some extra air in the lungs. Patients with 'dry' lungs are often dehydrated and so they are often given intravenous fluids, and other treatments directed at the cause of their problem be it asthma, infection or other.

scan at their doctor's request. These patients have been counted in the control group (using the intention to treat rationale) .

1.2 Study Path – Clinical pathway for patients presenting with breathlessness

IN EMERGENCY DEPARTMENT

1 Elderly patient arrives, reporting dyspnoea

2 Placed in cubicle – category 1, 2, and 3

3 Nurse performs observations, applies comprehensive monitoring, inserts IV line, draws blood and performs ECG

4 Junior doctor, occasionally senior, takes history, reviews ECG, arranges blood tests, examines patient and orders chest x-ray in most cases

5 Trial- credentialed clinician marks impression of 'wet or dry or other' with specification if relevant e.g. 'pneumothorax', 'effusion', 'poor cardiac function'. Communicates findings immediately to treating doctor.

6 Junior doctor makes diagnosis and commences treatment or consults with senior doctor and then commences treatment, senior doctor may communicate findings (of advanced USS) to junior immediately if relevant to care (e.g. 'pneumothorax')

- → *Diagnosis of 'Dry' (0-9 B line visible) or 'Subclinical'*
- → *Diagnosis of 'Wet' (12 or more B lines visible in 2+ areas on both sides of the chest) OR sub clinically wet but with enlarged left atrium and/or ventricle and/or tachycardia>120*
- → *Diagnosis of dual pathology*

7 Adjust patient management based on the response to the initial treatment or as test results become available

8 Patient is referred to:
   a. medical registrar (hospital) for ongoing treatment (x%)
   b. transferred to another hospital (y%)
   c. discharged if definitive care has provided significant improvement (uncommon, z%)

9 On a weekly basis, research assistant reviews study book on USS machine

IN HOSPITAL

10 Other items to ensure record keeping such as consent form, CXR documents, review of episode of care and actual cause of dyspnoea, report length of stay and ongoing monitoring.

Data source: CIE using LUS+ 2014 Trial Booklet, Version 6, protocol V2 and with input from Dr Kylie Baker.

- **The extent of the resources in training the junior or inexperienced clinicians was modest.** Each received a four-hour training session and was required to submit 10 practice scans with correctly identified Wet versus Dry condition diagnosis. There was a small incidence of retraining, where ultrasound findings were identified as wrong. The retraining extended to TPCH but not PAH as PAH had their own ongoing routine ultrasound teaching sessions (not specific to lung but including lung).

- **Once diagnosed, the treatment pathway is determined primarily by the Wet/Dry diagnosis and managed similarly to the Usual Care pathway.** It was hoped that an earlier diagnosis would be possible with the intervention, however the study results show no discernible difference in the timing of diagnosis. (private communication)

It is important to note that the fixed costs of the intervention and the training of medical officers may have multiple or long-term payoffs that extend beyond the study. If the medical officers continue to use their new skills in ultrasound for other techniques it can be surmised that the impact of the initial training investment may continue.

A longer-term objective of the research is to examine the potential for safe removal of chest x-rays as 'standard' in the diagnostic and treatment pathway, when replaced with the intervention protocol (ultrasound scan).

Population, intervention, comparator and outcome

Table 1.3 provides the 'PICO' table defining the population, intervention, comparator and outcome parameters.

The literature review that supports the PICO and guides the economic analysis is set out in appendix A.

1.3 Population, intervention, comparator and outcome (PICO) description

Category	Description
Population	Patients presenting with breathlessness to ED; over 60 years [a]; non-trauma patients; consent given; heart failure suspected
Intervention	Ultrasound with count of B lines, plus cardiac view added to conventional workup (listed in comparator)
Comparator	Chest X-ray AND pathology AND ECG AND examination AND history
Outcome	Diagnostic accuracy, length of stay; cost of care; rate of re-presentation and re-admission in 30 days; patient outcomes

[a] In doing this, the study is specifically looking for heart failure patients.

Note: Cardiac views were encouraged in all patients in the Study path, however the cardiac views are difficult to teach and only a proportion were useful (less than 30 per cent).

Source: CIE.

Population

The population considered in the analysis includes non-trauma patients aged over 60 years who present to the Emergency Department with breathlessness.

Breathlessness, or *dyspnoea*, can be caused by a range of conditions, including acute coronary syndrome, heart failure, diffuse interstitial syndrome, pleural effusion, focal interstitial syndrome, alveolar consolidation, pneumothorax, anaemia, anxiety and infection.[3]

3 Cibinel, G.A., Casoli, G., Elia, F., Padoan, M., Pivetta, E., Lupia, E. & Goffi, A. 2012, 'Diagnostic accuracy and reproducibility of pleural and lung ultrasound in discriminating

Given the clinical setting of this research, the population for the study does not exclude conditions which ultrasound is unlikely to improve diagnostic accuracy, such as fibrosing lung disease, bilateral pneumonitis and non-cardiogenic pulmonary oedema because they cannot be detected immediately. It is noted that, if excluded, diagnostic accuracy of ultrasound for patients presenting with breathlessness increases, including to more than 85 per cent. This information, although desirable, is not always available at the initial clinical assessment. The intention of the study was to replicate actual practice, so these patients were not excluded, adding an extra degree of challenge to the protocol.

It is noted that trauma patients (which are often very serious although few) were excluded from the study and that by examining patients over 60 years of age, this would lead to a higher than otherwise rate of cardiogenic pulmonary oedema.

Intervention

The intervention involves ultrasound with count of B-lines and cardiac views (see box 1.4).

Ultrasound is conducted and interpreted by a *junior doctor or ultrasound-naïve clinician* who has undertaken a four-hour training session and ten practice scans.

1.4 Understanding lung ultrasound

Lung ultrasound can be readily available (portable and light weight), interpreted in real time, and unlike chest radiography and lung computed tomography (CT), is free of radiation hazards.[4]

Ultrasound energy is rapidly dissipated by air, with use of ultrasound on a patient with healthy aerated lungs only able to detect the pleura (represented by a bright white horizontal line). In healthy lungs, the pleura line moves horizontally with respiration, a phenomenon known as lung sliding. If the lungs are compromised, the ultrasound will detect vertical lines known as B-lines, in addition to the pleura. The number of B-lines increases with a decrease in air content and an increase in lung density.

Important to the description of the intervention is that:

- the observation of bilateral pleural effusions and abnormalities was not included in the training (or diagnostic protocol). This may trade a small margin of diagnostic accuracy for the ability to simplify the use of ultrasound for adoption by junior doctors with a short training period, and

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cardiogenic causes of acute dyspnea in the Emergency Department', *Internal and Emergency Medicine*, vol. 7, no. 1, pp. 65-70.; Russell, F.M., Ehrman, R.R., Cosby, K., Ansari, A., Tseeng, S., Christain, E., Bailitz, J. & Stahmer, S.A. 2015, 'Diagnosing Acute Heart Failure in Patients With Undifferentiated Dyspnea: A Lung and Cardiac Ultrasound (LuCUS) Protocol', *Academic Emergency Medicine*, vol. 22, no. 2, pp. 182-191.

4 Saraogi, A. 2015, 'Lung ultrasound: Present and future', Lung India: official organ of Indian Chest Society, vol. 32, no. 3, pp. 250-257.

- there has been some variability in the scale and frequency of training provided across sites, which may have a bearing on interpretation of lung ultrasound.

While the training and protocol included cardiac views of all patients, there was a low proportion of cardiac scans that provided useful pictures (at less than 30 per cent). In terms of the 'intervention', the proficiency is driven by the extent of training provided to the doctor over a four-hour initial session, plus a further ten scans taking around 5-10 minutes each. Approximately 30 people completed both training and proctored scans.

At Prince Charles Hospital, and Ipswich, a further one hour upskill exercise was offered at 6 months following the initial training. A second one hour upskill session was provided at 12 months after the initial training. At the Princess Alexandra Hospital, however, only the first initial four-hour session was conducted, with the consultants subsequently providing the teaching during their regular ultrasound training program. The training materials were made available online for revision, and on desktops at each hospital. Despite the attempts to standardise training, the Ipswich hospital staff are likely to have benefited from the presence of a highly proficient mentor on staff.

Comparator

The comparator involves chest x-ray, pathology and ECG, as well as examination and history taking. For ethical reasons, a lung/cardiac/ IVC ultrasound was not with-held in those suspected of having pneumothorax, providing a competent sonologist and senior doctor was available. These techniques are more complex than the intervention protocol taught to the junior doctors.

In the participating hospitals, the following timeframes apply:

- an ECG (performed by nurses and shown to a senior doctor within 10 minutes) is usually available within 15 minutes
- blood tests may be available within one to two hours of testing
- a chest x-ray is usually performed within two hours of the request, and is then read by the junior/senior medical officer, while
- the turnaround of a chest x-ray report (from the radiologist) varies widely, from less than 24 hours for larger hospitals to one week for the smaller, regional hospitals such as Ipswich Hospital.

There is no difference in the in-hospital care between the intervention and comparator.

Outcomes

The outcomes of interest for this report include cost of care, rate of 30-day re-presentation and re-admission, length of stay and patient outcomes (for example, mortality, or development of complications). These outcomes will be used to measure the economic impacts of the intervention.

2 Identifying and quantifying the cost and outcomes

Patients receiving usual care compared to the intervention (lung ultrasound) may (or may not) have different management (inputs), timing of inputs, and outcomes such as hospital Length of Stay (LOS), cost of care for that admission and health outcomes and associated funding implications (measured by the rate of re-admission).

Based on the literature review undertaken for this study, it has been found that:

- **studies rarely tease out 'correct' and 'incorrect' diagnosis, and rarely provide the degree of improvement (assumed to occur) with the use of the intervention. This makes it difficult to make conclusions as to the reliability of the presence or absence of relationships between a correct diagnosis and outcomes**
- **there are other subtle factors which may play a role in the impact of an intervention on outcomes such as patient severity across groups, the degree of uncertainty (milder disease) associated with patient diagnosis across both the intervention and control groups and associated responses, and care following hospital, and**
- **days in hospital following diagnosis may be relevant to measure instead of re-admission rates).**

The impact of diagnostic accuracy

As shown in chart 2.1, the initial diagnosis is compared with the diagnosis at discharge. An incorrect diagnosis may have a different impact on patient outcomes to that of a correct diagnosis.

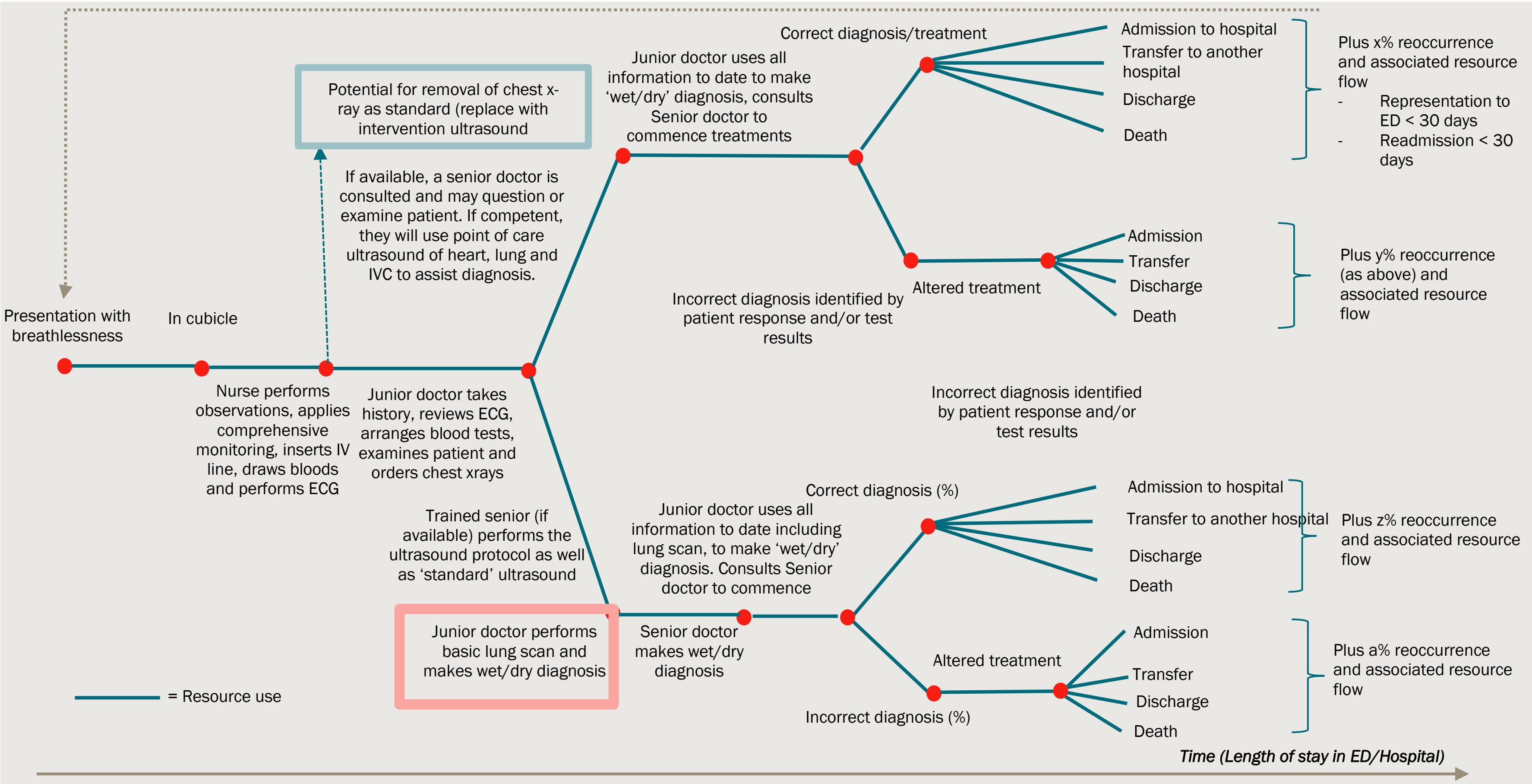
This study looks for any differential rate of accuracy in the diagnosis for both Usual Care and the intervention and aims to identify a relationship between diagnostic rates and cost/patient outcomes, controlling for any difference in patient severity between correctly diagnosed and incorrectly diagnosed patients where possible.

Outcomes such as cost and patient wellbeing may be approximated by the length of stay, however the effect of 'inter-facility transfer' and in-hospital death must be factored in.

While length of stay is closely related to cost, an examination of the cost data[5] is required to ascertain whether an incorrect diagnosis is associated with higher levels of resource use per admission.

5 The cost data is captured according to the following categories: theatre; sterilisation; specialist procedures; anaesthetics; high dependency units; medical/nursing input; allied health; pathology; medical imaging; pharmacy department, ED and miscellaneous.

2.1 Resource flow and clinical outcomes in ED and hospital under Usual Care and Study Path [Tertiary, specialist cardiothoracic, regional]



Note: A chest x-ray was standard in both groups, however, noting that the study will seek to comment on the cost effectiveness of removing the chest x-ray.

Estimating economic outcomes of lung ultrasound

A literature review has been conducted to estimate the expected economic outcomes associated with using lung ultrasound for diagnosing older, non-trauma patients who present to the Emergency Department with dyspnoea.

The search strategy was aligned to the PICO format, where outcomes included cost, length of stay, re-admission, health outcomes or economic evaluation. The question being examined is to what extent a timelier or more accurate diagnosis using ultrasound impacts patient or cost outcomes.

From the seven studies included in the full literature review, only two provided a metric of the impacts of point-of-care ultrasound. Yet neither of those studies quantified the impacts for patient care, such as cost impact, associated with better diagnostic accuracy from ultrasound.

A 2017 study by Zanobetti et al showed that the addition of lung ultrasound to usual Emergency Department care for the diagnosis of dyspnoea leads to a timelier diagnosis which could, in theory, reduce the time taken to administer the correct Wet/Dry treatment. A 2013 study by Goff et al found a greater level of diagnostic accuracy with lung ultrasound compared to clinical assessment and identified a change in the management of patients with respect to medication, testing and disposition plan but did not quantify the cost of this.

The CIE also undertook an expanded literature search and review to examine how a more accurate diagnosis in the ED may lead to better outcomes. That is, we kept the same PICO, except for the intervention, where we relaxed the assumption that an ultrasound is the method of achieving a higher diagnostic accuracy.

From the adjusted search, a total of 10 studies were ‘included’ after a full literature review. Studies were included if they provided a clinical evaluation or meta-analysis that contributed to the question of whether a correct diagnosis led to altered outcomes for the patient, and hospital/ health care system.

Table 2.2 provides a summary of the literature identified, including any key internal and external validity considerations.

Outcomes measured included hospital and ICU admission, time to discharge and hospital length of stay, in-hospital and 30-day mortality, two-year or three-year mortality rates, 30-day readmission rates, cost of care in hospital, cost of care over two years and so forth.

2.2 Summary of the extended literature review

Study	Summary of risk of bias/ Key findings
Formal literature search	
Lam et al, 2010. Meta-analysis: effect of B-type natriuretic peptide testing on clinical outcomes in patients with acute dyspnea in the emergency setting.	Meta-analysis – conducted well
	Data from five Randomised Controlled Trials showed that using BNP testing had a modest effect on management of patients presenting to the Emergency Department. The pooled effect on all-cause hospital mortality was inconclusive, while admission rates decreased in the tested group compared to the control group (but not statistically significant), and length of hospital and critical care unit was modestly reduced, by 0.6-1.2 days.
Trinquart, L. (2011). Natriuretic peptide testing in EDs for managing acute dyspnea: a meta-analysis.	Meta-analysis – conducted well
	Natriuretic peptides testing had a limited impact on the outcome of patients presenting to the ED with acute dyspnea (focusing on duration in the ED, time to discharge and length of stay). The study states that there was **'no impact on readmission rates and mortality'.** However, it notes that one study reported a non-significant reduction in the risk of readmission at 60 days, and a nonsignificant reduction of risk of secondary hospitalisation in the intervention arm in one study. It is also stated that it 'could be of use to older patients' and a subgroup of patients that could benefit from them, including those with intermediate suspicion of heart failure with a physician estimated probability between **20-80%, representing 30 per cent of emergency patients** and those associated patients with a specifically higher mortality rate.
Mueller et al, 2004. Medical and economic long-term effects of B-type natriuretic peptide testing in patients with acute dyspnea.	Randomised controlled trial known as the BASEL trial Adequate sequence generation and incomplete outcome data addressed by authors. No blinding to treating physicians and uncertain allocation concealment (time to discharge possibly influenced), unclear if free of selective reporting, and bias. Distinguishes true readmissions from secondary admissions in patients who had not been admitted initially. Importantly, however, as treatment occurred earlier due to the intervention, the findings should be cautiously transferred.
	The main source of decreased hospital/ICU admission rates (across all studies). The use of B-type natriuretic peptide levels in conjunction with other clinical information reduced the time to the initiation of the most appropriate therapy, the need for hospitalization and intensive care, time to discharge, and the total cost of treatment. There is no reporting of the change in diagnostic accuracy, however, it is implied that the intervention is more accurate than history or other laboratory/physical findings to identify heart failure (HF) as the cause and that there was a higher rate of obstructive pulmonary disease identified in the B-type natriuretic peptide group than the control group, implying this also. Final diagnosis was less frequently HF in the intervention group than in control group. Possibly indicates that greater certainty in the diagnosis (increased confidence) led to the change in resource use.

Study	Summary of risk of bias/ Key findings
Breidthardt, C. 2007. Medical and economic long-term effects of B-type natriuretic peptide testing in patients with acute dyspnea.	A prospective observational study using the BASEL study (Mueller, 2004). This study was not included in the Trinquart et al meta-analysis possibly since the patient cohort is similar and to include would double count the effect of this study.
	BNP testing induced changes in initial management, including a reduction in the initial hospital rate, the use of ICU, and initial time to discharge. Cumulative all-cause 720-day mortality was not different between the BNP group and the control group, however morbidity (reflected by days in hospital at 360 days) was significantly lower in the BNP group compared to the control group; at 12 days versus 16. The total treatment cost at 360 days (driven by lower days in hospital) was significantly improved in the control group ($10 144 versus $12 748). The reduction in in-hospital days in the BNP group was due to lower days due to dyspnea.
Mueller, C. et al, 2006. Cost-effectiveness of B-type natriuretic peptide testing in patients with acute dyspnea.	A further prospective observational study based on the BASEL trial. (See above, Mueller et al, 2004)
	The major finding was that at 180 days, there were fewer total days in hospital, at both initial presentation and maintained until 180 days. Costs excluded medications as these were determined to be more attributed to the baseline.
Rutten et al (2008) - N-terminal pro-brain natriuretic peptide testing in the emergency department: beneficial effects on hospitalization, costs, and outcome.	Adequate sequence generation and allocation concealment. Incomplete outcome data addressed and **free of selective reporting.** Uncertain blinding to participants, treating physicians and outcome assessors. Did not distinguish true readmissions from secondary admissions in patients who had not been admitted initially.
	NT-proBNP testing for heart failure in the ED reduces the time to discharge and is associated with a trend toward cost reduction.
Schneider et al (2009) - B-type natriuretic peptide testing, clinical outcomes, and health services use in emergency department patients with dyspnea: a randomized trial.	Patients were blinded to the intervention however clinicians and those assessing the trial outcomes were not. In 2 Australian teaching hospital ED setting. Transfer of result (that there was no impact of BNP testing) would depend on whether BNP testing alters the management of the patients (did not in this trial). Its conclusion that there is no support for routine use of BNP testing may be reasonable in this context, where there is the lack of data for improved management, and the author states that it may be of benefit to patient subgroups.
	A heart failure diagnosis was significantly more common in the BNP group than those in the control group (48.4 per cent, compared to 41.2 per cent) and that BNP discriminated accurately between patients with and without heart failure. There was **no change** of patients in the emergency department (initial treatment planning), in terms of use of medications such as appropriate heart failure medication. There were no statistically significant between-group differences in hospital admission rates or length of admission. The overall 30-day mortality rate was 6.9 per cent in the control group and 6.5 per cent in the BNP group but nonsignificant; and readmission rates were 15 per cent in the BNP group and 18 per cent in the control group but nonsignificant.

Study	Summary of risk of bias/ Key findings
Green et al (2008), Clinical uncertainty, diagnostic accuracy, and outcomes in emergency department patients presenting with dyspnea.	A key limitation of the study is that it is undertaken retrospectively without a control group to show change in actual outcomes.
	The data shows that there is a clear association between the phenomenon of “clinical uncertainty” and adverse outcomes, which may be more deleterious in those who have ADHF. Clinical uncertainty was present in 31 per cent of the 592 dyspneic patients evaluated in this trial. Among dyspneic patients in the ED, clinical uncertainty is associated with increased morbidity and mortality, especially in those with heart failure. Clinical certainty of Heart Failure was ranked between 0 to 100 per cent by clinicians with the range of 21-79 per cent identified as clinical uncertainty. Patients judged with clinical uncertainty (approximately 31 per cent) had more hospital admissions, longer hospital length of stay and increased 1-year morbidity and mortality, especially those with Acute Decompensated Heart Failure (ADHF). The study found that the addition of NT-proBNP testing to clinical judgment may reduce diagnostic uncertainty in this setting.
Meisel S, et al (2012). Pre-admission NT-proBNP improves diagnostic yield and risk stratification - the NT-proBNP for Evaluation of dyspnoeic patients in the Emergency Room and hospital (BNP4EVER) study	Testing of the NT-pro-BNP testing did not affect admission, LOS, 2-year survival or recurrent cardiac events, but improved diagnosis at discharge and allowed risk stratification, including in the ADHF-likely group. Notes that medium length of stay was short, which may explain the lack of observed benefit. Accuracy of diagnosis of ADHF on discharge was one in four missed without NT-proBNP testing, compared to one in three missed without NT-proBNP testing. Also, correct diagnosis of ADHF in the ‘below-median group’ of NT-proBNP was associated with a better outcome at 16 months. This suggests that testing makes the recognition of ‘missed’ cases easier, particularly those with milder disease and to identify those with very high levels at considerable risk of a negative outcome. The authors suggest the need to combine correct diagnosis and proven therapy with long term clinic visits (as implemented in clinical trials), for the optimal prognosis. More beta blockers were used in those properly diagnosed as ADHF-likely patients. The authors suggest **that in the absence of outpatient clinic visits**, a correct diagnosis at hospital discharge in ADHF-likely patients may not ensure improvement in survival.
Grey literature review	
Ray et al (2006). Acute respiratory failure in the elderly: etiology, emergency diagnosis and prognosis.	The study finds that inappropriate initial treatment in the emergency room was associated with increased mortality in elderly patients with ARF. The study included any patient aged 65 or older with dyspnea. It identified that there were incorrect diagnoses in 20 per cent of patients, but with inappropriate treatment occurring in **32 per cent of the patients.** For those with receiving inappropriate initial treatment, there was a higher rate of mortality of 25 per cent, compared to 11 per cent. Inappropriate initial treatment had a statistically significant relationship with death ($p < 0.002$), with 25 per cent of those receiving incorrect initial treatment suffering mortality in hospital compared to 11 per cent in those with appropriate treatment. In addition, the study found that undertreatment of the causes of ARF (breathlessness) was associated with higher morbidity and mortality, with a ratio of $p<0.002$. Note also that the rate of patients with initial inappropriate treatment was higher than the rate of patients with an initial missed diagnosis (of 14 per cent). Furthermore, there was no causal link demonstrated between inappropriate initial treatment and outcomes.

Study	Summary of risk of bias/ Key findings
Mozzini et al, 2017. Lung ultrasound in internal medicine efficiently drives the management of patients with heart failure and speeds up the discharge time	This study reported that lung ultrasound is a useful tool for the assessment of heart failure through the quantification of B lines. The research evaluated whether the use of lung ultrasound reduced the time to discharge, promoted efficient dosing of diuretic therapy and was superior to amino-terminal portion of B type natriuretic peptide (NT-proBNP) for monitoring heart failure recovery. Findings indicated that the **shorter discharge time** for the ultrasound group, compared to the chest X-ray group, was statistically significant (median of 7 (3 to 10), compared to 8 (4 to 17), respectively). Patients in the ultrasound group also underwent **more diuretic modulations** and there was a stronger association between partial pressure of oxygen in arterial blood and B-lines compared to the association with NT-proBNP (both on admission and discharge). The authors conclude that the study confirms that the use of lung ultrasound can be effective in **tailoring diuretic therapy** and **reducing discharge time** in heart failure patients. Sixty patients were included in the chest X-ray cohort and 60 patients in the lung ultrasound cohort. All patients underwent transthoracic echocardiography upon admission to classify left ventricular ejection fraction. In terms of internal validity, the study has a well-defined question, however the results of the study may be less applicable to an emergency department setting where less experienced physicians would be conducting the lung ultrasound examinations. The authors acknowledge that the findings may not be replicable in the emergency department where physicians are time poor and the ultrasound operator may have less information on the patient's clinical condition. Moreover, the study involved multiple lung ultrasounds over several days, a testing regimen which would not occur in an ED setting. Given that it is not possible to determine to what extent the lung ultrasound at admission alone led to reduced discharge times, the applicability of the study's findings to our research is reduced. Nonetheless, the finding that "the study stresses the real need for appropriate timing and modality of LUS in Internal Medicine" is appropriate.

Source: CIE.

Inclusion and exclusion process

We excluded studies for which the timing of diagnosis was the key observation, to enable comparison of the impact of improved diagnostic accuracy after the introduction of ultrasound. In this study lung ultrasound was not associated with any documented change in the timing of diagnosis.

The literature review included studies designed to identify heart failure, as this corresponds to identification of general Wet/Dry condition. However, we excluded those research questions which were irrelevant to our purpose, for instance those that examined:

- the diagnosis/prognostic marker of other specific conditions such as pulmonary thromboembolism, pneumonia or chronic obstructive pulmonary disease, or
- where there was no clear relationship between the intervention and diagnostic accuracy; for instance, those looking at prognosis following an intervention treatment such as serelaxin/high-sensitivity troponin T assay
- where the population base was not exclusively patients with dyspnoea as the primary presenting symptom (for instance, Nunez et al 2006).[6]

[6] Nunez, S. et al, 2006. Unscheduled returns to the emergency department: an outcome of medical errors? *Quality and Safety in Health Care*. April 2015 (2): 102-108.

While a broad search was undertaken, where the form of the intervention was relaxed, virtually all studies included, excluding one, looked at the use of natriuretic peptide testing in the ED to promote improved diagnosis and management of heart failure.

The CIE included studies that assessed the usefulness of B-type natriuretic peptide (BNP) or its N-terminal fragment (NT-proBNP), in terms of impact on patient and health care outcomes. This was less preferable than finding studies that looked directly at the value of correct diagnosis of a patient, but this indirect comparison showed what has (and has not been proven) in terms of interventions (aimed to promote 'better diagnosis and management' in hospital) and patient outcomes.

Findings relevant to the economic evaluation

The utility and assessment of BNP closely parallels the utility and findings regarding novice lung ultrasound. Both are used on a similar population, for similar indications namely - early in the assessment of breathless patients to detect heart failure. Both modalities have false negatives and positives and a zone of uncertainty.

The BNP literature is useful because there are more evaluations of patient outcomes and costs, possibly aided by more industry sponsorship. The prognosis and outcomes associated with correct and incorrect diagnosis by BNP might be extrapolated to correct and incorrect diagnosis by lung ultrasound.

The drivers of admission are more likely due to patient symptoms and assessment of severity, rather than test results.[7]

One study (Miesel et al, 2012) identifies that more beta blockers were used in those properly diagnosed as ADHF-likely patients.[8] However, not all studies (such as Schneider et al) showed a change in the management of patients in the ED with the use of the intervention.[9]

The extended literature review, which identified many studies relating to natriuretic peptide testing, can be related to the use of ultrasound as both interventions are intended to increase diagnostic accuracy. When it is achieved, an improvement in diagnostic accuracy should improve the appropriateness of the treatment pathway for patients, which is hypothesised to deliver an improvement in patient outcomes.

A major limitation of the literature reviewed was that the change in diagnostic accuracy was not well documented, such that it is difficult to specifically identify the causal factor behind any improvement or lack thereof (such as behavioural factors) of the intervention.

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[7] Meisel et al, 2012. *Pre-admission NT-proBNP improves diagnostic yield and risk stratification - the NT-proBNP for Evaluation of dyspnoeic patients in the Emergency Room and hospital (BNP4EVER) study.* Eur Heart J Acute Cardiovasc Care. 2012

[8] Meisel et al, 2012.

[9] Schneider, H., 2009. B-type natriuretic peptide testing, clinical outcomes, and health services use in emergency department patients with dyspnea: a randomized trial. *Ann Intern Med.* 2009; 150:365-371.

Nonetheless, the extended literature review provides the following evidence about the relationship between diagnostic accuracy and patient outcomes.

- The main source of ***decreased hospital/ICU admission rates*** (across all studies) is Mueller et al (2004), and an impact on hospital rate of admission would not be expected from improved diagnostic accuracy.
- The literature supports that ***length of hospital and critical care unit stay*** is modestly reduced, typically by a half to full day. This is contributed to by the Randomised controlled trial known as the BASEL trial (Mueller et al, 2004) where treatment occurred earlier due to the intervention (shown in other studies not to affect patient outcomes). However, where no change in Length of Stay has been identified, such as Meisel et al (2012), this may be because the length of stay is already relatively short.
- Studies have shown an impact on ***cost of hospital stay*** based on the BASEL trial (by Mueller et al, 2004, and subsequent studies such as by Breidthardt, as well as Rutten et al 2008).
- There is no conclusive evidence of any impact on the ***rate of re-admissions*** (see Trinquart, and Schneider), however one study reports a non-significant reduction in risk of readmission at 60 days and a nonsignificant reduction of risk of secondary hospitalisation in the intervention arm (Trinquart et al, 2011).
- There are some indicators of longer term benefits.
  - Breidthardt (based on the BASEL trial) found that the ***cumulative all-cause 720-day mortality*** was not different between the BNP group and the control group, however ***morbidity*** (reflected by days in hospital at 360 days) was significantly lower in the BNP group compared to the control group, at 12 days versus 16.
  - Mueller (based on the BASEL trial) found that at 180 days, there were ***fewer total days in hospital***, at both initial presentation and until 180 days.
  - Green et al (2008) shows that patients judged with clinical uncertainty (approximately 31 per cent) had more ***hospital admissions, longer hospital length of stay and increased 1-year morbidity and mortality***, especially those with Acute Decompensated Heart Failure (ADHF). Note, however, a key limitation of the study is that it is undertaken retrospectively without a control group to show change in actual outcomes.
  - Meisel S, et al (2012) shows that correct diagnosis of ADHF in the 'below-median group' of NT-proBNP was associated with a better ***outcome at 16 months***. Note that Meisel uses 'correct' versus 'incorrect' diagnosis to establish a more direct understanding of impact.
- The review shows that there is no clear impact on patient mortality. Miesel et al state that in the absence of outpatient clinic visits (other factors), a correct diagnosis at hospital discharge in ADHF-likely patients may not ensure improvement in survival.

Overall, as stated in Meisel et al (2012), the impact of natriuretic peptide testing in the ED on hospital diagnosis at discharge and on long-term outcome is 'lacking'.

3 Primary data analysis and cleaning

Data was collected from 430 older patients between May 2014 and October 2016 who presented to the ED at three hospitals in Queensland.

Before use, data was subject to data analysis and a process of removing outliers from the sample.

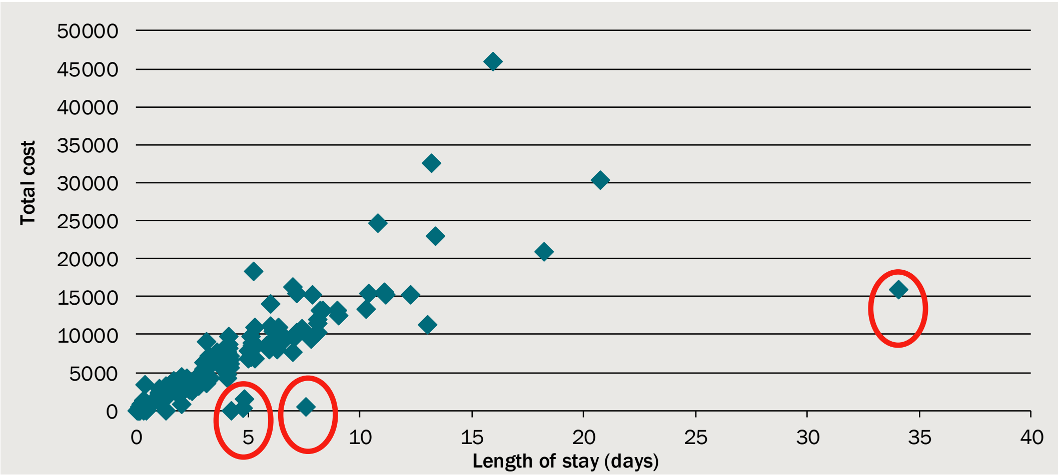
Data analysis

The CIE reviewed the patient data provided by Dr Kylie Baker and identified a range of outliers whose results were deemed to be implausible due to the cost data. To make this determination, we analysed total cost and length of stay which identified patients that fell outside a reasonable range. After review, those excluded based on implausible cost data were LUS2009, LUS1015, LUS1018, LUS1132, LUS1197, LUS2106 and LUS1028.

Two further observations were excluded on the basis that there was no cost data provided: TPCH4061 and TPCH4062. Other 'outliers' that were reviewed but included after further considerations were LUS1240, LUS1057, LUS1018, TPCH4023 and LUS1126.

An example of the analysis conducted on the outliers is provided below in chart 3.1, for individuals in the Control group with a Correct Diagnosis. Those that are highlighted in red were deemed to be unlikely. The same analysis was repeated across the Control group with an Incorrect Diagnosis, and for the Intervention groups.

3.1 Analysis of 'outliers' in Control/Correct data set



Data source: CIE.

Assessment of the sample

Patient groups were examined to assess the potential for sampling effects across key project parameters, including triage category, age and sex.

This analysis (in table 3.2) shows that there are inevitably differences in the patient sample, regarding patient age, that may contribute to the outcomes observed at the PAH and TPCH. However, sex and patient triage are relatively comparable across the control and intervention groups.

3.2 Average age, sex and PT Triage Category

Hospital	Average age	Average sex	Average PT Triage Category
PAH			
Control	74.7	1.4	2.7
Intervention	78.4	1.3	2.8
Ipswich			
Control	75.5	1.4	2.8
Intervention	75.8	1.6	2.7
TPCH			
Control	74.9	1.5	2.7
Intervention	78.9	1.4	2.7

Note: For sex, a "1" is given for males and a "2" is given for females. Triage category is a severity estimate score between 1 (critical) and 5(non-urgent) given to each arriving ED patient. Most breathless patients receive a '2' or '3'.

Recruited (n) post exclusion	Site 1 (132)	Site 2 (96)	Site 3 (211)	Total (n = 439)
Median age	75.5 (IQR 69-83)	78 (IQR 70- 85)	75 (IQR 67-82)	75 (IQR 68-83)
Male sex (%)	89 (67%)	52 (54%)	115 (54%)	256 (58%)
Admitted (%)	118 (89%)	92(96%)	191 (90%)	401(91%)
EDLOS [a] median (IQR minutes)	4 hours 13 mins (IQR 190-396)	3 hours 55 mins (IQR 187-329)	2 hours 25 mins (IQR 95-201)	3 hours 17 mins (IQR 133-277)
Entire LOS [b] (IQR minutes)	67 hours 48 min (IQR 1815 –7401)	76 hours 44 min (IQR 1547–6384)	67 hours 24 min (IQR 523 –8730)	71 hours 40 min (IQR 1446-8582)
Pulmonary oedema (%)	44 (33%)	38 (40%)	50(24%)	132 (30%)
Dual pathology	12	12	19	43
Died in hospital (n)	5	2	6	13
Six most common discharge diagnoses (diagnosis related groups)	HF+ ‡ shock HF+shock (major) COAD § (minor) COAD (major) Resp. neoplasm Resp. infection (major)	COAD (catastrophic) Resp. infection (major) COAD (minor) COAD (major) HF+shock(major) HF+shock (minor)	COAD (minor) HF+shock (minor) COAD (major) HF+shock (major) Chest pain less than 5 days Resp.infection (major)	

Recruited (n) post exclusion	Site 1 (132)	Site 2 (96)	Site 3 (211)	Total (n = 439)
Approximate Average Daily Presentations 2014-2016	168 (adults only)	220 (adults/paeds)	155 (adults/paeds)	-

[a] Emergency Department length of stay. [b] Length of Stay. ‡ Heart Failure and shock. § Chronic Obstructive Airways Disease
Source: CIE.

Analysis of DRGs across sample

The CIE analysed the potential for differences in the makeup of the Diagnosis-Related Groups (DRGs) to determine the potential for differences in the severity (and associated cost) of patient conditions across the various samples that may drive the outcomes observed (see table 3.3). This involved mapping of the DRGs to the National Hospital Cost Data Collection for 2015-16, with respect to the average length of stay, and average cost per DRG. In summary, the analysis suggests that patient condition across the sample is unlikely to significantly impact the observations for the study.

- As shown below, for the PAH, slightly more days may be expected for the control group than intervention group, however the average cost is very similar and therefore there is unlikely to be any significant difference across the sample.
- For Ipswich, the control group would be predisposed to a slightly higher cost than the intervention group, however in the order of approximately 5 per cent.
- For the TPCH, the patient DRGs suggest that the intervention group may be typically more expensive to treat, however, in the order of a modest 5 per cent.

3.3 Expected average and median length of stay and cost per hospital stay based on DRGs in the control and intervention groups

	Average length of stay	Average cost per DRG	Median length of stay	Median cost per DRG
	Days	$	Days	$
PAH				
Control - Average	5.0	8 623	4.2	7099
Intervention -Average	5.2	8 758	4.2	7194
Difference between Control and Intervention	0.1	135	0.0	95
Ipswich				
Control - Average	4.3	7 408	3.6	5570
Intervention - Average	4.2	7 033	3.6	5570
Difference between Control and Intervention	-0.1	- 375	0.0	0
TPCH				
Control - Average	4.4	7 402	3.7	6318
Intervention - Average	4.6	7 734	4.1	6781

	Average length of stay	Average cost per DRG	Median length of stay	Median cost per DRG
	Days	$	Days	$
Difference between Control and Intervention	0.2	332	0.4	463

Note: There are 9 patients in the TPCH data set whose DRGs cannot be correlated to the National Hospital Cost Data Collection.

Source: CIE.

4 Study results

Overall, diagnostic accuracy was improved by the intervention.

Cost comparisons between the intervention and the control with respect to *correct* diagnoses are mixed and somewhat inconclusive.

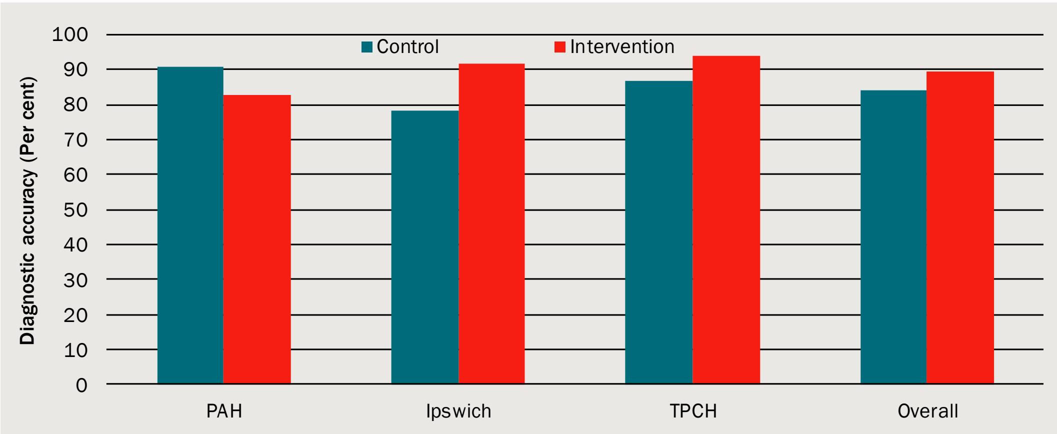
This study does, however, demonstrate that an *incorrect* diagnosis is costlier than a correct diagnosis.

Impact on diagnostic accuracy

The overall average impact of the intervention on diagnostic accuracy is positive, at **5.6 per cent**, ranging from -8.1 per cent to +13.7 per cent across hospitals, with:

- an *increase* in diagnostic accuracy at the TPCH of 6.8 per cent, from 87.0 per cent in the control group to 93.8 per cent in the intervention group
- an *increase* in diagnostic accuracy at the Ipswich hospital of 13.7 per cent, from 78.1 per cent in the control group to 91.8 per cent in the intervention group, and
- a *reduction* in diagnostic accuracy at the PAH of 8.1 per cent, from 90.9 per cent in the control group to 82.8 per cent in the intervention group.

4.1 Impact of intervention on diagnostic accuracy



Data source: CIE.

Length of Stay

The average length of stay for patients with an incorrect diagnosis is longer on average across all 3 hospitals, although there is notable variation by hospital (see table 4.2).

Interestingly, the average length of stay is *higher* in the intervention group than the control group, mainly due to the increased length of stay among those with a correct diagnosis in the intervention group. This difference is not significant (shown later in table 4.5), and less so when the rate of death and inter-hospital transfer is factored in using survival curve analysis.[10]

4.2 Length of stay in ED and total, across trial hospitals

	Average hours in ED				Average length of stay			
	PAH	Ipswich	TPCH	All hospitals	PAH	Ipswich	TPCH	All hospitals
				Hours				Days
Control								
Correct	4.7	2.4	4.4	3.6	3.4	3.3	4.4	3.6
Incorrect	4.7	3.1	3.5	3.4	3.4	5.4	3.4	4.7
Intervention								
Correct	5.3	2.8	4.5	4.0	3.6	3.9	4.7	4.0
Incorrect	6.0	1.2	4.6	3.2	7.6	2.2	4.4	4.3
Overall								
Correct	5.0	2.6	4.4	3.8	3.5	3.6	4.6	3.8
Incorrect	5.6	2.3	3.9	3.3	6.1	4.0	3.7	4.5
Control	**4.7**	**2.6**	**4.2**	**3.6**	**3.4**	**3.7**	**4.2**	**3.7**
Intervention	**5.4**	**2.5**	**4.5**	**3.9**	**4.3**	**3.6**	**4.7**	**4.1**

Note: The results for PAH, where the length of stay was longer for incorrect diagnoses, were influenced by an intervention outlier whereby a patient stayed for 30 days awaiting respite placement. Long stay outliers were not excluded, as cost analysis aimed to weigh the effect of correct diagnosis against other factors such as placement capacity.

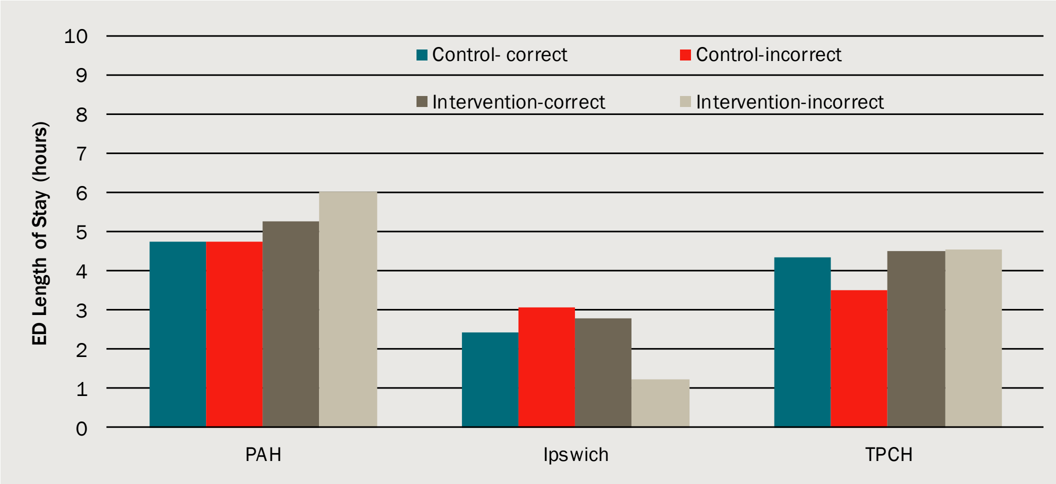
Source: CIE.

The estimates for average length of stay in the ED and the overall length of stay for each hospital are shown in chart 4.3 and chart 4.4.

The length of stay is longer in the intervention group compared to control group, across all three hospitals, for correct diagnoses and for incorrect diagnoses in two of three cases.

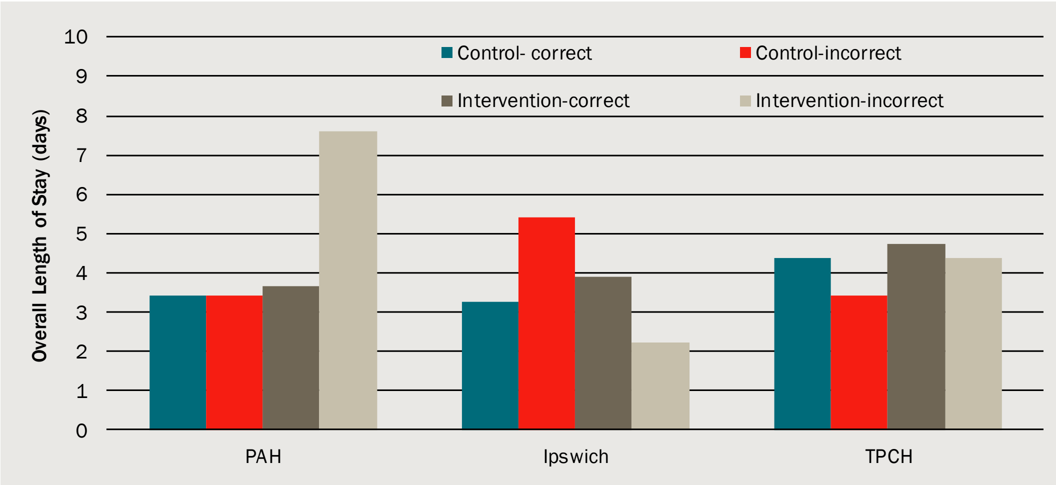
10 Personal communication.

4.3 Average length of stay in ED (hours), across three hospitals



Data source: CIE.

4.4 Average length of stay overall (days), across three hospitals

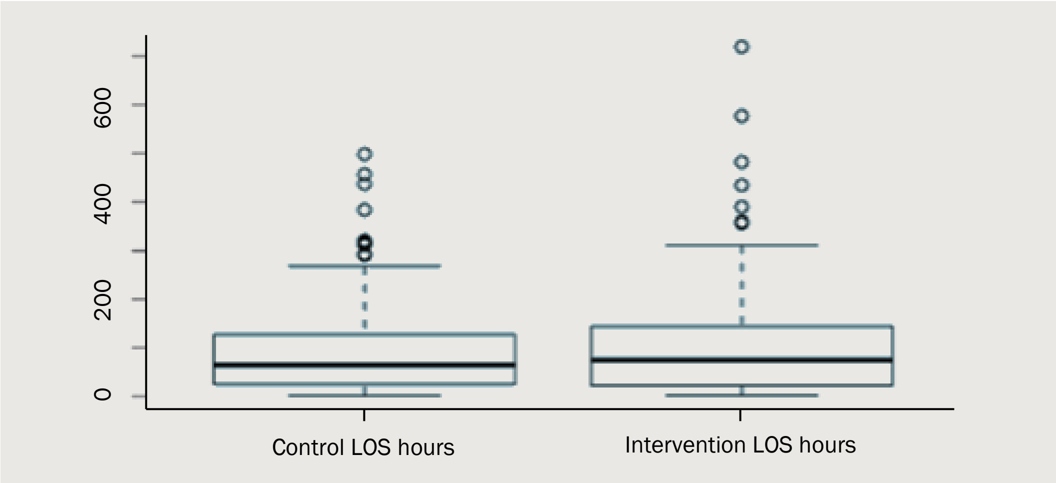


Data source: CIE. Intervention-incorrect column for PAH is influenced by outlier with 30 day stay awaiting respite.

Statistical analysis of the distribution in length of stay and hospital costs across all hospitals and between the intervention and control group show no significant difference (charts 4.5 and 4.6), nor with breakdown per individual hospital.[11]

11 Personal communication.

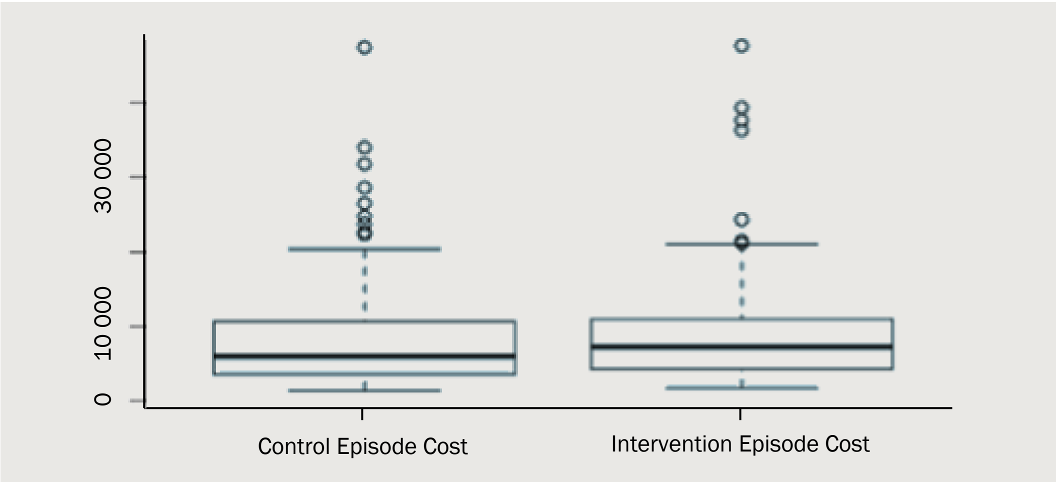
4.5 Distribution of data on length of stay across all hospitals



Note: Y axis is calibrated in hours. Not significant Wilcoxon Rank sum W =22269.5, p = 0.5142.

Data source: Dr Kylie Baker.

4.6 Distribution of hospital costs across all hospitals



Note: Y axis is calibrated in dollars. Not significant Wilcoxon rank sum W = 22226.5, p= 0.4929.

Data source: Dr Kylie Baker.

Rate of representation to ED and re-admission

The rate of representation to ED and re-admission is shown in table 4.7. It shows no positive correlation between an incorrect diagnosis and higher rates of re-presentation or re-admission. In fact, those with an incorrect diagnosis are less likely to return to ED or hospital.

The rates of ED representation and ED readmission in the control and intervention groups are similar. However, there is only a very small (most likely, insignificant) reduction in the rate of re-presentation to the ED in the intervention group.

4.7 Rate of ED representation and re-admission

Across ALL hospitals	ED representation within 30 days	Re Admittance within 30 days	Patient sample	Rate of ED Representation	Rate Readmission
	No	No	No	Frequency of representations	Frequency of readmissions
Total Correct	169	153	362	47%	42%
Total Incorrect	17	16	67	25%	24%
Total Control	97	86	217	45%	40%
Total Intervention	89	83	212	42%	39%

Source: Source: CIE.

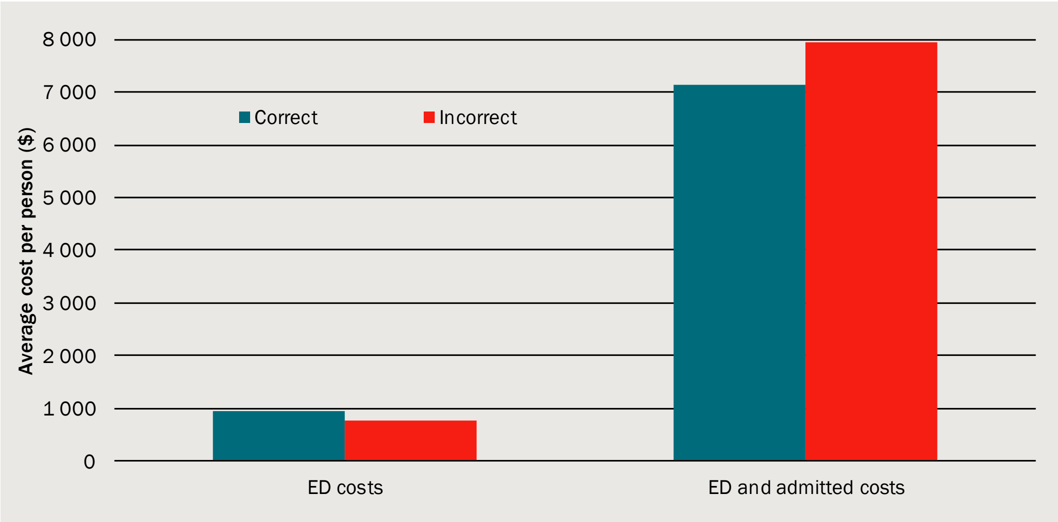
Cost

The section below outlines the outcomes of the study in terms of costs associated with the ED, admission and across all patients presenting to the ED (admitted and non-admitted). It suggests that an incorrect diagnosis results in more expensive admissions cost per person, on average, however the introduction of the ultrasound protocol does not deliver a more cost-effective outcome than the control group while reliance on chest x-ray continues.

Correct versus incorrect diagnosis

As presented in chart 4.8, while an incorrect diagnosis results in marginally lower ED costs, when ED and admitted costs are included, costs per patient are higher.

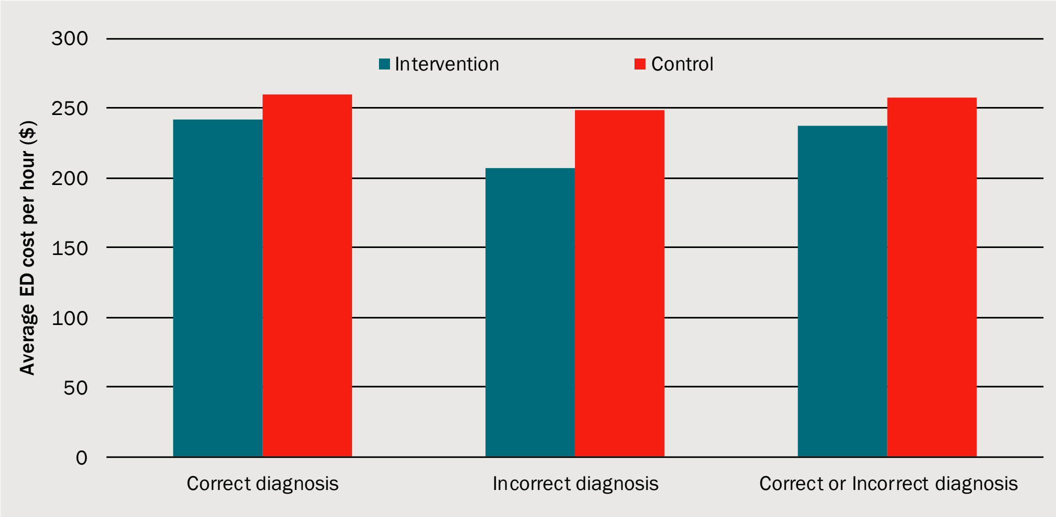
4.8 Average ED and hospital costs per patient by diagnostic accuracy



Data source: CIE.

Given that costs depend on length of stay, a more useful presentation of results is average costs per hour in the ED. As shown in chart 4.9, there is no conclusive pattern in ED costs per hour in terms of diagnostic accuracy, although hourly costs of the invention are moderately below those of the control group.

4.9 Average ED costs per hour by diagnostic accuracy



Data source: CIE.

ED costs per hour by hospital are shown in table 4.10, along with average costs per day for admitted patients. Again, there is no definitive pattern in the cost impact of diagnostic accuracy for admitted patients, which varies depending on the hospital.

4.10 Average Cost per day or hour for patients admitted or presenting

				ED costs				Admitted costs
	PAH	Ipswich	TPCH	All hospitals	PAH	Ipswich	TPCH	All hospitals
	$/person presenting to ED/hour in ED on average				$/admitted person/day on average			
Control								
Correct	241	315	227	260	1 957	1 882	1 541	1 817
Incorrect	196	252	308	249	1 646	1 644	1 485	1 634
Intervention								
Correct	200	312	222	242	2 051	1 680	1 582	1 746
Incorrect	173	271	267	207	1 484	3 220	1 663	2 161
Overall								
Correct	219	313	224	251	1 997	1 775	1 562	1 779
Incorrect	180	256	292	229	1 516	2 102	1 580	1 847
Control	**237**	**299**	**236**	**258**	**1 926**	**1 818**	**1 541**	**1 781**
Intervention	**192**	**308**	**224**	**238**	**1 904**	**1 837**	**1 587**	**1 793**

Note: The results for PAH, where the length of stay was longer for incorrect diagnoses, were influenced by an outlier whereby a patient stayed for 30 days.

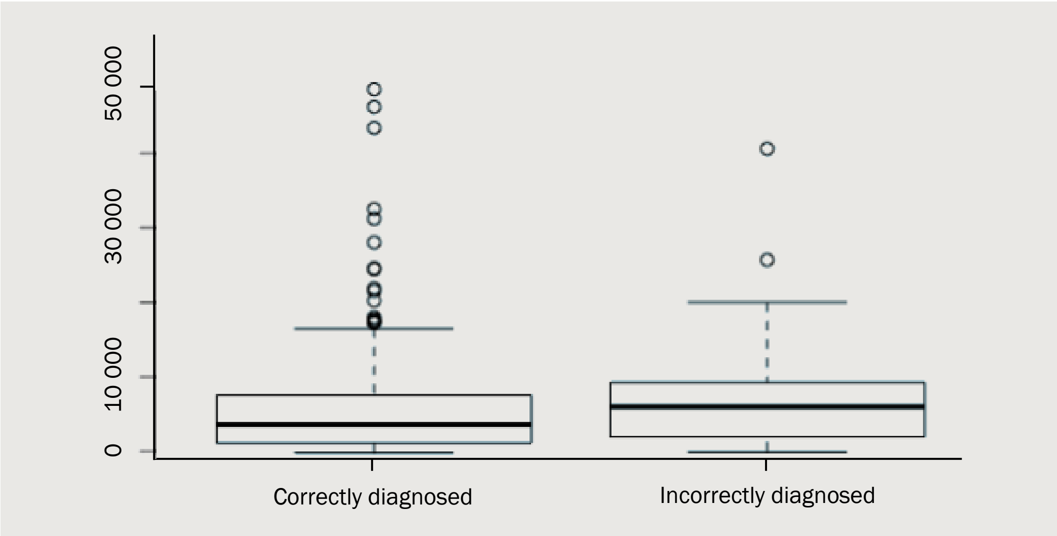
Source: CIE.

Cost per admitted person

Observations on the cost per admitted person are presented for comparative purposes only, and it is acknowledged that there would be many factors that impact on costs per stay over-and-above diagnostic accuracy.

This is consistent with a key finding from the literature that although possibly significant, improved diagnostic accuracy is not expected to substantively impact on hospital length of stay (chart 4.11) or rate of admission.[12]

4.11 Hospital length of stay in minutes, comparing those correctly with those incorrectly diagnosed



Note: Y axis calibrated in minutes. Wilcoxon rank sum w=9237.5, p= 0.04423

Data source: Dr Kylie Baker.

That said, the average cost per admitted person in each subgroup is higher for those with an incorrect diagnosis than those with a correct diagnosis in two out of the three hospitals (table 4.12).

For both the PAH and TPCH, the intervention group was more expensive than the control. In the case of Ipswich, a minor reduction in the average cost per admitted person was evident for the intervention group, but again, average costs per admitted person are not statistically significantly impacted by diagnostic accuracy.

These changes were not reflected by the medians (chart 4.13).

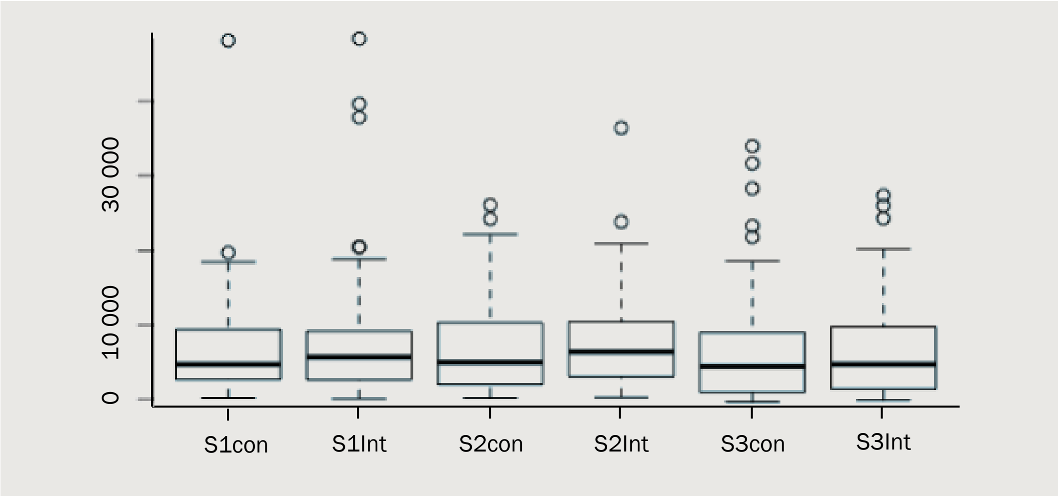
12 See Mueller et al (2004).

4.12 Average Cost per admitted person in subgroup (excluding ED)

Overall	*PAH*	*Ipswich*	*TPCH*
	$/admitted person	$/admitted person	$/admitted person
Control - Correct	6 686	6 149	6 716
Control - Incorrect	5 636	8 916	5 049
Intervention - Correct	7 471	6 543	7 470
Intervention - Incorrect	11 283	7 136	7 310
Total across hospital	**7 240**	**6 701**	**7 004**
Total Correct (Control and Intervention)	**7 035**	**6 355**	**7 112**
Total Incorrect (Control and Intervention)	**9 290**	**8 441**	**5 897**
Total Control	**6 583**	**6 796**	**6 527**
Total Intervention	**8 233**	**6 598**	**7 460**

Source: CIE.

4.13 Range and median costs per admission divided by hospital, control and intervention



Note: Y axis calibrated in dollars. S1 = PAH, S2 = TPCH, S3 = Ipswich, con = control, int = intervention.

Data source: Dr Kylie Baker.

Patient outcomes

Patient outcomes including discharge, internal transfer or death in hospital were recorded. Table 4.14 suggests that there is a slight increase in the rate of death with an incorrect diagnosis, although the degree of significance is unclear.

4.14 Outcomes associated with correct and incorrect diagnosis

Count	PAH	Ipswich	TPCH	Total
Correct diagnosis				
Back to usual residence “1”	103	143	72	318
Interfacility transfer “2”	3	24	11	38
Interfacility transfer “3”	2	2	0	4
Death in hospital “4”	5	2	2	9
Rate of outcome “4” (Death)	4.4%	1.2%	2.4%	2.4%
Total	**113**	**171**	**85**	**369**
Incorrect diagnosis				
Back to usual residence “1”	15	27	8	50
Interfacility transfer “2”	2	6	1	9
Interfacility transfer “3”	0	0	0	0
Death in hospital “4”	0	2	0	2
Rate of outcome “4” (Death)	0.0%	5.7%	0.0%	3.3%
Total	**17**	**35**	**9**	**61**

Note: Destination at discharge 1 = back to usual residence, 2 and 3 are interfacility transfers, and 4 is death in hospital. The original intention of codes ‘2’ and ‘3’ was to differentiate between transfers to a private hospital and transfers to a ‘step down’ facility, but the electronic information system proved too inconsistent. All that can be said of these patients was that they were not yet well enough to be discharged back to their usual place of residence.

Source: CIE.

Charts 4.15 and 4.16 show that the intervention group has a lower rate of death than the control group (at 1.4 per cent compared to 3.7 per cent) which is not statistically significant.

4.15 Outcomes – Control

Count	PAH	Ipswich	TPCH	Total
Back to usual residence “1”	58	82	40	180
Interfacility transfer “2”	3	19	5	27
Interfacility transfer “3”	1	1	0	2
Death in hospital “4”	4	3	1	8
Total	**66**	**105**	**46**	**217**
Rate of outcome “4” (Death)	6.1%	2.9%	2.2%	3.7%

Note: Destination at discharge 1 = back to usual residence, 2 and 3 are interfacility transfers, and 4 is death in hospital.

Source: CIE.

4.16 Outcomes – Intervention

Count	PAH	Ipswich	TPCH	Total
Back to usual residence “1”	60	88	40	188
Interfacility transfer “2”	2	11	7	20
Interfacility transfer “3”	1	1	0	2
Death in hospital “4”	1	1	1	3
Total	**64**	**101**	**48**	**213**
Rate of outcome “4” (Death)	1.6%	1.0%	2.1%	1.4%

Note: Destination at discharge 1 = back to usual residence, 2 and 3 are interfacility transfers, and 4 is death in hospital.
Source: CIE.

Conclusion

The study suggests that an incorrect diagnosis is more expensive than a correct one, and the intervention (ultrasound protocol) achieved a higher diagnostic accuracy in two of the three hospitals, though by a small amount overall. The introduction of the ultrasound protocol did not lead to a reduction in cost.

The CIE would recommend that further consideration is given as to why the cost of the intervention group may have been higher for patients with a correct diagnosis.

There may be a basis for normalising these costs, but the bias associated with this would need to be examined in consultation with a statistician.

The relatively minor impact of diagnostic accuracy on both costs and outcomes suggests that factors other than diagnostic accuracy impact on length of stay. Management decisions and placement options may be a better target of investigation, rather than improved diagnosis.

5 *Assessment of cost effectiveness*

A key finding of this study is that diagnostic accuracy has a small impact on length of stay and cost outcomes, and a *correct* diagnosis is more cost effective than an *incorrect* diagnosis.

The intervention is not shown to be cost effective in this format. This is due to the large size of the sample of 'correct' diagnosis relative to incorrect diagnosis, and underlying differences in the cost of a correct diagnosis between the interventional and control group, which is not explained by the difference in diagnostic approach.

Effectiveness

The effectiveness of the intervention (ultrasound protocol) compared to the standard treatment protocol (control) is reflected in its effect on diagnostic accuracy, and cost.

Overall, the diagnostic accuracy of the intervention was improved in two of the three hospitals, which the results showing:

- an *increase* in diagnostic accuracy at the TPCH of 6.8 per cent, from 87.0 per cent in the control group to 93.8 per cent in the intervention group
- an *increase* in diagnostic accuracy at the Ipswich hospital of 13.7 per cent, from 78.1 per cent in the control group to 91.8 per cent in the intervention group, and
- a *reduction* in diagnostic accuracy at the PAH of 8.1 per cent, from 90.9 per cent in the control group to 82.8 per cent in the intervention group.

The study suggests that *length of stay* is increased, on average, for patients with an incorrect diagnosis. Overall, however, the length of stay was nonetheless higher in the intervention group due to:

- the impact of the lower diagnostic accuracy in the intervention group at the PAH, and
- the impact of the longer length of stay in the intervention group for both correct and incorrect diagnoses.

Costs

Overall comparisons in costs between the intervention and control group showed mixed, nondefinitive results.

Across all 3 hospitals, average hourly ED costs were 8 per cent lower for an incorrect diagnosis compared to a correct diagnosis, although the reverse was true for hospital admissions, where average costs per day were 4 per cent higher for an incorrect diagnosis. However, hospital variation was noted:

- average ED costs per person were the same for the intervention and control group, however, the cost of a correct diagnosis under the intervention was non-significantly higher than a correct diagnosis under the control ($969 versus $935 respectively)
- total average costs (ED and hospital) per person presenting to the ED were highest for patients in the control group with an incorrect diagnosis ($8 145) followed by those with a correct diagnosis in the intervention group ($7 437), those in the intervention group with an incorrect diagnosis ($7 011) and those in the control group with a correct diagnosis ($6 830)
- differences in ALOS between the comparator and control group for a correct diagnosis were marginal (half a day longer for the control group).

Given the importance of LOS on costs, costs per day (hospital) and per hour (ED) were calculated to assess the impacts of the intervention. It was found that:

- the intervention was associated with reduced hourly costs in the ED per patient presenting at the PAH (-19 per cent) and TPCH (-5 per cent), but not at Ipswich (+3 per cent), with an average reduction across all hospitals of 8 per cent per hour per presenting patient, and
- the intervention was associated with a minor impact on total admission costs per day (+1 per cent), with minimal hospital variation (ranging from -1 per cent to +3 per cent).

For the purposes of this study, the cost of the equipment is a sunk cost, as they are already on hand for other purposes, while the main investment is the time of both the clinicians and doctors in facilitating and undertaking training. The cost and time dimensions included in this study included:

- four hours of training, undertaken by a 'trial-credentialed clinician' that performs the intervention ultrasound scan, usually a *junior doctor*
- time for the submission of 10 practice scans with correctly identified Wet versus Dry condition diagnosis, and
- additional retraining, Ipswich and TPCH (but not PAH[13]), when prompted by an incorrect ultrasound plus a further one hour upskill exercise at 6 months and 12 months following the initial training.

Assumptions regarding the cost of staff training are set out in table 5.1.

5.1 Assumptions: estimating the cost of staff training

Assumption	PAH	Ipswich	TPCH
Staff training — initial			
Hours of training	4	4	4
Time required to complete practice scans (hours)	1.2	1.2	1.2
Average hours per staff	**5.2**	**5.2**	**5.2**

13 The PAH had their own ongoing routine ultrasound teaching sessions (not specific to lung scans but including lung scans).

Assumption	PAH	Ipswich	TPCH
Staff training — ongoing			
Number of staff	10	10	10
Retraining session offered at 6 months (hours)	4	4	4
% participating staff	0%	25%	25%
Upskill exercise at 6 months following initial training (hours)	1	1	1
% participating staff	25%	25%	25%
Upskill exercise at 12 months (hours)	1	1	1
% participating staff	25%	25%	25%
Total hours	5	15	15
Average hours per staff	**0.5**	**1.5**	**1.5**
Total costs for staff participating in training			
Total hours of training per staff (average)	5.7	6.7	6.7
Average cost per staff per hour	72.4	72.4	72.4
Total cost per staff trained	**410**	**483**	**483**
Total cost for staff trainer			
Total hours of training per staff (average)	5.7	6.7	6.7
Cost per hour	74.7	74.7	74.7
Total cost per staff trained	**423**	**498**	**498**
Total training program cost			
Total value of the fixed investment per staff trained	**833**	**981**	**981**
Total value of the fixed investment	**8 335**	**9 806**	**9 806**

Source: CIE.

Lessons from the study results

The analysis suggests that it is difficult to make conclusions regarding the cost impact of the intervention where the trial outcomes are predominantly driven by the cost of those with a correct diagnosis. Thus, the impact of the change in diagnostic accuracy is only minimal compared with the overall cost differential of the trial groups. What is more relevant is the impact of diagnostic accuracy on length of stay and cost outcomes, as confirmed by this study.

The impact of diagnostic testing on confidence levels would potentially be influenced by the extent of training and interpretation of those results by practitioners. Any future study could look to identify impact on sub groups such as those with uncertainty around heart failure.

It is noted that in the case of the PAH, the intervention led to a worse rate of diagnostic accuracy. This tertiary hospital had the best diagnostic accuracy within the control group, suggesting that their processes were already robust and therefore little benefit accrued from an extra test. Ipswich, with the worst control group accuracy, had the most to gain.

A Studies included in the review

Studies identified in the literature review to support the PICO

A summary of the 7 studies identified through the search strategy (restriction to studies with the ultrasound being the intervention) is provided below.

A.1 Studies assessing the economic impact of diagnostic techniques for dyspnoea in the emergency setting

Studies
PubMed
Title: Bedside lung ultrasound versus chest X-ray use in the emergency department **Author:** Unluer, E.E. & Karagoz, A. **Year:** 2014 **Country:** Turkey **Setting:** Emergency Department **Population:** Case study of a dyspnoeic patient with a normal chest X-ray result **Intervention:** Bedside lung ultrasound **Outcomes measured (relevant to the PICO):** Cost of intervention
Title: Effectiveness of chest radiography, lung ultrasound and thoracic computed tomography in the diagnosis of congestive heart failure **Author:** Cardinale, L., Priola, A.M., Moretti, F. & Volpicelli, G. **Year:** 2014 **Country:** Italy **Setting:** Emergency Department **Population:** Patients with hydrostatic pulmonary edema due to congestive heart failure **Intervention:** Lung ultrasound, chest X-ray and CT **Outcomes measured (relevant to the PICO):** Cost of intervention
Title: Real-time lung ultrasound for the diagnosis of alveolar consolidation and interstitial syndrome in the emergency department **Author:** Volpicelli, G., Silva, F. & Radeos, M. **Year:** 2010 **Country:** Italy **Setting:** Emergency Department **Population:** Patients with pulmonary disease **Intervention:** Lung ultrasound **Outcomes measured (relevant to the PICO):** Time saving and cost of intervention
Title: Usefulness of lung ultrasound in the bedside distinction between pulmonary edema and exacerbation of COPD **Author:** Volpicelli, G., Cardinale, L., Garofalo, G. & Veltri, A. **Year:** 2008 **Country:** Italy

Studies
Setting: Emergency setting **Population:** Patients with pulmonary edema or exacerbation of chronic obstructive pulmonary disease **Intervention:** Bedside lung ultrasound **Outcomes measured (relevant to the PICO):** Feasibility and cost efficiency
Cochrane
Title: Immediate versus delayed integrated point-of-care-ultrasonography to manage acute dyspnea in the emergency department **Author:** Pirozzi, C., Numis, F.G., Pagano, A., Melillo, P., Copetti, R. & Schiraldi, F. **Year:** 2014 **Country:** Italy **Setting:** Emergency Department **Population:** Patients presenting to emergency department with dyspnea **Intervention:** Lung ultrasound **Outcomes measured (relevant to the PICO):** mortality, days of hospitalisation in emergency medicine department and transfers to other wards
Manual searching
Title: Has lung ultrasound an impact on the management of patients with acute dyspnea in the emergency department? **Author:** Goffi, A., Pivetta, E., Lupia, E., Porrino, G., Civita, M., Laurita, E., Griot, G., Casoli, G. & Cibinel, G.A. **Year:** 2013 **Country:** Italy **Setting:** Emergency department **Population:** Adult patients presenting to the Emergency Department with acute undifferentiated dyspnea **Intervention:** Lung Ultrasound **Outcomes measured (relevant to the PICO):** change in patient management due to improved diagnostics (prescribing of new medicine, holding of medicine that would have otherwise been prescribed, new procedure initiation)
Title: Point-of-care Ultrasonography for Evaluation of Acute Dyspnea in the ED **Author:** Zanobetti, M., Scorpiniti, M., Gigli, C., Nazerian, P., Vanni, S., Innocenti, F., Stefanone, V.T., Savinelli, C., Coppa, A., Bigiarini, S., Caldi, F., Tassinari, I., Conti, A., Grifoni, S. & Pini, R. **Year:** 2017 **Country**: Italy **Setting:** Emergency department **Population:** Adult patients presenting with dyspnea **Intervention:** Point-of-care lung ultrasound **Outcomes measured (relevant to the PICO):** time to diagnosis

Source: CIE.

Additional studies identified as relevant to the economic evaluation

A summary of the 10 studies identified through the search strategy (no restriction on the intervention) is provided below. The outcomes that are specifically of interest and those shown in bold.

A.2 Studies assessing the economic impact of diagnostic techniques for dyspnoea in the emergency setting

Studies
PubMed
Title: Meta-analysis: effect of B-type natriuretic peptide testing on clinical outcomes in patients with acute dyspnea in the emergency setting. **Author:** Lam, L., Cameron, L., Schneider, H., Abramson, M., Muller, C., and Krum, H. **Year:** 2010 **Country:** **Setting:** Meta-analysis (including five trials conducted in 5 countries – Australia, Switzerland, Canada, the Netherlands, and the United States - different study settings) **Population:** Patients presenting with acute dyspnea **Intervention:** Two trials used the NT pro-BNP test, while 3 trials used the BNP test **Outcomes measured (relevant to the PICO):** Admission rates, length of stay in hospital and critical care unit, **all-cause mortality in hospital and at 30/60 days**; Re-admission **Result:** Data from 5 Randomised Controlled Trials showed using BNP testing had a modest effect on management of patients presenting to the emergency department
Title: Clinical uncertainty, diagnostic accuracy, and outcomes in emergency department patients presenting with dyspnea **Author:** Green, S., Martinez-Rumayor, A., Gregory, S. **Year:** 2008 **Country:** Massachusetts General Hospital, Boston **Setting:** From the ProBNP Investigation of Dyspnea in the Emergency Department (PRIDE) study **Population:** Dyspneic patients **Intervention:** Amino-terminal pro-B-type natriuretic peptide (NT-proBNP) **Outcomes measured (relevant to the PICO):** Hospitalisation, length of stay in hospital, and **outcomes**
Title: Pre-admission NT-proBNP improves diagnostic yield and risk stratification - the NT-proBNP for Evaluation of dyspnoeic patients in the Emergency Room and hospital (BNP4EVER) study **Author:** Meisel SR, Januzzi JL, Medvedovski M, Sharist M, Shochat M, Ashkar J, Peschansky P, Haim SB, Blondheim DS, Glikson M, Shotan A. **Year:** 2012 **Country:** Not stated?? **Setting:** **Population:** BNP4Ever – Individuals over 18 years, presenting with evidence of dyspnoea (excluding those with known causes such as trauma, COPD, acute myocardial infarction or pneumonia **(NOTE: NOT strictly meeting our criteria)** **Intervention:** NT-proBNP testing **Outcomes measured (relevant to the PICO):** Admission, length of stay, in-hospital mortality, discharge diagnosis, and **long-term outcome (therapy at discharge and two-year outcome)**
Title: Natriuretic peptide testing in EDs for managing acute dyspnea: a meta-analysis. **Author:** Trinquart L, Ray P, Riou B, Teixeira A. **Year:** 2011 **Country:** Meta-analysis including four randomised controlled trials (Switzerland, Canada, Netherlands, Australia) **Setting:** Various (two single-centre trials, one at 7 centres, one at 2 centres) **Population:** Patients presenting to ED with dyspnoea

Studies
Intervention: Use of B-type natriuretic peptide or N-terminal fragment **Outcomes measured (relevant to the PICO):** Hospital admission rate, time to discharge, length of hospital stay, **mortality**, and **rehospitalisation rates**, and **total direct medical costs**
Title: B-type natriuretic peptide testing, clinical outcomes, and health services use in emergency department patients with dyspnea: a randomized trial. **Author:** Schneider HG, Lam L, Lokuge A, Krum H, Naughton MT, De Villiers Smit P, Bystrzycki A, Eccleston D, Federman J, Flannery G, Cameron P. **Year:** 2009 **Country:** Australia **Setting:** 2 teaching hospital emergency departments **Population:** Acute severe dyspnea **Intervention:** BNP testing or no testing **Outcomes measured (relevant to the PICO):** Admission rates, length of stay, and emergency department medications (primary outcomes); **mortality** and **readmission rates (secondary outcomes)**
Title: N-terminal pro-brain natriuretic peptide testing in the emergency department: beneficial effects on hospitalization, costs, and outcome. **Author:** Rutten JH, Steyerberg EW, Boomsma F, van Saase JL, Deckers JW, Hoogsteden HC, Lindemans J, van den Meiracker AH. **Year:** 2008 **Country:** The Netherlands **Setting:** Erasmus Medical College, Rotterdam **Population:** Patients with acute dyspnea presenting to the emergency department (average age of 59 years) **Intervention:** **Outcomes measured (relevant to the PICO):** Time to discharge from the hospital and costs related to hospital admission; and 30-day mortality
Title: Medical and economic long-term effects of B-type natriuretic peptide testing in patients with acute dyspnea. **Author:** Breidthardt T, Laule K, Strohmeyer AH, Schindler C, Meier S, Fischer M, Scholer A, Noveanu M, Christ M, Perruchoud AP, Mueller C. **Year:** 2007 **Country:** **Setting:** Follow up analysis of the B-Type Natriuretic Peptide for Acute Shortness of Breath Evaluation (452 patients) **Population:** Patients presenting to ED with acute dyspnea but the mean age was 71 years **Intervention:** 'Rapid' BNP testing **Outcomes measured (relevant to the PICO): Effect on long term mortality, effect on morbidity (in terms of days in hospital), and economic outcome at 12 months**
Title: Cost-effectiveness of B-type natriuretic peptide testing in patients with acute dyspnea **Author:** Mueller C, Laule-Kilian K, Schindler C, Klima T, Frana B, Rodriguez D, Scholer A, Christ M, Perruchoud AP. **Year:** 2006 **Country:** Switzerland **Setting:** Secondary care. **Population:** Patients presenting to the hospital emergency department with acute dyspnoea (excluding trauma, severe renal disease and cardiogenic shock) **Intervention:** 'Diagnosis' – with B-type natriuretic peptide (BNP) testing **Outcomes measured (relevant to the PICO): Cost of total treatment at 180 days; all-cause mortality**
Title: The use of B-type natriuretic peptide in the management of elderly patients with acute dyspnoea. **Author:** Mueller C, Laule-Kilian K, Frana B, Rodriguez D, Rudez J, Scholer A, Buser P, Pfisterer M, Perruchoud AP. **Year:** 2005 **Country:** Switzerland **Setting:** Acute Shortness of Breath Evaluation (BASEL) study – ED of University hospital **Population:** Shortness of breath as primary complaint and no obvious traumatic cause (excluding patients with severe renal disease, cardiogenic shock and those requesting early transfer) **Intervention:** BNP testing **Outcomes measured (relevant to the PICO):** Time to discharge; and total cost of treatment

Studies
Manual searching
Title: Acute respiratory failure in the elderly: etiology, emergency diagnosis and prognosis **Author:** Ray, P, Birolleau, S., Lefort, Y., Becquemin, M-H., Beigelman, C., Isnard, R., Teixeira, A., Arthaud, M., Riou, B., and Boddaeart, J. **Year:** 2006 **Country:** **Setting:** Emergency department **Population:** **Intervention:** Standard care in both groups, with record of those receiving inappropriate versus non- inappropriate initial care and the rate of mortality **Outcomes measured (relevant to the PICO):** mortality
Title: Lung ultrasound in internal medicine efficiently drives the management of patients with heart failure and speeds up the discharge time **Author:** Mozzini, C., Perna, M., Pesce, G., Garbin, U., Pasini, A., Ticinesi, A., and Nouvenne, A. **Year:** 2017 **Country**: Italy **Setting:** Emergency department, University hospital **Population:** Italy **Intervention:** Lung ultrasound versus chest x ray **Outcomes measured (relevant to the PICO):** Time to discharge, diuretic therapy dosage, amino-terminal portion of B type natriuretic peptide (NT-proBNP) levels in monitoring HF recovery

Source: CIE.

B Collection and appraisal of the economic literature

A literature search was conducted to identify any published or unpublished studies relevant to the PICO. The databases utilised included:

- PubMed
- Cochrane
- ScienceDirect
- International Health Technology Assessment Agencies (NICE, SMC and CADTH), and
- manual searching of ResearchGate, Google Scholar and PubMed.

Inclusion and exclusion criteria

An inclusion and exclusion criteria was established to determine the appropriateness of each study identified in the literature search (table B.1). To be included, a study was required to consider the use of ultrasound in diagnosing adults presenting to the Emergency Department with undifferentiated dyspnoea. The outcomes of interest included time to diagnosis, length of stay, mortality, re-admission rate and associated costs. Studies that *only* looked at the accuracy of lung ultrasound without evaluating any economic or resource utilisation outcomes were excluded.

B.1 Inclusion and exclusion criteria

Criteria	Example of inclusion	Example of exclusion
Study type	Case study, RCT, Review	Clinical guidelines
Population	Adults presenting with dyspnoea	Paediatric population, trauma patients
Setting	Emergency Department	Pre-hospital, Intensive care unit, nursing home
Intervention	Lung ultrasound	Protocols and clinical prediction rules
Comparator	CT, chest X-ray, echocardiography, electrocardiography	Dyspnoea management strategies, innovative blood tests
Outcome measured	Time to diagnosis, length of stay, mortality, re-admissions, cost of intervention, cost of management	Only focused on accuracy of diagnostic technique

Source: CIE.

Search strategy

PubMed

PubMed was searched on the 9th of February 2018. The search terms entered the PubMed Advanced Search Builder and corresponding number of returned results are presented in table B.2. A total of 47 publications were identified. Following title and abstract review, 43 were excluded, with:

- 2 excluded due to inappropriate population (paediatric)
- 33 excluded due to inappropriate outcome (e.g. antibiotic use, radiation exposure, intervention accuracy, epidemiological study)
- 4 excluded due to inappropriate setting (e.g. low resource settings, out-of-hospital care), and
- 4 excluded due to inappropriate intervention (pre-test probability protocol and clinical prediction rule).

The final 4 studies that were deemed relevant to the PICO are presented in table A.1.

B.2 PubMed Search strategy

No.	Search term	No. of results
#1	Breathlessness	45 420
#2	Dyspnea	49 148
#3	Dyspnoea	49 166
#4	Emergency department	212 413
#5	Emergency room	89 513
#6	Ultrasound	1 393 809
#7	Lung ultrasound	86 540
#8	B lines	52 178
#9	Chest X-ray	78 289
#10	Electrocardiography	197 916
#11	Cost	743 789
#12	Re-admission	1 162
#13	Length of stay	110 873
#14	Health outcomes	313 783
#15	Economic evaluation	94 276
#16	#1 or #2 or #3	51 748
#17	#4 or #5	218 613
#18	#6 or #7 or #8 or #9 or #10	1 631 042
#19	#11 or #12 or #13 or #14 or #15	1 101 305
#20	#16 and #17 and #18 and #19	47

Note: Search conducted on 9th of February 2018.

Source: CIE.

Cochrane database

The Cochrane database was searched on the 12th of February 2018 using the terminology "lung ultrasound in the emergency department". Twenty-four results were identified. Of these, one publication was deemed relevant to the PICO (table A.1) and twenty-three were excluded, with:

- 6 excluded due to inappropriate population (paediatric, young women)
- 14 excluded due to inappropriate outcome (e.g. intervention accuracy, case studies, chest tube insertion)
- 2 excluded due to inappropriate intervention (tricuspid annual plane systolic excursion), and
- 1 excluded due to duplication with a PubMed search result previously excluded.

ScienceDirect

The ScienceDirect database was searched on the 12th of February 2018 using the terms presented in table B.3. No relevant publications were identified.

B.3 Science direct search terms

No.	Search terms	No. of results
1. General search, excl. paediatrics	((breathlessness or dyspnoea or dyspnea) and (ultrasound or lung ultrasound or b lines or chest x-ray or electrocardiography) and ((emergency department or emergency room) and (cost or re-admission or length of stay or health outcomes or economic evaluation) and not (children or infants or paediatric or paediatric))	200
2. Search 1 with date restriction	Pub date > 2012 and ((breathlessness or dyspnoea or dyspnea) and (ultrasound or lung ultrasound or b lines or chest x-ray or electrocardiography) and ((emergency department or emergency room) and (cost or re-admission or length of stay or health outcomes or economic evaluation) and not (children or infants or paediatric or paediatric))	54
3. Date restriction, and no restriction on population (i.e. paediatrics not excluded)	pub-date > 2012 and ((breathlessness or dyspnoea or dyspnea) and (ultrasound or lung ultrasound or b lines or chest x-ray or electrocardiography) and ((emergency department or emergency room) and (cost or re-admission or length of stay or health outcomes or economic evaluation)	254

Note: Search conducted on the 12th of February 2018.

Source: CIE.

Health technology assessment agencies

Three Health Technology Assessment Agencies were searched on the 9th of February 2018. No relevant publications were identified (table B.4).

B.4 Health Technology Assessment Agency search strategies

Country	Agency	Search terms	Relevant publications
England	NICE	"dyspnea", "breathlessness", "emergency department", "lung ultrasound", "chest X-ray"	0
New Zealand	PHARMAC	"dyspnea", "breathlessness", "emergency department", "lung ultrasound", "chest X-ray"	0
Canada	CADTH	"dyspnea", "breathlessness", "emergency department", "lung ultrasound", "chest X-ray"	0

Note: Search conducted on 9th of February 2018.
Source: CIE.

Manual searching

A manual search was conducted using Google Scholar, ResearchGate and PubMed to capture any studies that may have been missed in the systematic literature review. A summary of the search terms used is presented in table B.5. The search terms were sufficiently broad to capture any outstanding studies. Two additional studies that met the PICO criteria were identified.

B.5 Manual review search terms

Search terms
Dyspnoea in the emergency department
Lung ultrasound in the emergency department
Dyspnea in the emergency department
Diagnosis of breathlessness in the emergency department
Economic evaluation of lung ultrasound in the emergency department

Note: Search conducted on 14th of February 2018.
Source: CIE.

Included studies

Most of the studies 'included' in the literature review considered lung ultrasound as a time efficient alternative to standard care, with results able to be interpreted at time of assessment. Whilst this is expected to lead to cost savings, and reduced time to treatment, no studies quantified the benefits of this, with only one study estimating actual time savings.[14] Each of the studies is detailed below.

Ultimately, upon review of the full text, only two studies were subject to further review (an internal and external validity evaluation).

Two studies, Zanobetti et al (2017) and Goff et al (2013), were suitable for inclusion in the review.

Zanobetti et al 2017

Zanobetti et al. (2017) measured the time taken to formulate a diagnosis for 2 683 adult patients who presented to the Emergency Department with dyspnoea. A comparison was made between ultrasound diagnosis and usual Emergency Department care (vital signs, medical history, physical exam, 12-lead ECG, chest x-ray, CT, echocardiogram and blood sampling). The study was performed by ten emergency physician sonographers who had previously attended an 80-hour training course and had a minimum of two years of experience. Thus, the results need to be qualified for the transferability to our study.

- For the diagnosis of acute coronary syndrome, pleural effusion, pericardial effusion and pneumothorax, there was no significant difference in sensitivity and specificity between ultrasound and usual care. However, the authors acknowledged that this was likely due to the high level of experience and training of the doctors who were conducting the ultrasound.
- Further, standard assessment was superior in the diagnosis of asthma/COPD (likely due to medical history taking rather than radiological tests) and pulmonary embolism (best indicated by CT pulmonary angiography).

For each patient, time of entry to the Emergency Department, time taken to perform and assess the ultrasound, and the time taken to complete the usual care diagnosis were recorded. The study made the following conclusions:

- The time needed to complete the ultrasound was significantly less than the standard protocol in that study's context (24±10 minutes compared to 186±72 minutes, respectively).
- Ultrasound could be safely used to minimise delays in treatment administration for patients presenting to the ED with dyspnoea.

However, the study did not address any other outcomes relevant to the search criteria (i.e. cost of care, length of stay or health outcomes).

14 Zanobetti, M., Scorpiniti, M., Gigli, C., Nazerian, P., Vanni, S., Innocenti, F., Stefanone, V.T., Savinelli, C., Coppa, A., Bigiarini, S., Caldi, F., Tassinari, I., Conti, A., Grifoni, S. & Pini, R. 2017, 'Point-of-care ultrasonography for evaluation of acute dyspnea in the emergency department', *Chest*.

Goff et al 2013

Goff et al. (2013) assessed the impact of lung ultrasound on patients who presented to the Emergency Department with dyspnoea. The study compared clinical assessment[15] with lung ultrasound in 50 adult patients (with a median age of 80.5 years). Noting that some patients had more than one diagnosis, the conditions diagnosed included diffuse interstitial syndrome (58 per cent of cases), pleural effusion (52 per cent), focal interstitial syndrome (18 per cent), alveolar consolidation (14 per cent) and pneumothorax (8 per cent).

Agreement between reference diagnosis and lung ultrasound was higher than reference diagnosis and standard clinical assessment for all three categories of diagnosis. That is, respective agreement between lung ultrasound versus reference diagnosis and standard clinical assessment verse reference diagnosis, was:

- 100 per cent compared to 70.6 per cent for acute decompensated heart failure
- 100 per cent versus 56.5 per cent for respiratory disorders and,
- 80 per cent versus 10 per cent for combined dyspnoea.

Lung ultrasound changed the main clinical diagnosis in 44 per cent of cases, with an associated change in patient management for 58 per cent of patients. A new drug was prescribed in 19 cases, medication was withheld in 10 cases, 6 cases involved a change in testing and 5 involved a change in disposition plan.

While the study did not address any other outcomes relevant to the search criteria (i.e. cost of care, length of stay, re-admission or health outcomes), it can be implied that improved accuracy in diagnosis has an impact on resource use in this context and may lead to better outcomes.

Excluded studies

The following five studies were identified but ultimately eliminated as:

- the comparator was not sufficiently consistent;
- the study was not a clinical or economic evaluation/ was a case study; and/or
- the study focused on clinical rather than outcome parameters with no actual outcomes reported.

Unler and Karagoz et al. (2014) was excluded on the basis that it was undertaken on patients with a normal chest x ray.

Pirozzi et al (2014) examined the question of whether an earlier ultrasound conducted within one hour of arrival to ED, compared to an immediate ultrasound plus standard care, contributed to a change in patient outcomes. While diagnostic accuracy was improved, there was no change in patient outcomes. However, the comparator of an ultrasound for that study does not provide a relevant comparator for this study.

[15] There are no details in the study about what is included in the clinical assessment.

The remaining studies, including Cardinale et al. (2014), Volpicelli et al. (2010) and Volpicelli et al. (2008), commented on the time savings associated with the use of lung ultrasound for diagnosing dyspnoea in the Emergency Department, but did not explicitly measure the costs or consequences.

The section below discusses these studies.

Pirozzi et al 2014

Pirozzi et al. (2014) compared the use of immediate ultrasound plus routine blood work and instrumental tests (standard care[16]) with standard care plus delayed ultrasound (within 1 hour of presentation) in patients presenting to the Emergency Department with dyspnoea. The study analysed two factors: whether it makes a difference to diagnostic accuracy to include the ultrasound in the standard diagnosis protocol (part 1) and whether there is a difference in clinical outcomes (of mortality, discharge and length of hospitalisation) from providing ultrasound immediately at the entry in to the ED or after a short delay of around one hour (part 2).

The primary outcome of the study was to determine if the addition of point-of-care ultrasound would improve diagnostic capabilities. The study found that use of ultrasound has a remarkable impact on diagnostic accuracy. The percentage of wrong *initial diagnosis* was 5 per cent[17] in group 1 (immediate ultrasound) and 50 per cent in group 2 after 'standard care' but prior to the ultrasound. The ultrasound involved examination of the lung, cardiac, inferior vena cava and inferior limb vein. The three investigators who performed the ultrasound were well trained in emergency ultrasonography.

The secondary outcome was to determine whether the timing of the ultrasound (immediate versus within an hour) would impact on mortality, transfer rates, discharge rates and days of hospitalisation. There was no difference in clinical outcomes between immediate versus delayed use (mortality, discharge, transfers and length of hospitalisation). However, the design of the study was not particularly informative for our purposes, with this study's *comparator* for analysing outcomes associated with correct/early diagnosis being an *ultrasound* after delivery, like our study's intervention (Study Path care).

Unluer et al 2014

Unluer et al. (2014) presented a case study of a 47-year-old woman presenting to the Emergency Department with dyspnoea. The woman was initially assessed with a chest X-ray; however, the results were unremarkable. A bedside lung ultrasound was conducted, demonstrating bilateral pleural effusion, followed by a confirmatory CT. The authors concluded that Emergency Department use of bedside lung ultrasound is helpful for diagnosing early pleural and peripheral lung disease, with benefits including the low

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16 Standard care approximates Usual Care under this study. Trauma and paediatric patients were excluded from the study. The patient group included those over 18 years.

17 The three investigators were well trained in emergency ultrasonography, indicating that the results may not be transferable to a typical Emergency Department setting

cost of administration and the ability to avoid transferring a patient to a radiology department (however, these benefits are not quantified).

Similarly, Cardinale et al. (2014) compared the efficacy of chest radiography, lung ultrasound and thoracic CT in the diagnosis of congestive heart failure. The authors discussed the usefulness of lung ultrasound in the emergency department setting, highlighting how it allows for prompt diagnostic evaluation. Given it is a case study, however, this limits the ability to use such results for generalisation.

Volpicelli et al (2010)

Volpicelli (2010) describes innovative uses of lung ultrasound for the diagnosis of alveolar consolidations and interstitial syndrome, based on findings from the literature. The study does not assess patient outcomes, but discusses how real-time diagnosis of alveolar interstitial syndrome may have immediate effects on the management of ED patients (in terms of timely administration of appropriate treatment). The authors completed the review in recognition of the time and cost savings associated with the use of ultrasound in the Emergency Department.

Volpicelli et al (2008)

Volpicelli et al. (2008) reviewed the usefulness of bedside lung ultrasound in the diagnosis of different cases of acute dyspnoea in the Emergency Department, with a focus on COPD and pulmonary oedema. Based on published literature, the study describes how to conduct and interpret lung ultrasound and reports the sensitivity and specificity of its application in alveolar interstitial syndrome. The authors discussed the potential for bedside and real-time diagnosis of alveolar-interstitial syndrome to lead to better management of critically ill patients, due to the reduction of dangerous delays in therapy administration or ineffective therapy administration and reduced workload of radiologists.

Critical appraisal of included studies

The identified studies have been considered in further detail to determine the transferability of the findings to our project. This involved assessing the degree to which the results are likely to be true and free of bias. More specifically, we evaluated each study for:

- internal validity: the extent to which the design and conduct of the study is likely to have prevented bias, and
- external validity: the extent to which the results provide a correct basis for generalisation to the Australian context.[18]

Each study had a clearly defined study question and accurate measurement of outcomes. Sensitivity analysis was only presented in Zanobetti et al. (2017). Both studies, Zanobetti et al. (2017) and Pirozzi et al. (2014), used investigators that were well trained and

18 http://community.cochrane.org/glossary#letter-V

experienced in ultrasonography, limiting the applicability of the results to broader contexts (for example, in settings with less trained or experienced physicians).

A summary of the findings and key internal and external validity considerations is provided below.

B.6 Internal and external validity of selected studies

Study / Results	Internal and external validity
Zanobetti et al. (2017)	
▪ There was no significant difference in sensitivity and specificity between ultrasound and usual care for the diagnosis of acute coronary syndrome, pleural effusion, pericardial effusion and pneumothorax ▪ Standard assessment was superior in the diagnosis of asthma/COPD and pulmonary embolism. ▪ The time needed to complete the ultrasound was significantly less than the standard protocol (24±10 minutes compared to 186±72 minutes respectively) ▪ Ultrasound could be safely used to minimise delays in treatment administration for patients presenting to the Emergency Department with dyspnoea	▪ The study question was well-defined ▪ Time to diagnosis was measured accurately ▪ Sensitivity analysis presented ▪ Study doctors were very well trained (80-hour training course, including 150 each of ultrasound and echocardiogram tests in the Emergency Department) ▪ A minimum of 2 years' experience. This indicates that the results of the study may not be applicable to a generic Emergency Department setting, where physicians may be less experienced in ultrasound. ▪ Patients who were not admitted after presentation to the Emergency Department were not considered in the study. These patients may have had more easily identifiable conditions, potentially decreasing the time to diagnosis difference between the two interventions. Number of averted hospitalisation is an important outcome of interest for our study, hence the exclusion of non-admitted patients in this study limits the transferability of the findings and may overestimate the benefits of ultrasound.
Goff et al. (2013)	
▪ Agreement between reference diagnosis and lung ultrasound was higher than reference diagnosis and standard clinical assessment for all three categories of diagnosis (acute decompensated heart failure, respiratory disorders and combined dyspnoea) ▪ Lung ultrasound changed the main clinical diagnosis in 44 per cent of cases. This was associated with a change in patient management for 58 per cent of patients: – a new drug was prescribed for 19 cases – medication was withheld in 10 cases – 6 cases had a change in testing, and – 5 had a change in disposition plan.	▪ The study captured how a more accurate diagnosis has direct impacts for patient management (particularly in areas of medicine prescribing, test ordering and disposition planning). This is likely to be generalisable to other Emergency Department settings. ▪ Study question was well-defined. ▪ Change in patient management due to improved diagnostics (prescribing of new medicine, holding of medicine that would have otherwise been prescribed, new procedure initiation) was measured accurately. ▪ No sensitivity analysis was presented.

Source: CIE.

C Statistical analysis

Assessment of whether hospital admission and ED costs differed between the intervention and comparator

There was no statistical evidence that hospital admission and ED costs differed between the intervention and the comparator.

C.1 Comparing admission costs

	Sample size	Average cost in the comparator group	Average cost in the intervention group	p value
	n	$	$	Prob=|z|
Patients who were discharged home	331	6 854	7 146	0.4007
Patients who were transferred to another facility	49	4 019	8 787	0.2935 [a]
Patients who died	11	12 235	5 796	0.3074 [a]
All patients	**391**	**7 703**	**7 243**	**0.2688**

[a] small size limits the power of this test

Note: using the Wilcoxon's Rank Sum Test (Mann-Whitney U Test)

Source: CIE.

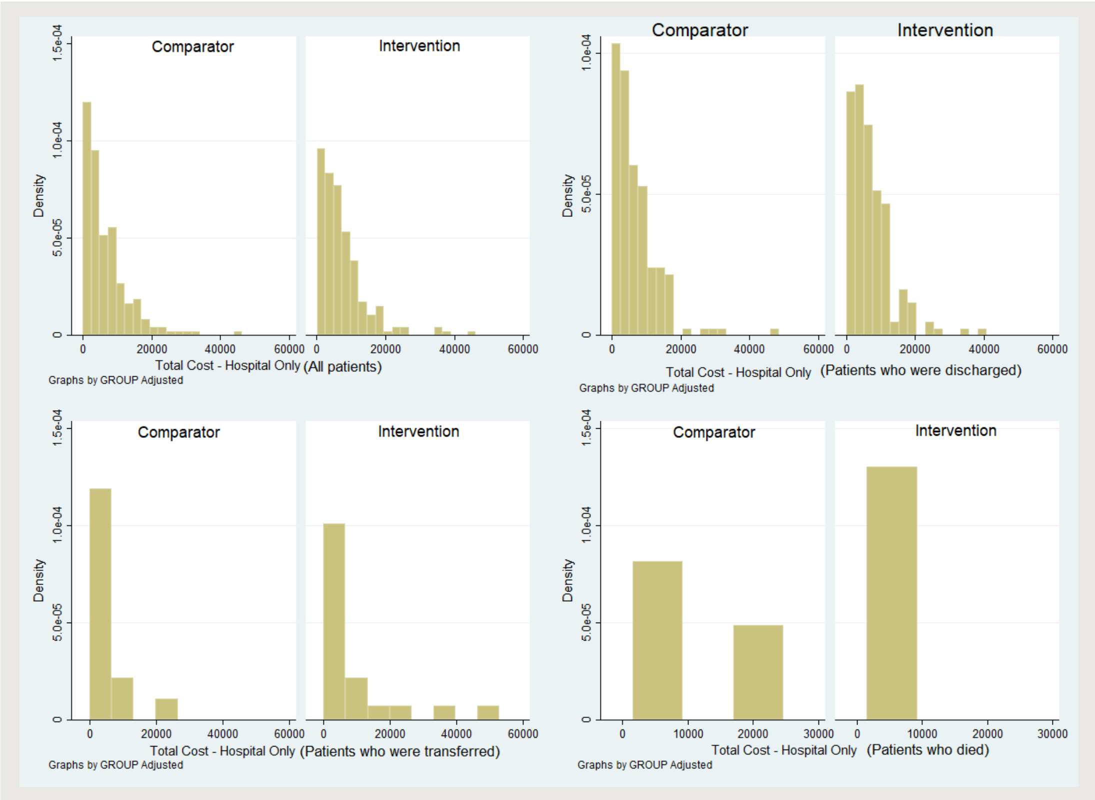
C.2 Comparing ED costs

	Sample size	Average cost in the comparator group	Average cost in the intervention group	p value
	n	$	$	
Patients who were discharged home	367	925	925	0.5027 [a]
Patients who were transferred to another facility	51	868	892	0.9316 [b]
Patients who died	11	1 125	1 164	0.8379 [b]
All patients	**429**	**976**	**994**	**0.5074** [a]

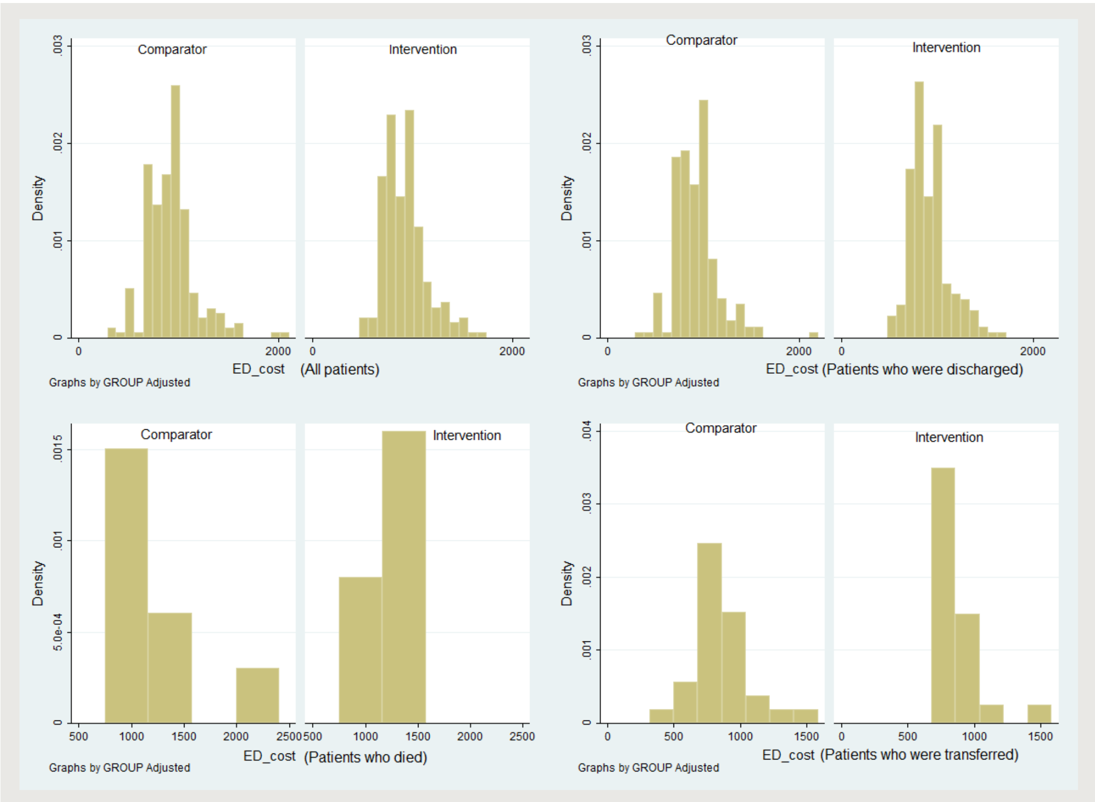
[a] independent t test T > t [b] Wilcoxon's Rank Sum Test (Mann-Whitney U Test) Prob=|z|

Source: CIE.

C.3 Distribution of admission costs



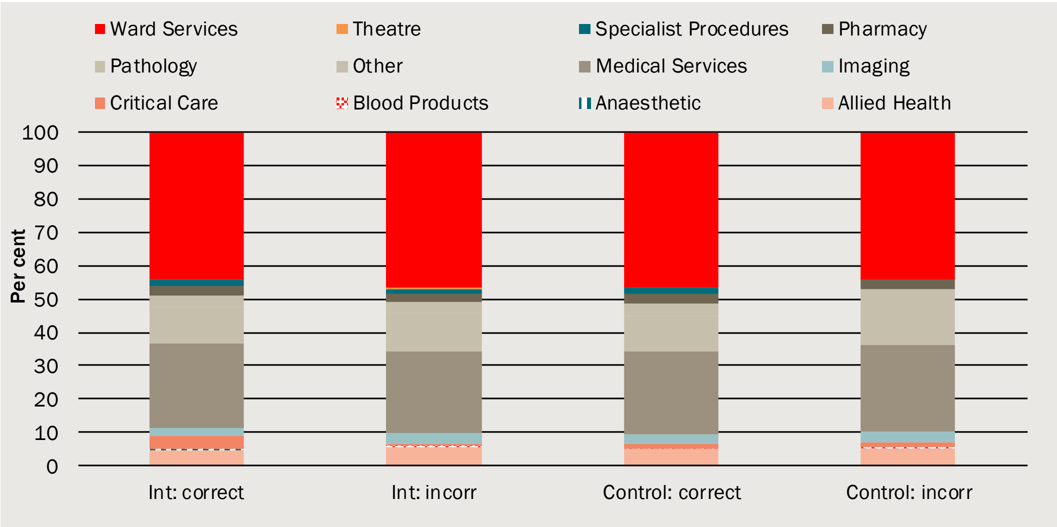
C.4 Distribution of ED costs



Data source: CIE.

D Cost breakdown

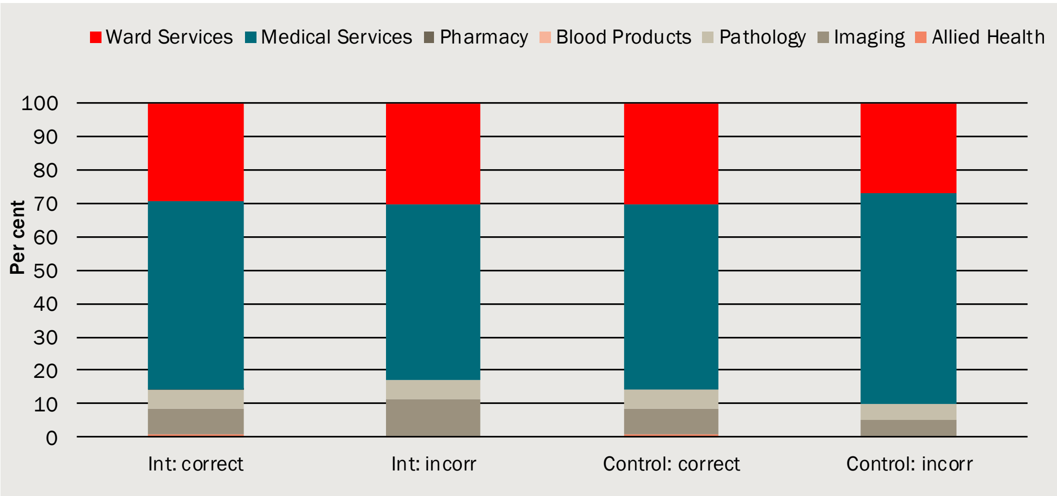
D.1 Average hospital costs: by group, by correct/incorrect diagnosis



Note: Int= intervention; incorr=incorrect diagnosis

Data source: CIE.

D.2 Average ED costs: by group, by correct/incorrect diagnosis



Note: Int= intervention; incorr=incorrect diagnosis

Data source: CIE.

D.3 Break down of Hospital only average costs ($)

Group	Diagnosis	Hospital	Allied Health	CSSDtot	Anaesthetic	Blood Products	Critical Care	Imaging	Medical Services	Other	Pathology	Pharmacy	Specialist Procedures	Theatre	Ward Services	Total Cost
			$	$	$	$	$	$	$	$	$	$	$	$	$	$
Detailed breakdown																
Control	Correct diagnosis	Ipswich	276	0	0	0	0	136	1 267	782	248	103	0	0	2 587	**5 399**
Control	Incorrect diagnosis	Ipswich	389	0	18	14	174	349	2 125	1 147	416	249	0	0	3 646	**8 528**
Control	Correct diagnosis	PAH	324	0	4	8	82	198	1 766	532	208	149	5	0	2 853	**6 129**
Control	Incorrect diagnosis	PAH	398	0	0	0	0	42	1 731	541	75	114	0	0	2 735	**5 636**
Control	Correct diagnosis	TPCH	300	0	0	0	273	150	1 481	407	186	327	483	6	2 935	**6 549**
Control	Incorrect diagnosis	TPCH	278	0	0	27	0	35	1 169	389	14	257	37	0	2 001	**4 207**
Intervention	Correct diagnosis	Ipswich	243	2	9	3	153	208	1 393	839	262	120	9	4	2 563	**5 808**
Intervention	Incorrect diagnosis	Ipswich	498	0	0	0	0	465	1 551	981	337	109	0	0	3 195	**7 136**
Intervention	Correct diagnosis	PAH	340	0	17	3	0	61	1 763	640	201	130	0	43	3 004	**6 202**
Intervention	Incorrect diagnosis	PAH	651	0	0	0	0	335	2 843	1 294	325	235	0	0	5 600	**11 283**
Intervention	Correct diagnosis	TPCH	330	0	0	4	789	134	1 676	422	219	286	482	3	2 793	**7 138**
Intervention	Incorrect diagnosis	TPCH	181	0	0	60	313	64	1 723	544	334	442	972	89	2 587	**7 310**

Group	Diagnosis	Hospital	Allied Health	CSSDtot	Anaesthetic	Blood Products	Critical Care	Imaging	Medical Services	Other	Pathology	Pharmacy	Specialist Procedures	Theatre	Ward Services	Total Cost
			$	$	$	$	$	$	$	$	$	$	$	$	$	$
By group and hospital only																
Control	All	Ipswich	301	0	4	3	38	183	1 455	862	285	135	0	0	2 819	**6 084**
Control	All	PAH	331	0	4	7	74	183	1 763	533	196	146	4	0	2 842	**6 084**
Control	All	TPCH	297	0	0	3	237	135	1 440	404	164	318	425	5	2 813	**6 243**
Intervention	All	Ipswich	262	2	8	2	135	233	1 455	858	271	117	8	4	2 650	**6 005**
Intervention	All	PAH	393	0	14	3	0	108	1 948	752	222	148	0	36	3 450	**7 075**
Intervention	All	TPCH	321	0	0	8	759	130	1 679	429	226	295	513	8	2 780	**7 149**
By group and diagnostic accuracy only																
Intervention	Correct diagnosis	All	291	1	9	3	263	149	1 566	682	234	163	120	15	2 743	**6 240**
Intervention	Incorrect diagnosis	All	531	0	0	8	43	345	2 220	1 078	331	218	133	12	4 315	**9 233**
Control	Correct diagnosis	All	297	0	1	3	87	159	1 478	617	221	168	108	1	2 751	**5 892**
Control	Incorrect diagnosis	All	372	0	12	14	114	243	1 894	913	289	227	6	0	3 208	**7 292**
By group only																
Intervention	All	All	315	1	8	4	235	172	1 654	730	246	166	119	14	2 920	**6 584**
Control	All	All	309	0	3	4	91	173	1 545	665	232	177	91	1	2 825	**6 118**

Source: CIE.

D.4 Break down of Hospital only average costs (Per cent)

Group	Diagnosis	Hospital	Allied Health	CSSDtot	Anaesthetic	Blood Products	Critical Care	Imaging	Medical Services	Other	Pathology	Pharmacy	Specialist Procedures	Theatre	Ward Services	Total Cost
			Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent
Detailed breakdown																
Control	Correct diagnosis	Ipswich	5	0	0	0	0	3	23	14	5	2	0	0	48	**100**
Control	Incorrect diagnosis	Ipswich	5	0	0	0	2	4	25	13	5	3	0	0	43	**100**
Control	Correct diagnosis	PAH	5	0	0	0	1	3	29	9	3	2	0	0	47	**100**
Control	Incorrect diagnosis	PAH	7	0	0	0	0	1	31	10	1	2	0	0	49	**100**
Control	Correct diagnosis	TPCH	5	0	0	0	4	2	23	6	3	5	7	0	45	**100**
Control	Incorrect diagnosis	TPCH	7	0	0	1	0	1	28	9	0	6	1	0	48	**100**
Intervention	Correct diagnosis	Ipswich	4	0	0	0	3	4	24	14	5	2	0	0	44	**100**
Intervention	Incorrect diagnosis	Ipswich	7	0	0	0	0	7	22	14	5	2	0	0	45	**100**
Intervention	Correct diagnosis	PAH	5	0	0	0	0	1	28	10	3	2	0	1	48	**100**
Intervention	Incorrect diagnosis	PAH	6	0	0	0	0	3	25	11	3	2	0	0	50	**100**
Intervention	Correct diagnosis	TPCH	5	0	0	0	11	2	23	6	3	4	7	0	39	**100**
Intervention	Incorrect diagnosis	TPCH	2	0	0	1	4	1	24	7	5	6	13	1	35	**100**

Group	Diagnosis	Hospital	Allied Health	CSSDtot	Anaesthetic	Blood Products	Critical Care	Imaging	Medical Services	Other	Pathology	Pharmacy	Specialist Procedures	Theatre	Ward Services	Total Cost
			Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent
By group and hospital only																
Control	All	Ipswich	5	0	0	0	1	3	24	14	5	2	0	0	46	**100**
Control	All	PAH	5	0	0	0	1	3	29	9	3	2	0	0	47	**100**
Control	All	TPCH	5	0	0	0	4	2	23	6	3	5	7	0	45	**100**
Intervention	All	Ipswich	4	0	0	0	2	4	24	14	5	2	0	0	44	**100**
Intervention	All	PAH	6	0	0	0	0	2	28	11	3	2	0	1	49	**100**
Intervention	All	TPCH	4	0	0	0	11	2	23	6	3	4	7	0	39	**100**
By group and diagnostic accuracy only																
Intervention	Correct diagnosis	All	5	0	0	0	4	2	25	11	4	3	2	0	44	**100**
Intervention	Incorrect diagnosis	All	6	0	0	0	0	4	24	12	4	2	1	0	47	**100**
Control	Correct diagnosis	All	5	0	0	0	1	3	25	10	4	3	2	0	47	**100**
Control	Incorrect diagnosis	All	5	0	0	0	2	3	26	13	4	3	0	0	44	**100**
By group only																
Intervention	All	All	5	0	0	0	4	3	25	11	4	3	2	0	44	**100**
Control	All	All	5	0	0	0	1	3	25	11	4	3	1	0	46	**100**

Source: CIE

D.5 Break down of average ED only costs ($)

Group	Diagnosis	Hospital	Allied Health	Imaging	Pathology	Blood Products	Pharmacy	Medical Services	Ward Services	Total Cost
			$	$	$	$	$	$	$	$
Detailed breakdown										
Control	Correct diagnosis	Ipswich	1	8	14	0	0	568	172	**763**
Control	Incorrect diagnosis	Ipswich	0	4	14	0	0	581	173	**772**
Control	Correct diagnosis	PAH	12	127	65	3	0	509	429	**1 144**
Control	Incorrect diagnosis	PAH	0	114	40	0	0	430	349	**932**
Control	Correct diagnosis	TPCH	18	115	113	0	0	445	298	**989**
Control	Incorrect diagnosis	TPCH	14	108	145	0	0	488	331	**1 086**
Intervention	Correct diagnosis	Ipswich	1	14	20	0	0	595	178	**807**
Intervention	Incorrect diagnosis	Ipswich	0	7	12	0	0	577	160	**756**
Intervention	Correct diagnosis	PAH	8	118	60	3	1	470	396	**1 056**
Intervention	Incorrect diagnosis	PAH	0	114	75	0	0	469	388	**1 046**
Intervention	Correct diagnosis	TPCH	13	127	110	2	0	446	303	**1 001**
Intervention	Incorrect diagnosis	TPCH	8	341	125	0	0	444	301	**1 217**
By group and hospital only										
Control	All	Ipswich	1	7	14	0	0	571	173	**765**
Control	All	PAH	11	126	62	3	0	502	422	**1 125**
Control	All	TPCH	18	114	117	0	0	450	302	**1 002**
Intervention	All	Ipswich	1	13	18	0	0	594	176	**802**
Intervention	All	PAH	7	118	62	2	1	469	395	**1 054**
Intervention	All	TPCH	13	140	111	2	0	446	302	**1 014**

Group	Diagnosis	Hospital	Allied Health	Imaging	Pathology	Blood Products	Pharmacy	Medical Services	Ward Services	Total Cost
			$	$	$	$	$	$	$	$
By group and diagnostic accuracy only										
Intervention	Correct diagnosis	All hospitals	6	70	53	1	0	524	269	**923**
Intervention	Incorrect diagnosis	All hospitals	1	106	59	0	0	505	293	**964**
Control	Correct diagnosis	All hospitals	8	71	52	1	0	521	285	**938**
Control	Incorrect diagnosis	All hospitals	2	41	41	0	0	539	230	**853**
By group only										
Intervention	All	All hospitals	5	73	52	1	0	523	270	**925**
Control	All	All hospitals	7	66	50	1	0	524	276	**925**

Source: CIE

D.6 Break down of average ED only costs (Per cent)

Group	Diagnosis	Hospital	Allied Health	Imaging	Pathology	Blood Products	Pharmacy	Medical Services	Ward Services	Total Cost
			Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent
Detailed breakdown										
Control	Correct diagnosis	Ipswich	0	1	2	0	0	74	23	**100**
Control	Incorrect diagnosis	Ipswich	0	1	2	0	0	75	22	**100**
Control	Correct diagnosis	PAH	1	11	6	0	0	44	38	**100**
Control	Incorrect diagnosis	PAH	0	12	4	0	0	46	37	**100**
Control	Correct diagnosis	TPCH	2	12	11	0	0	45	30	**100**
Control	Incorrect diagnosis	TPCH	1	10	13	0	0	45	30	**100**
Intervention	Correct diagnosis	Ipswich	0	2	2	0	0	74	22	**100**

Group	Diagnosis	Hospital	Allied Health	Imaging	Pathology	Blood Products	Pharmacy	Medical Services	Ward Services	Total Cost
			Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent
Intervention	Incorrect diagnosis	Ipswich	0	1	2	0	0	76	21	**100**
Intervention	Correct diagnosis	PAH	1	11	6	0	0	44	38	**100**
Intervention	Incorrect diagnosis	PAH	0	11	7	0	0	45	37	**100**
Intervention	Correct diagnosis	TPCH	1	13	11	0	0	45	30	**100**
Intervention	Incorrect diagnosis	TPCH	1	28	10	0	0	36	25	**100**
By group and hospital only										
Control	All	Ipswich	0	1	2	0	0	75	23	**100**
Control	All	PAH	1	11	6	0	0	45	37	**100**
Control	All	TPCH	2	11	12	0	0	45	30	**100**
Intervention	All	Ipswich	0	2	2	0	0	74	22	**100**
Intervention	All	PAH	1	11	6	0	0	45	37	**100**
Intervention	All	TPCH	1	14	11	0	0	44	30	**100**
By group and diagnostic accuracy only										
Intervention	Correct diagnosis	All hospitals	1	8	6	0	0	57	29	**100**
Intervention	Incorrect diagnosis	All hospitals	0	11	6	0	0	52	30	**100**
Control	Correct diagnosis	All hospitals	1	8	6	0	0	56	30	**100**
Control	Incorrect diagnosis	All hospitals	0	5	5	0	0	63	27	**100**
By group only										
Intervention	All	All hospitals	1	8	6	0	0	57	29	**100**
Control	All	All hospitals	1	7	5	0	0	57	30	**100**

Source: CIE

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