NICE advice

i STAT CG4+ and CHEM8+ cartridges for point-of-care testing in the emergency department

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Summary

The i-STAT is a handheld analyser used with a range of single-use cartridges for testing blood at the point of care, such as in the emergency department. This briefing focuses on 2 of these cartridges. The CG4+ cartridge detects lactate and several blood gases, whereas the CHEM8+ cartridge detects a number of blood electrolytes, haematocrit, haemoglobin and total CO_2. Five studies used the CG4+ cartridge; of these only 1 assessed diagnostic test accuracy. Two studies used the CHEM8+ cartridge to assess renal function; 1 of the 2 studies also used the CG4+ cartridge to analyse blood gases. In the latter 2 studies, there was a statistically significant reduction in the median time for patients to be declared ready to leave the emergency department after the tests had been introduced as one component of a redesigned emergency department service. The i-STAT analyser costs £5191. CG4+ cartridges cost £12.49 per test and CHEM8+ cartridges cost £19.54 per test (excluding VAT).

Product summary and likely place in therapy	Accuracy and effectiveness
• The i-STAT is an in vitro whole-blood analyser that uses single-use cartridges for critical care tests at the point of care, such as blood gases, electrolytes, metabolites and coagulation. • The CG4+ and CHEM8+ cartridges could be used as a component of the patient pathway in the emergency department, as an alternative to laboratory-based or other point-of-care tests, where the speed of access to test results is a limiting factor in improving patient throughput.	• Seven studies using i-STAT with findings relevant to the emergency department setting are included in this briefing. Five used the CG4+ cartridge, 1 used the CHEM8+ cartridge and the other used both CG4+ and CHEM8+ cartridges. • A prospective cohort study in 1 US emergency department assessed the diagnostic test accuracy of lactate in serum measured using the CG4+ cartridge for predicting mortality in 669 patients with suspected sepsis. Analysis showed that the lactate measurement using the i-STAT was accurate for clinical decision-making compared with the laboratory test. • One prospective cohort study in a US medicine and pathology laboratory assessed the correlation between 5 different systems used for lactate analysis, including the i-STAT CG4+ cartridge. The Vitros system was used as a reference standard. Of the 90 samples tested, the i-STAT lactate values of 85 samples (94%) fell within the same risk category as the Vitros value.

	• Two studies evaluated the i-STAT CG4+ cartridge in non-emergency department settings. A before-and-after study found that post-operative mortality rates in young children and babies changed from 6.2% before i-STAT CG4+ lactate testing was introduced to 2.4% after. Test turnaround time was 2 minutes using the i-STAT CG4+. A prospective cohort study in 446 intubated intensive care adult patients found that partial pressure of oxygen and carbon dioxide as measured by the CG4+ cartridge could be considered acceptable surrogates to laboratory measurements.

	• One before-and-after study in a US emergency department compared bedside lactate testing using i-STAT CG4+ with laboratory testing in patients with suspected sepsis. Eighty patients in the i-STAT CG4+ group were compared with 80 patients in the laboratory group. There was a statistically significant reduction in time to intravenous fluid administration in the i-STAT group compared with the laboratory group. No statistically significant difference was found in time to intravenous antibiotics between the 2 groups.

	• In the only UK-based reports, 2 before-and-after studies assessed the impact of a redesigned emergency department service, including the addition of point-of-care testing using the i-STAT, on the amount of time patients spent in the department. Both found a statistically significant reduction in the median time for patients to be declared ready to leave when the i-STAT CHEM8+ and CG4+ cartridges were used. In the context of the overall service redesign, the contribution of the point-of-care testing to the reduced turnaround time cannot be evaluated separately. Both studies were supported by the manufacturer.

Technical and patient factors	Cost and resource use
• i-STAT is a handheld battery-operated, reusable analyser. Samples are processed automatically and results are provided in 2 minutes. • The CG4+ cartridge measures lactate, pH, bicarbonate, base excess, oxygen saturation, the partial pressures of oxygen and carbon dioxide and total carbon dioxide. • The CHEM8+ cartridge measures sodium, potassium, chloride, total carbon dioxide, anion gap, ionised calcium, glucose, urea nitrogen, creatinine, lactate, haematocrit and haemoglobin. • The i-STAT cartridges are single-use and each cartridge requires 2 to 3 drops of blood.	• The CG4+ cartridge costs £12.49 per test, excluding VAT. • The CHEM8+ cartridge costs £19.54 per test, excluding VAT. • The i-STAT analyser costs £5191, excluding VAT.

Introduction

From April 2014 to March 2015 there were almost 14.6 million recorded attendances at major emergency departments (EDs) in England (NHS England 2015). The indicators used to assess ED performance include ambulance offload times, the numbers of patients on trolleys in relation to designated assessment spaces, and if more than 10% of patients have waited more than 2 hours for admission (College of Emergency Medicine 2011).

From October to December 2014, the number of patients seen within 4 hours of attending an NHS ED was 92.6%, below the target of 95% (NHS England 2015). This, together with Accident and Emergency Quality Indicators data (Health and Social Care Information Commission 2015), suggests that crowding presents increasing difficulties for NHS EDs.

Crowding occurs in EDs from time to time and is associated with increased mortality, reduced quality of care, increased length of stay for non-elective admissions and staff burnout. An ED is considered to be crowded if ambulances cannot offload patients, there are long delays for patients to be seen by a doctor, there are more patients on trolleys than

there are cubicle spaces, or if patients are waiting for more than 2 hours for an inpatient bed after a decision has been made to admit them to hospital (College of Emergency Medicine 2014). NHS targets state that 95% of patients should wait no longer than 4 hours in an ED (measured quarterly), and no ED patients should wait more than 12 hours on a trolley.

Crowding can be related to input factors (how many patients attend the ED), throughput factors (how patients flow through the ED) and output factors (how patients leave the ED; College of Emergency Medicine 2014). Interventions to improve patient throughput include those aimed at streaming or fast-tracking patients, such as team triage, nurse requested X-rays and point-of-care testing. A systematic review concluded that there was moderate quality evidence that fast-tracking patients with less severe symptoms leads to shorter waiting times and length of stay in the ED, and fewer patients leaving the ED without being seen by a doctor, but evidence on other interventions was limited (Oredsson et al. 2011). Point-of-care testing was seen to improve turnaround time but there was limited evidence to show any effect on length of ED stay. Point-of-care tests with rapid turnaround of results have the potential to lead to faster clinical decision-making and increased patient throughput in the ED. They could have a role in managing crowding in the ED and improving the quality of ED care (Rooney and Schilling 2014).

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

CE marking

The CG4+ and CHEM8+ cartridges (Abbott) are classified as IVD General in vitro diagnostic medical devices (98/79/EC). The CG4+ cartridge was CE marked in October 2003 and the CHEM8+ cartridge in December 2006.

Description

The i-STAT is a handheld, in vitro analyser designed to be used at the patient's bedside (point-of-care) for testing arterial, venous or capillary whole blood. It takes single-use cartridges containing chemically sensitive biosensors on a silicon chip that are configured for test-specific indicators. i-STAT test cartridges are available for a broad range of diagnostic and treatment indicators including blood gases, electrolytes, metabolites and coagulation markers. Blood samples do not need to be processed before testing and results are available in around 2 minutes.

The i-STAT system has the following components, accessories and consumables:

- i-STAT analyser – a handheld, battery-operated and fully automated analysis platform, consisting of a LCD screen and keypad. Two versions of the i-STAT analyser are available: a wireless internet version (the i-STAT Wireless, which can upload the results wirelessly) and a non-wireless version (with which test results can be uploaded when the analyser is placed in the i-STAT downloader/recharger).
- i-STAT cartridges – single-use, disposable cartridges for whole-blood testing. They are inserted into the analyser after the blood sample has been applied. A large number of cartridges are available to test the most common test-specific indicators in different combinations. Cartridges include tests for blood gases, electrolytes, metabolites and coagulation.
- i-STAT downloader/recharger – acts as a cradle for the analyser, automatically uploading data (with the non-wireless analyser) and recharging its batteries.
- Electronic simulator – for checking the performance of the i-STAT analyser.
- TriControls – a set of control solutions at 3 clinically relevant concentrations of test-specific indicators for verifying each cartridge type.
- i-STAT data manager – data management software for cartridges, where test records can be transmitted to and then be printed or transmitted to the laboratory/hospital information system.
- i-STAT printer – an optional portable printer which enables the operator to print results at the point of care.

This briefing report focuses on 2 i-STAT cartridges, the CG4+ and CHEM8+, which are most relevant to the NHS ED setting.

The CG4+ cartridge provides the following chemistry test and blood gas measures:

- lactate
- pH
- the partial pressure of carbon dioxide (PCO_2)
- the partial pressure of oxygen (PO_2)
- total carbon dioxide (TCO_2; calculated)
- bicarbonate (HCO_3; calculated)
- base excess (calculated)
- oxygen saturation (sO_2; calculated).

The CHEM8+ cartridge provides the following electrolyte and haematology tests:

- sodium
- potassium
- chloride
- urea nitrogen/urea
- glucose
- creatinine
- ionised calcium
- total carbon dioxide (TCO_2)
- anion gap (calculated)
- haematocrit
- haemoglobin (calculated).

Detailed information on the cartridges and tests is available on the manufacturer's website, including their intended use, methods and performance data on the tests.

To use a test cartridge, the operator and patient information is entered into the i-STAT analyser using the keypad. Two or 3 drops of blood (between 65 and 95 microlitres) are applied to the cartridge using a syringe before the cartridge is inserted into the i-STAT analyser. The test starts automatically once the cartridge is inserted in the analyser. All the tests are run simultaneously and results are available in around 2 minutes for both the CG4+ and CHEM8+ cartridges. Before running a test, each cartridge initiates a series of pre-set quality control diagnostics, from monitoring the quality of the sample to validating the reagent. Test results are displayed on the LCD screen of the analyser and can be uploaded automatically, either wirelessly with the i-STAT Wireless or when the analyser is placed in the i-STAT downloader/recharger. The data can be transmitted from multiple analysers in many patient care areas to the i-STAT Data Manager, a dedicated desktop computer with the i-STAT central data application installed. The data can be printed, stored, organised, edited and transferred to a laboratory information system or other computer system such as a hospital information system to aid patient record keeping.

The manufacturer's instruction suggests that an electronic quality control check of the performance of each i-STAT analyser should be done once on each day of use, or as needed. This is carried out with an electronic simulator (either internal or external), which tests the analyser's cartridge signal-reading function. When the specified time has passed since the last electronic simulator test the internal test will automatically be performed when a cartridge is inserted and before the sample is tested. This adds about 20 seconds to the testing cycle. The external electronic simulator is a device in a cartridge form. It is inserted into the cartridge port to perform the check. Using the external electronic simulator adds about 60 seconds to the test cycle. The electronic simulator check simulates 2 levels of electrical signals that stress the analyser's cartridge signal detection function both below and above measurement ranges. This provides an independent check of the analyser's ability to take accurate and sensitive measurements of voltage, current and resistance from the cartridge. An analyser will pass or fail this electronic test depending on whether or not it measures these signals within limits specified in the analyser software.

The integrity of i-STAT cartridges can be verified using 2 of the 3 TriControls, which are control fluids formulated at 3 clinically relevant levels with known concentrations of the test-specific indicators. Cartridges can be verified on 1 representative cartridge from each new batch of cartridges and by comparing the results to the expected values published by the manufacturer in the value assignment sheets. To verify the CG4+ and CHEM8+ cartridges, level 1 (low concentration) and level 3 (high concentration) controls are used.

Both versions of the i-STAT analyser have the following specifications:

- dimensions of 209h x 64w x 52d mm and weight of 520 g
- LCD display
- keypad with a set of buttons for operating the i-STAT analyser, including keys to enter information into the analyser and access the analyser's menu
- battery-operated using two 9 volt lithium batteries
- communication link: infrared transmitter and receiver.

Both versions also have the same operator features:

- Operator and patient information can be entered via a barcode scanner.
- Screen prompts provide the user with step-by-step instructions during the entire testing process, displaying data in large type for easy reading.
- An operator ID code to lock and unlock the i-STAT analyser. This operator lockout helps prevent unauthorised users from performing or viewing test results.

Setting and intended use

The i-STAT analyser and cartridges can be used for multiple indications in multiple settings. The focus of this briefing is the intended use of the CG4+ and CHEM8+ cartridges in the ED setting to aid the diagnosis or exclusion of numerous potentially serious diseases and clinical conditions. The CG4+ cartridge is used for the measurement of blood gases and lactate that are indicative of the following conditions:

- respiratory disturbances and metabolic and respiratory-based acid-base disturbances (blood gases)
- hypoxia, shock, heart attack, severe congestive heart failure, renal failure, uncontrolled diabetes, or sepsis (lactate).

The CHEM8+ cartridge is used for tests of blood chemistry, haematology, ionised calcium and total CO_2 to help diagnose:

- conditions that manifest electrolyte and acid-base disorders (blood chemistry and TCO_2)
- anaemia, erythrocytosis, and blood loss related to trauma and surgery (haematocrit and haemoglobin)
- parathyroid disease, various bone diseases, chronic renal disease, tetany, and disturbances related to surgical and intensive care (ionised calcium).

The manufacturer stated that the analysers and cartridges should be used by healthcare professionals trained and certified to use the system. Each end-user should attend an end-user training class in order to receive certification for the i-STAT system. The class includes hands-on demonstration and a competency assessment.

Current NHS options

In the majority of NHS EDs, standard blood tests (such as those available with the CHEM8+ cartridge) are obtained from accredited hospital laboratories, usually on site. Blood gases and lactate measurements are also analysed in hospital laboratories, although a specialist commentator stated that most EDs now have standalone analysers to measure lactate when testing for sepsis. Standalone blood gas analysers are also used in intensive care units where blood gases are measured frequently.

NICE is aware of other CE-marked point-of-care test devices that appear to fulfil a similar function to the i-STAT CG4+ and CHEM8+ cartridges on an individual test basis. These include handheld devices but also desktop analysers which can be used to provide point-of-care tests in the ED. Examples of these devices include:

- Radiometer ABL800 FLEX analyser (Radiometer) – desktop blood gas analyser.
- HemoCue 201+ meters (HemoCue) – portable systems that are used to measure haemoglobin.
- FreeStyle Optium (Abbott) – portable blood glucose monitoring system.
- FreeStyle Mini (Abbott) – portable blood glucose monitoring system.
- epoc Blood Analysis System (Epocal) – portable blood gas and electrolyte testing.
- RAPIDLab 348EX Blood Gas System (Siemens Healthcare Diagnostics) – desktop blood gas analyser.

- RAPIDPoint 500 system (Siemens Healthcare Diagnostics) – desktop blood lactate assay.

Costs and use of the technology

The list price of the technology and consumables or maintenance required to use the products, excluding VAT, are as follows:

- i-STAT analyser: non-wireless £5191, i-STAT Wireless £6191.
- i-STAT downloader/recharger: £1100.
- CG4+ cartridge: £12.49 per cartridge (unit size: box of 25 cartridges).
- CHEM8+ cartridge: £19.54 per cartridge (unit size: box of 25 cartridges).
- electronic simulator: £243.73.
- TriControls: £20.31 (box of 10 glass ampules).
- i-STAT printer: £335.
- service after 1 year warranty: £1298 per analyser per year.

The unit size for both CG4+ and CHEM8+ cartridges is 25 cartridges. The TriControls are supplied in a box of 10 glass ampules at a single concentration level (level 1, 2 or 3). Each level of TriControls needs to be purchased separately. Each analyser must be verified using a single cartridge. The TriControls used for both the CG4+ CHEM8+ cartridges are not stable, so a separate ampule must be used for each analyser being tested, although up to 3 i-STAT analysers can be verified if tested simultaneously. Cartridges are verified by analysing level 1 and level 3 of the appropriate control on each new batch of cartridges and by comparing the results with the expected values published by the manufacturer. Verification of cartridges is not a manufacturer's system instruction but a suggestion to comply with quality assurance requirements.

The data management software is an optional component of the i-STAT. It can be purchased from a third-party vendor if an open system is needed to connect multiple devices. The software is typically installed in a server but could be installed on a computer with the correct specifications.

Likely place in therapy

The i-STAT analyser with the CG4+ and CHEM8+ cartridges could be used in emergency departments to reduce the time taken for results compared with the same tests done in the hospital laboratory.

Specialist commentator comments

One specialist commentator stated that because the i-STAT system is a compact and relatively simple machine to use, it can be a valuable addition to an ED if a blood gas analyser is not available, or if the time taken to get results from the laboratory regularly delays decision-making. It could also be of benefit in minor injury units without access to on-site laboratory services.

One commentator mentioned that almost all EDs have point-of-care blood gas machines already, so the benefits of these cartridges in reducing time to discharge are overstated. Another commentator stated that if on-site laboratory services are available and results are generally ready in a reasonable timescale, the i-STAT does not confer a huge advantage to the speed of decision-making or total length of ED stay.

Two specialist commentators stated that the CHEM8+ and CG4+ cartridges do not include some of the additional tests that are used to help decide if a patient can be sent home safely, such as d-dimer, troponin and white cell count, although cardiac troponin I is available on another i-STAT cartridge. Therefore, even with the i-STAT, other tests may be needed in some instances. One specialist commentator was of the opinion that the i-STAT analyser may also take up clinical time to carry out quality control checks and to test the sample, rather than leaving this to laboratory staff outside the ED.

Another specialist commentator stated that from a financial point of view, the cost per test when using the i-STAT is much higher than an on-site laboratory analysis.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. In producing guidance, NICE aims to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

Young children, older people and people with chronic conditions are more likely to need the services of an ED. These groups in particular will benefit from improvements in the quality of ED care. Using point-of-care tests could contribute to quality of care if outcomes such as time to a clinical decision improve. Age is a protected characteristic under the 2010 Equality Act.

Evidence review

Clinical and technical evidence

Regulatory bodies

A search of the Medicines and Healthcare Products Regulatory Agency website revealed that no manufacturer Field Safety Notices or Medical Device Alerts for this device. No reports of adverse events were identified from a search of the US Food and Drug Administration (FDA) database: Manufacturer and User Device Facility Experience (MAUDE).

Clinical evidence

A literature search for evidence identified 7 studies that used the i-STAT analyser with either the CG4+ or CHEM8+ cartridges for point-of-care tests. Of these studies, 5 used the CG4+ cartridge (Shapiro et al. 2010; Rossi and Khan 2004; Thomas et al. 2009; Karon et al. 2007; Singer et al. 2014), 1 used the CHEM8+ cartridge (Jarvis et al. 2015), and the other used both CG4+ and CHEM8+ cartridges (Jarvis et al. 2014). Another study (Shephard et al. 2012) also used the CHEM8+ cartridge, but was excluded because it did not report outcomes relevant to this briefing.

Four studies were identified where the papers do not report which tests were used but

where it is likely, based on information from the company and from specialist commentators, that either the i-STAT CHEM8+ or CG4+ cartridges were used. For completeness, a brief summary of each study is in table 15.

The Shapiro et al. (2010) study (tables 1 and 2) was a prospective cohort study in an urban tertiary care ED in the USA, carried out between May 2006 and March 2007. It aimed to study the feasibility and accuracy of the i-STAT using CG4+ cartridges for bedside serum lactate measurements, and to determine if other measurements (pH and base excess) are predictive of mortality. It was off-label use of the i-STAT CG4+ cartridge, because serum is not an approved sample type for the i-STAT CG4+ cartridge. A convenience sample of 699 adults attending the ED with suspected sepsis during the study period was included. Lactate measurements were taken using the CG4+ cartridge and a mandatory confirmatory lactate measurement was done by the hospital's clinical laboratory.

Of the 699 patients in the cohort, 34 (4.9%) died. The area under the curve in receiver operating curve (AUROC) analysis for mortality prediction was 0.72 for i-STAT lactate, 0.70 for laboratory lactate, 0.60 for pH measurement and 0.60 for base excess. A Bland–Altman plot showed that the lactate measurement using i-STAT was accurate for clinical decision-making compared with the laboratory test. The i-STAT lactate measurement was on average 0.32 mmol/l lower than laboratory lactate (standard deviation 0.45; 95% confidence interval [CI] -0.35 to 0.98) with the limits of agreement ranging from −1.1 to 0.50. The i-STAT lactate was highly correlated with the laboratory lactate with an r value of 0.97.

The study by Rossi and Khan (2004; tables 3 and 4) was a before-and-after study conducted in a cardiac intensive care unit in a paediatric hospital in the USA. It aimed to evaluate the combination of 2 strategies, goal-directed therapy and point-of-care blood lactate testing using the i-STAT CG4+ cartridge, in improving outcomes for young children (aged under 1 year) and babies (under 1 month) after congenital heart surgery. Group A (851 patients) had surgery before the i-STAT was implemented in the care unit and group B (378 patients) had surgery after implementation. Measurements included overall mortality at 30 days after surgery, blood lactate levels, cardiopulmonary bypass times and aortic cross-clamp times.

The study found that overall mortality was significantly lower for group B (2.4%) compared with group A (6.2%; p=<0.007). A significant reduction in mortality between group B and group A was observed in babies (4.3% compared with 12%, p=0.008), but the reduction did not reach significance in young children (0.9% compared with 2.6%, p value not

reported).

The turnaround time for lactate was 120 seconds using the i-STAT system and 15 minutes to 2 hours with the laboratory test.

The study by Karon et al. (2007; tables 5 and 6) was a cohort study conducted in the USA. It compared lactate values obtained from laboratory (plasma-based assays) and point-of-care (whole blood) platforms to determine whether clinically relevant discrepancies might occur between the values obtained from the 2 methods.

Whole-blood specimens were obtained from patients in the ED and intensive care unit (n=90), and were analysed using 3 different methods: the Radiometer ABL 715 blood gas analyser, the i-STAT (with CG4+ cartridge), and the Nova analyser. All tests were done within 1–2 minutes of each other and within 1 hour of the blood sample being taken. Within 5 minutes of whole-blood analysis, the blood specimens were centrifuged. The plasma was separated and kept on ice. Plasma lactate was analysed using the Integra Roche analyser and the Vitros analyser within 1 hour of plasma separation. It was unclear how the samples and patients were selected.

The authors found that correlation between lactate methods was good, with slopes of best fit of 0.87–1.06 and intercepts of 0.1–0.2 mmol/l lactate for all 4 methods compared with the Vitros.

At high lactate values (>6 mmol/l), the i-STAT system showed negative bias (relative to the Vitros), and reported lower lactate results compared with the Vitros and Integra.

Of the 90 samples tested, the i-STAT lactate values for 85 of the samples (94%) fell within the same risk category as the Vitros value.

The study by Thomas et al. (2009; tables 7 and 8) was a prospective cohort study conducted in a level 1 trauma centre in the USA. It evaluated the 'measure of treatment agreement' – the number of standard clinical laboratory arterial blood gas measurements that prompted changes in mechanical ventilator support therapy compared with the number of portable device measurements that would have prompted the same or different changes. The study included 446 intubated adult intensive care unit patients. Measurements taken with the i-STAT system (using the CG4+ cartridge for arterial O_2 saturation, PO_2, pH and PCO_2) and 2 other test devices (for peripheral capillary O_2 saturation and end-tidal CO_2) were compared with paired standard laboratory

measurements for arterial CO_2, PO_2, pH and PCO_2.

Testing for equivalence found that the i-STAT PO_2, i-STAT pH and i-STAT PCO_2 measurements were deemed 'equivalent' surrogates to paired laboratory analysis.

The measure of treatment agreement between the i-STAT and paired laboratory blood gas values was 73% for arterial O_2 saturation, 97% for PO_2, 88% for pH and 95% for PCO_2. Based on a minimum of 95% treatment agreement, only the i-STAT PO_2 and the i-STAT PCO_2 measurements were considered acceptable surrogates to those done in the laboratory.

The study by Singer et al (2014; tables 9 and 10) was also a before-and-after study done in an ED in the US. It assessed the effects of bedside point-of-care lactate measurement using the i-STAT CG4+ cartridge on the time to administration of intravenous fluids and antibiotics in adult ED patients with suspected sepsis. Bedside point-of-care lactate measurement in a convenience sample of 80 patients with suspected sepsis presenting in the ED was compared with laboratory lactate measurement in the first 80 consecutive patients with suspected sepsis presenting the ED 12 months before the introduction of the bedside lactate testing. Only patients who had an initial lactate level of ≥2 mmol/l were included in the study. Of these, patients whose initial lactate level was 4 mmol/l or greater were transferred to the critical care area for further evaluation and management. The primary outcome measure was time to intravenous fluid and time to intravenous antibiotics.

The study found that introducing the bedside point-of-care lactate testing had a statistically significant reduction in median (interquartile) time to intravenous fluid administration compared with the laboratory lactate testing (55 [34–83] minutes compared with 71 [42–110] minutes; p=0.03). No statistically significant difference in median (interquartile) time to intravenous antibiotics administration was observed between the two groups (89 [63–182] minutes in the point-of-care testing group compared with 97 [55–160] minutes in the laboratory testing group; p=0.59).

The study by Jarvis et al. (2014; tables 11 and 12) was a before-and-after study conducted in an ED in a district general hospital in the UK with approximately 65,000 ED attendances a year. The study assessed the introduction of a rapid consultant-led assessment model supported by point-of-care testing (phase 2, between 30 September and 18 October 2013, n=787) and how it affected the time patients spent in the ED, when compared with nurse-led triage (phase 1, between 1 April and 24 May 2013, n=3835). The rapid

assessment used point-of-care testing for the analysis of renal function (using the i-STAT CHEM8+ cartridge), blood gases (using the i-STAT CG4+ cartridge) and full blood counts (using another assay).

The study found that there was a significant reduction of 53 minutes (or 41.1%) in the median time for patients to be declared ready to leave the ED in phase 2 compared with phase 1 (p=0.0025).

The authors conducted another very similar study, Jarvis et al. (2015; tables 13 and 14), which was a before and after study in a seemingly identical setting. It assessed the impact of introducing point-of-care testing for renal function on the length of time patients spend in the ED. It consisted of 2 consecutive phases: phase 1 (between 1 April and 24 May 2013, n=3835), during which renal function was tested using the hospital's centralised laboratory analyser (which seemed to be identical to the phase 1 in the Jarvis et al. [2014] study), and phase 2 (between 28 May 2013 and 29 September 2013, n=7033) during which renal function was tested using the i-STAT with the CHEM8+ cartridge.

The study found that there was a significant reduction of 20 minutes (or 15.5%) in the median time for patients to be declared ready to leave the ED in phase 2 compared with phase 1 (p=0.0025).

Recent and ongoing studies

One in-development trial of i-STAT for point-of-care testing was identified in the preparation of this briefing (Clinicaltrials.gov identifier: NCT02189096). The trial is not yet open to participants. The condition is sepsis and the interventions are the use of a standard single National Early Warning Score and sepsis screening, and point-of-care lactate measurement.

Costs and resource consequences

No published evidence on resource consequences was identified. Savings with point-of-care testing could be achieved by improving patient flow, ED throughput and clinical decision-making. In practice, point-of-care testing is often introduced as part of complex ED service redesign.

Two reports of what appears to be the same service improvement project (Jarvis et al. 2014 and Jarvis et al. 2015) report before-and-after results when a rapid consultant-led

assessment model supported by point-of-care testing with i-STAT was introduced in a UK district general hospital ED. The rapid assessment used point-of-care testing for the analyses of renal function (using the i-STAT CHEM8+ cartridge), blood gas (using the i-STAT CG4+ cartridge) and full blood counts (using another assay) with a median reduction of 53 minutes (or 41.1%) in the time for patients to be declared ready to leave the ED. Analysis of renal function using the i-STAT CHEM8+ cartridge resulted in a median reduction of 20 minutes for patients to be declared ready to leave the ED.

Strengths and limitations of the evidence

Seven relevant studies were identified: 5 used the i-STAT CG4+ cartridge, 1 used the CHEM8+ cartridges, and the other used both the i-STAT CG4+ and CHEM8+ cartridges.

All the studies were cohort studies, with 3 being prospective single arm and the other 4 using a before-and-after comparison model. Of the 3 single-arm cohort studies, 1 study used convenience sampling, which may not be representative of the study population (Shapiro et al. 2010). It was also unclear how the test samples and patients were selected in the Karon et al. (2007) study.

Of the 5 studies that used the CG4+ cartridge, 3 studies assessed the correlation between different test methods (Karon et al. 2007; Thomas et al. 2009; Singer et al. 2014). One study assessed mortality following the implementation of a patient management strategy based on lactate measurements using the i-STAT CG4+cartridge compared with the strategy implemented without the point-of-care test (Rossi and Khan 2004). Only 1 study evaluated the diagnostic test accuracy of the test, by measuring the AUROC analysis for mortality prediction against a laboratory test (Shapiro et al. 2010).

In the study by Singer et al. (2014), sample size was calculated for the 2 comparison groups. The investigators who determined ultimate diagnosis and severity of sepsis, source of infection, Sequential Organ Failure Assessment (SOFA) scores, Modified Early Warning Scores (MEWS) scores, length of stay, and in-hospital mortality were masked to study group and lactate levels. There were no statistically significant differences between the comparison groups in the majority of baseline demographic and clinical characteristics. However, the reported time from arrival to laboratory testing results and the time from order to laboratory testing results were significantly shorter in the i-STAT CG4+ group than in the laboratory group, so there may have been influences other than the testing on the general care and clinical process (for example, improved time to decide to take a test). The paper also reported a statistically significant lower mortality rate in the 'after' group

than in the 'before' group. However, like other before-and-after studies in the briefing, it is possible that any difference noted between the groups was because of other unmeasured confounding variables rather than introduction of the point-of-care testing. No studies on the diagnostic test accuracy or performance characteristics of the i-STAT CHEM8+ cartridge were identified.

Both the study that used CHEM8+ and CG4+ cartridges (Jarvis et al. 2014) and the study that used only CHEM8+ cartridges (Jarvis et al. 2015) evaluated the impact of introducing point-of-care testing on the length of time patients spent in ED. This also involved a redesign of the service. Although these studies had positive results, the use of the i-STAT for point-of-care testing was only 1 part of a complex service redesign and the impact of i-STAT alone cannot be evaluated. Both studies were single institution before-and-after studies which provide relatively weak elements.

In 4 studies (Shapiro et al. 2010; Rossi and Khan 2004; Karon et al. 2007; Singer et al. 2014), the CG4+ cartridge was used for testing blood lactate levels. Currently, there is no reference standard for lactate measurement. In the Karon et al. (2007) study, the Vitros assay was used as the reference method, which might not be a perfect reference standard to assess diagnostic test accuracy. However, the use of this reference standard was not problematic because the aim of the study was to assess the agreement and discrepancies between different test methods.

In the Rossi and Khan (2004) study, lactate values using the i-STAT CG4+ cartridge were included as part of the post-operative management strategy for the patients after congenital heart surgery. Post-operative mortality was the primary outcome measure. The duration of the study from start (phase 1, before i-STAT was introduced) to finish (phase 2, with i-STAT) was nearly a decade. It was unclear whether there might have been confounding factors contributing to the difference in the mortalities observed between the 2 phases, other than the introduction of the point-of-care lactate measurement.

Both Jarvis et al. studies (2014 and 2015) were conducted in a UK district general hospital, indicating that their results are likely to be generalisable to the NHS. The other 5 studies were conducted in the USA and may not be so reflective of NHS practice.

The Shapiro et al. (2010) and Singer et al. (2014) studies were funded by the manufacturer. For the Singer et al. (2014) study, the manufacturer was also consulted during the design of the study; furthermore, the first author of this study is on the speaker's bureau of the manufacturer. In the Jarvis et al. (2014) study, the manufacturer donated the i-STAT CG4+

and CHEM8+ cartridges used. One of the authors of this study also served as an expert speaker and received honoraria from the manufacturer, and the Jarvis et al. (2015) study was supported by a grant from the manufacturer.

With regards to the 4 studies/articles that were outlined for completeness, it is uncertain whether they contribute to the evidence base due to uncertainty about whether the point-of-care tests used are within the scope of the MIB. In studies where the i-STAT testing was used with other devices as part of service redesign package, the i-STAT's individual contribution to the overall service improvement is uncertain. Furthermore, with the exception of the randomised controlled trial, these articles reported only a limited amount of data. The briefing was restricted to exclude studies in which the cartridges were unspecified; selection bias could be introduced if only a number of selected studies were included from those studies in which the cartridges were unspecified.

Overall, current published evidence on the diagnostic accuracy of the i-STAT CG4+ and i-STAT CHEM8+ tests is sparse although the manufacturer provides some information on test performance for each individual test on its website. Each of the identified studies had diverse patient groups, settings, test-specific indicators tested, reference standards or comparison tests used, treatment strategies based on the test results, and outcome measures.

Relevance to NICE guidance programmes

The use of i-STAT is not currently planned into any NICE guidance programme.

NICE has issued the following relevant guidance which includes recommendations for physiological measurement (including oxygen saturation, biochemical analysis such as lactate, blood glucose, base deficit, arterial pH) for patients in adults in hospital with acute illness:

- Acutely ill patients in hospital: recognition of and response to acute illness in adults in hospital (2007) NICE guideline CG50.

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Search strategy and evidence selection

Search strategy

- Databases were searched including Ovid Embase (1974 to 2015 April 21), Ovid MEDLINE(R) (1946 to April Week 2 2015), and Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations (April 21, 2015). The keywords "i stat" and "i-STAT" were used for the searches.
- The internet was searched using the above keywords.

- ClinicalTrials.gov, WHO ICTRP, and Current Controlled Trials were searched for ongoing trials.
- Information provided by the manufacturer was thoroughly checked for relevant studies. Information provided by the manufacturer in supporting this briefing was checked to identify any further information.
- The manufacturer's website was thoroughly investigated.

Evidence selection

The inclusion criteria were as follows:

Patients: patients presenting at emergency departments.

Intervention: the CG4+ and CHEM8+ cartridges using the i-STAT analyser for blood test (manufactured by Abbott). Studies using other cartridges or unspecified cartridges were excluded.

Comparator:

- laboratory based blood sample analysis
- any other point-of-care blood analyser which can measure the same range of tests.

Outcomes: any relevant efficacy and safety clinical outcomes, including:

- diagnostic accuracy/test characteristics
- time to gain a test result
- resources required to gain a test result
- effect on the patient pathway.

Study design: published clinical studies including controlled and observational studies will be included. Systematic reviews and meta-analyses will be used for identifying relevant primary studies only. Proof of concept and non-English language studies will be excluded.

Appendix

Contents

Table 1 Overview of the Shapiro et al. (2010) study

Study component	Description
Objectives/ hypotheses	To study the feasibility and accuracy of a point-of-care analyser (i-STAT with CG4+ cartridge) capable of performing bedside serum lactate measurements to identify emergency department (ED) patients at risk of sepsis, and to determine whether other measurements (pH, base excess) are predictive of mortality. [a]
Study design	Prospective cohort study.
Setting	A tertiary care ED in an urban hospital in the USA. Recruitment dates from May 2006 to March 2007.
Inclusion/ exclusion criteria	A convenience sample of adult (age 18 years or older) ED patients with suspected infection during the study period of 1 May 2006 and 15 March 2007 who had a POC lactate measurement obtained with a mandatory confirmatory lactate measurement performed by the hospital's clinical laboratory. Exclusion criterion: absence of suspected infection.
Primary outcomes	In-hospital mortality. The AUCs for mortality prediction for parameters including: point-of-care lactate, laboratory lactate, pH value, and base excess.
Statistical methods	AUC for ROC curve; Bland–Altman statistics along with a correlation coefficient; relative risk with 95% confidence intervals.
Conclusions	A point-of-care testing device provides a reliable and feasible way to measure serum lactate at the bedside. The pH and base excess were less helpful.

Abbreviations: AUC, area under the curve; ED, emergency department; n, number of patients; POC, point of care; ROC, receiver operating characteristic.

[a] Serum is not an approved sample type for the i-STAT CG+ cartridge.

Table 2 Summary of results from the Shapiro et al. (2010)

Patients included	n=699 patients, mean age 60.4 years (95% CI 58.9 to 61.2), who were a prospective cohort of a convenience sample of adult (age 18 years or older) ED patients with suspected infection during the study period of 1 May 2006 and 15 March 2007 who had a point-of-care lactate measurement obtained (i STAT with CG4+ cartridge) with a mandatory confirmatory lactate measurement performed by the hospital's clinical laboratory.
Primary outcomes	A Bland–Altman plot showed that point-of-care lactate measurements were accurate for clinical decision-making compared with the laboratory lactate test. There was an average bias for point-of-care lactate of 0.32 (SD 0.45) mmol/l lower than laboratory lactate, with the limits of agreement ranging from -1.1 to 0.50 (the range over which 95% of the differences between the point-of-care and laboratory lactate will be contained). The point-of-care lactate was highly correlated with the laboratory lactate (r=0.9)7. A total of 699 patients were enrolled, 34 (4.9%) of whom died. The mean point-of-care lactate value was higher in those who died (3.2 mmol/l; 95% CI 2.05–4.37) than those who lived (1.65 mmol/l; 95% CI 1.56–1.74). Mean laboratory lactate levels also differed between those who died and survivors: 3.83 mmol/l (2.20–5.47) compared with 1.95 mmol/l (1.86–2.04), respectively, as did pH: 7.42 (7.42–7.43) compared with 7.37 (7.33–7.42), respectively. Base excess did not show a statistically significance difference: 1.71 (1.32–2.10) compared with 0.62 (-4.09–2.85), respectively. The AUCs for mortality prediction: point-of-care lactate 0.72, laboratory lactate 0.70, pH measurement 0.60, and base excess 0.60. Bland–Altman showed that mean lactate by the point-of-care test was 0.32 (95% CI-0.35–0.98) lower than that by laboratory test, with agreement Kappa=0.97.
Abbreviations: AUC, area under the curve; CI, confidence interval; ED, emergency department; n, number of patients; SD, standard deviation.	

Table 3 Overview of the Rossi and Khan (2004) study

Study component	Description
Objectives/ hypotheses	To evaluate the impact of the combination of two strategies, goal-directed therapy (GDT) and point-of-care blood lactate testing using the i-STAT CG4+ cartridge, on improving outcomes for babies (younger than 1 month) and young children (younger than 1 year) after congenital heart surgery.
Study design	Before-and-after study. Blood lactate measurements were performed serially for 24 hours after surgery. Post-operative management of patients was based on serial lactate determinations i.e., based on a lactate value, medical therapy was escalated, diminished or left unchanged. Outcome data were collected prospectively. Mortality at 30 days after surgery was compared for patients undergoing a GDT protocol and a group of historical cohorts. The operative risk for all operations was determined using the RACHS-1 scoring system.[a] The reference value for arterial blood lactate was 0.36–1.25 mmol/l for the i-STAT analyser.
Setting	A 16-bed cardiac ICU in a 268-bed free-standing paediatric hospital in the USA, between June 1995 and June 2003.
Inclusion/ exclusion criteria	Inclusion: all patients undergoing congenital heart surgery in the hospital from June 1995 through to July 2003. Exclusion criteria were not specified.
Primary outcomes	Overall mortality at 30 days after surgery; blood lactate level; cardiopulmonary bypass times and aortic cross-clamp times.
Statistical methods	Chi-square analysis was used to detected differences in mortality between groups. Mann–Whitney rank sum analysis was used to determine differences in demographic data between groups.

Patients included	Infants (under 1 year of age) and neonates (under 1 month of age) undergoing congenital heart surgery. Group A (June 1995–June 2001 before i-STAT was introduced): n=851; group B (July 2001–June 2003, after i-STAT was introduced): n=378. Patients in group B were smaller and younger than those in group A (median weight 3.8 kg compared with 4.3 kg, p<0.001; median age 42 days compared with 76 days, p=0.02).
Conclusions	The combination of goal-directed therapy and point-of-care testing significantly reduced mortality in patients after congenital heart surgery. This improvement was greatest in the youngest patients and those undergoing higher-risk surgery.
Abbreviations: GDT, goal-directed therapy; ICU, intensive care unit; n, number of patients; NS, not (statistically) significant. [a] RACHS-1, "Risk Adjustment for Congenital Heart Surgery" scoring system. RACHS-1 scoring was devised to categorise the risk for death associated with various congenital heart operations. RACHS-1 divides the surgeries into six categories, with category 1 being the simplest surgeries with the lowest mortality and category 6 being the surgeries with the highest mortality.	

Table 4 Summary of results from the Rossi and Khan (2004) study

	i-STAT	**Pre i-STAT**	**Analysis**
Total number of patients	n=378	n=851	
Primary outcome [a]			
• Overall mortality	2.4%	6.2%	p reported as " <0.007 "
• Overall mortality in neonates	n=164 4.3%	n=320 12%	p=0.008
• Overall mortality in infants	n=214 0.9%	n=531 2.6%	p=NS

• Overall mortality in patients undergoing high-risk operations (RACHS-1 groups 5 and 6) [b]	9%	30%	p=0.03
• Overall mortality in patients undergoing lower-risk operations (RACHS-1 groups 1 and 2) [b]	0.5%	1.5%	p=NS
The turn-around time for lactate	120 seconds	15 minutes to 2 hours	Not reported
Abbreviations: n, number of patients; NS, not (statistically) significant. [a] 95% confidence intervals not reported. [b] RACHS-1, "Risk Adjustment for Congenital Heart Surgery" scoring system. RACHS-1 scoring was devised to categorise the risk for death associated with various congenital heart operations. RACHS-1 divides the surgeries into six categories, with category 1 being the simplest surgeries with the lowest mortality and category 6 being the surgeries with the highest mortality.			

Table 5 Overview of the Karon et al. (2007) study

Study component	Description
Objectives/ hypotheses	To compare lactate values obtained from multiple central laboratory (plasma-based assays) and point-of-care (whole blood) platforms to determine whether clinically relevant discrepancies might occur if testing is performed on both plasma (central laboratory) and whole blood (point-of-care or blood gas analyser) platforms.

Study design	Prospective cohort study. Three whole blood lactate methods were compared with 2 plasma-based methods. The Vitros assay was used as the reference method. The 3 whole blood lactate methods: • **Radiometer:** Radiometer ABL 725 blood gas analyser; • **i-STAT:** using CG4+ cartridge • **Nova:** Lactate Plus. The 2 plasma-based methods: • **Integra:** Lactate Gen.2 performed on a Roche Cobas Integra 400 analyser • **Vitros:** Vitros LAC slide assay performed on a Vitros 250 analyser. Whole blood specimens obtained from patients in the ED and ICU (n=90) were analysed on the Radiometer methods, the i-STAT CG4+, and the Nova analyser within 1–2 minutes of each other. Samples were transported to the laboratory at ambient temperature and all whole blood analysis was completed within 1 hour of draw time. Within 5 minutes of the whole blood analysis, the specimens were centrifuged and plasma separated and kept on ice until testing on the Roche Integra and the Vitros 250 analysers could be completed (within 1 hour of plasma separation). Linearity and precision of each device or assay was also determined using material provided by the individual manufacturers. It was unclear how the samples or patients were selected.
Setting	Department of Laboratory Medicine and Pathology, Mayo Clinic College of Medicine, Rochester, USA.
Inclusion/ exclusion criteria	Not specified.
Primary outcomes	Correlation between lactate methods.

Statistical methods	Results were compared by least squares regression and Bland–Altmann plots and by comparing concordance within clinically relevant lactate ranges. [a]
Conclusions	The negative bias in i-STAT and Radiometer results may confound the interpretation of patient condition if multiple methods are used within the same institution.

Abbreviations: ED, emergency department; ICU, intensive care unit.

[a] Results were classified as low risk (lactate result, ≤2.2 mmol/l), intermediate risk (lactate result, 2.3–5.0 mmol/l), or high risk (lactate result, >5 mmol/l) based on available literature relating lactate levels to patient outcome.

Table 6 Summary of results from the Karon et al. (2007) study

Patients included	Patients in the ED and ICU (n=90). No further details were reported. It was unclear how the samples/patients were selected.
Primary outcomes	Correlation between lactate methods was good with slopes of 0.87–1.06 and intercepts of 0.1–0.2 mmol/l of lactate for all 4 methods compared with the Vitros (slopes of 0.87 for the i-STAT methods, with r^2=0.99 or more in each case). Intercepts were between lactate levels of 0.1 and 0.2 mmol/l for all methods. At high lactate values (>6 mmol/l), the Radiometer and i-STAT assays exhibited negative bias (relative to the Vitros), and the Radiometer and i-STAT methods reported lower lactate results compared with the Vitros and Integra. Among the 90 samples analysed on the Vitros, there were 29, 30, and 31 samples in the low-, intermediate-, and high-risk categories respectively. [a] The percentage of concordance (percentage of all samples that fell in the same risk category as the Vitros result): the Radiometer and i-STAT had 85 (94%) of 90 samples concordant with the Vitros result; for the Integra, 89 (99%) of 90 samples fell within the same risk category as the Vitros value; the Nova demonstrated 90% concordance (81/90) with the Vitros.

Abbreviations: ED, emergency department; ICU, intensive care unit; n, number of patients.

[a] Results were classified as low risk (lactate result, ≤2.2 mmol/l), intermediate risk (lactate result, 2.3–5.0 mmol/l), or high risk (lactate result, >5 mmol/l) based on available literature relating lactate levels to patient outcome.

Table 7 Overview of the Thomas et al. (2009) study

Study component	Description
Objectives/ hypotheses	To evaluate the "measure of treatment agreement" – the number of standard clinical laboratory arterial blood gas measurements that prompted changes in mechanical ventilator support therapy compared with number of portable device measurements that would have prompted the same or different changes.
Study design	Prospective cohort study. Treatment decisions made with arterial blood measurements by: • i-STAT cartridge CG4+: arterial oxygen saturation (saO_2), PO_2, pH, PCO_2 • Nonin 8500 M pulse oximeter: SpO_2 • Novametrix-610: end-tidal CO_2 ($ETCO_2$) were compared with the recommended treatment from paired arterial blood measurements by laboratory Radiometer ABL-725: $_saCO_2$, PO_2, pH, PCO_2.
Setting	A shock-trauma ICU at a level 1 trauma centre in the USA between 23 September 2002 and 13 November 2003.

Inclusion/ exclusion criteria	Intubated and ventilated adult patients admitted to the shock-trauma ICU were eligible for inclusion if they had an indwelling arterial catheter and if portable bedside measurements could be performed at the time of the first arterial blood gas sample. Patients were excluded if any measurements were missing from any of the study devices (Nonin, Novametrix, i-STAT, and Radiometer ABL 725) or if the arterial blood gas had been inadvertently run on another bench-top blood gas analyser other than the Radiometer ABL 725.
Primary outcomes	Association between portable and laboratory blood gas measurements.
Statistical methods	Regression scatter plots, Bland–Altman statistics.
Conclusions	The i-STATPO_2 and PCO_2 portable device measurements were acceptable as surrogates to standard clinical laboratory blood gas measurements in guiding protocol-directed ventilator management. The "measure of treatment agreement," based on standardised decisions and measurement thresholds of a protocol, provides a simple method for assessing clinical validity of surrogate measurements.
Abbreviations: ICU, intensive care unit.	

Table 8 Summary of results from the Thomas et al. (2009) study

Patients included	446 intubated adult ICU patients, mean age 48 (SD 19) years, males 57%. Admission category: infectious 11%, medical 17%; neurological 5%, psychological <1%, respiratory 11%, surgical 20%, and trauma 32%. Mean injury severity scores: 28 (SD 12). Hospital mortality: 18%.

Primary outcomes	Except for the Novametrix-610 $ETCO_2$ (r^2=0.460), correlation coefficients between portable and laboratory measurements were high ($r^2 \geq 0.755$). Testing for equivalence, the Nonin SpO_2, i-STAT PO_2, i-STAT pH, and i-STAT PCO_2 were deemed "equivalent" surrogates to paired laboratory measurements. The measure of treatment agreement between the portable and paired laboratory blood gas measurements were Nonin-SpO_2 (68%), i-STAT $_saO_2$ (73%), i-STAT PO_2 (97%), i-STAT pH (88%), i-STAT PCO_2 (95%), and Novametrix $ETCO_2$ (60%). Based on a minimum of ≥95% measure of treatment agreement, only the i-STAT PO_2 and the i-STAT PCO_2 were considered acceptable surrogates to the laboratory PO_2 and PCO_2.
Abbreviations: $ETCO_2$, end-tidal CO_2; ICU, intensive care unit; n, number of patients; SD, standard deviation.	

Table 9 Overview of the Singer et al. (2014) study

Study component	Description
Objectives/ hypotheses	To assess the effects of bedside POC lactate measurement (using the i-STAT CG4+ cartridge) on the time to administration of IV fluids and antibiotics in adult ED patients with suspected sepsis.
Study design	Before-and-after study. Bedside lactate measurement (using the i-STAT CG4+ cartridge) in a convenience sample of 80 patients presenting to the ED between January and September 2013 who met the study inclusion criteria, was compared with laboratory lactate measurement in the first 80 consecutive patients presenting to the ED12 months prior to introduction of the bedside lactate testing (starting from 1 calendar year prior to study initiation).
Setting	A suburban, academic tertiary care medical centre with annual ED attendance of approximately 90,000 people.

Inclusion/ exclusion criteria	Inclusion criteria In the 'before' group: the first 80 consecutive patients presenting to the ED12 months prior to the introduction of bedside lactate testing who also had an initial lactate level of ≥2 mmol/l (starting from 1 calendar year prior to study initiation). In the 'after' group: following the introduction of bedside lactate testing, patients attending the ED between January and November 2011 with suspected infection and at least 2 of the clinical criteria for the SIRS (including a temperature of ≥38°C, a temperature of ≤35°C, a heart rate of ≥90 beats per minute, a respiratory rate of ≥20 per minute, a systolic blood pressure < 90 mmHg, or an acute change in mental status) and with a bedside lactate level of at least 2 mmol/l. Exclusion criteria Patients who could not give consent or for whom consent could not be obtained from a legal guardian were excluded. Patient who received an intravenous antibiotic for suspected sepsis within the last 12 hours were also excluded.
Primary outcomes	Time from ED triage to iv fluids and antibiotic administration.
Statistical methods	Binary data were compared between groups with X^2 or Fischer's exact tests. Continuous data were compared with t-tests and Mann Whitney U tests as appropriate. A sample size calculation determined 80 patients in each of the study periods. The agreement between bedside POC and central lab lactates was analysed with scatterplots, correlation coefficients and Bland Altman analysis.
Patients included	n=80 in each group. Respiratory infection as the source of infection: 50% in the before group and 29% in the after group (p=0.01). There were no statistically significant differences in other baseline demographic and clinical characteristics.
Conclusions	Implementation of bedside POC lactate measurement in adult ED patients with suspected sepsis reduces time to test results and time to administration of IV fluids but not antibiotics. A significant reduction in mortality and ICU admissions was also demonstrated, which is likely to be due, at least in part, to POC testing.

Abbreviations: ED, emergency department; ICU, intensive care unit; IV, intravenous; POC, point-of-care; SIRS, systemic inflammatory response syndrome.

Table 10 Summary of results from the Singer et al. (2014) study[a]

	After (i-STAT CG4+)	Before (laboratory)	Analysis
Number analysed	n=80	n=80	
Primary outcomes			
Time to iv fluids (minutes)	55 (34–83)	71 (42–110)	p=0.03
Time to iv antibiotics (minutes) [b]	89 (54–156)	97 (55–160)	p=0.59
Secondary outcomes			
Test turnaround time (minutes)	34 (26–55)	122 (82–149)	p<0.001
Time from arrival to standard central laboratory results	71 (53–101) [c]	122 (82–149)	p<0.001
Time from order to standard central laboratory results	38 (26–53)	71 (53–91)	p<0.001
ICU admits, n (%) [d]	26 (33%)	41 (51%)	p=0.02
Total ED length of stay	352 (246–457)	326 (249–436)	p=0.50
ICU length of stay, days	3 (2–6)	4 (2–6)	p=0.90
Hospital length of stay, days [e]	7 (3–13)	8 (4–13)	p=0.27
Mortality	5 (6%)	15 (19%)	p=0.02

Abbreviations: ED, emergency department; ICU, intensive care unit; IV, intravenous; POC, point-of-care; n, number of patients.

[a] The data reported for 'time to', 'time from', and 'length of stay' days were in median (interquartile).

[b] Discrepancy between the data reported in the abstract and that in the table 2 of the paper.

[c] All patients in the prospective arm receiving a POC lactate test result also had their serum lactate levels measured in the central laboratory to assess the performance of the POC lactate assay compared with the standard of care. Treatment was initiated based on the POC result; it was not delayed or contingent on the value or the availability of the central lab serum lactate result.

[d] patients in whom the initial lactate level was 4 mmol/l or greater were transferred the critical care area for further evaluation and management.

[e] Excludes deaths.

Table 11 Overview of the Jarvis et al. (2014) study

Study component	Description
Objectives/ hypotheses	The authors hypothesised that nurse-led triage in the ED may not be the most efficient method of initiating care. The study assessed the impact of introducing a consultant-supported point-of-care rapid assessment model and point-of-care testing on the length of time patients spend in the ED.
Study design	A before-and-after study consisting of two consecutive phases: phase 1 during which patients were assessed and treated using a nurse-led triage model; phase 2 during which patients were assessed using a rapid assessment model. The rapid assessment model used point-of-care testing for full blood counts, renal function (i-STAT CHEM8+) and blood gases (i-STAT CG4+).
Setting	An ED in a district general hospital (major trauma unit) in the UK with an annual number of ED attendances of approximately 65,000. Phase 1: between 1 April 2013 and 24 May 2013. Phase 2: between 30 September 2013 and 18 October 2013.

Inclusion/ exclusion criteria	Not specified.
Primary outcomes	Time from the patient arriving in the ED to the point in time when all ED care is complete and the patients is deemed ready to move to the next destination of care.
Statistical methods	Chi square test; interpretations were based on α=0.05 and β=0.8. A 2-tailed sample size calculation estimated that 497 patients were required in both phases.
Patients included	Phase 1: n=3835, male 51.8%, mean age 42 years. Phase 2: n=787, male 50.2%, mean age 45 years. There was no statistically significant differences between the population characteristics examined, including age, gender, full blood counts, renal functions, blood gases, and proportion of arrived by ambulance and triage category.
Conclusions	The study demonstrates that a consultant-supported rapid assessment model using POCT significantly shortens the time patients spend in the ED.
Abbreviations: ED, emergency department; n, number of patients; POCT, point-of-care testing.	

Table 12 Summary of results from the Jarvis et al. (2014) study

	i-STAT CHEM8+/CG4+	**Nurse-led**	**Analysis**
Number analysed	n=787	n=3835	
Primary outcomes			
Median time from patients arriving in the ED to be declared "ED ready"	76 minutes	129 minutes	Median reduction=53 minutes or 41.1% (95% CI 39.7%–42.3%; p<0.0001)

Median time from arrival to the commencement of an assessment by a member of clinical staff (doctor or nurse)	4 minutes	12 minutes	Median reduction=8 minutes or 66.7% (95% CI 65.0%–68.3%; p<0.0001)
Median time from arrival in the ED to assessment by an ED physician	24 minutes	96 minutes	Median reduction=72 minutes or 75.0% (95% CI 74.6%–75.3%; p<0.0001)
Abbreviations: CI, confidence interval; ED, emergency department; n, number of patients.			

Table 13 Overview of the Jarvis et al. (2015) study

Study component	Description
Objectives/ hypotheses	To quantify the impact of introducing point-of-care testing for renal function on the length of time patients spend in the ED.
Study design	A before-and-after study. It consisted of two consecutive phases: phase 1 during which renal function was tested using the hospital's centralised laboratory analyser and phase 2 during which renal function analysis was tested using the bedside i-STAT CHEM8+ cartridge.
Setting	An ED in a district general hospital (major trauma unit) in the UK with an annual number of ED attendances of approximately 65,000. Phase 1: between 1 April 2013 and 24 May 2013. Phase 2: between 28 May 2013 and 29 September 2013.
Inclusion/ exclusion criteria	All patients attending the ED within the study period that were identified as requiring renal function analysis and did not have a minor injury were included in the data analysis. patients who presented with a minor injury were excluded.
Primary outcomes	Time for patients to be declared ready to leave the ED.

Statistical methods	Wilcoxon rank sum tests; interpretations were based on α=0.05 and β=0.8. A 2-tailed sample size calculation estimated that 155 patients were required in both phases.
Patients included	Phase 1: n=3835, male 51.8%, age 42 years (unclear whether mean or median). Phase 2: n=7033, male 52%, age 45 years (unclear whether mean or median).
Conclusions	The study demonstrates that using POCT for renal function in the ED was significantly quicker than using a centralised hospital laboratory. The use of a bedside POCT device enables clinicians to make informed clinical decisions in a timelier manner.
Abbreviations: ED, emergency department; CI, confidence interval; n, number of patients; POCT, point-of-care testing.	

Table 14 Summary of results from the Jarvis et al. (2015) study

	i-STAT CHEM8+	**Laboratory**	**Analysis**
Number analysed	n=7033	n=3835	
Primary outcomes			
Median time from patients arriving in the ED to be declared "ED ready"	109 minutes	129 minutes	Median reduction=20 minutes or 15.5% (95% CI 14.8%–16.2%; p=0.0025)
Median time from arrival to the commencement of an assessment by a member of clinical staff (doctor or nurse)	7 minutes	10 minutes	Median reduction=3 minutes or 30% (95% CI 29.1%–30.86%; p=0.0025)

Median time from arrival in the ED to assessment by an ED physician	80 minutes	90 minutes	Median reduction=16 minutes or 16.7% (95% CI 16.0%–17.4%: p=0.0025)
Abbreviations: CI, confidence interval; ED, emergency department; n, number of patients.			

Table 15 Outline of articles in which the POCT was probably the i-STAT CHEM8+ and/or CG4+ cartridges

Authors	Outline
Hsiao et al (2007)	In the study it was not specified which POCT devices were used, nor were the use of i-STAT and cartridges specified (one specialist commentator suggested that this study should be included in the briefing). The study was a randomised controlled trial comparing the effect of POCT with traditional laboratory methods on patient length of stay in a paediatric ED. A total of 225 patients presenting to a tertiary hospital ED in the US were included, 114 were in the POCT group and 111 in the routine laboratory analysis group. Time intervals were analysed including time spent in the waiting room, time waiting for first physician contact, and time waiting for blood draw. Similar waiting periods were noted in both groups for time spent in the waiting room, time waiting for first physician contact, and time waiting for blood draw. Statistically significantly less time was required in the POCT group compared with the laboratory group for results to become available to physicians (65.0 minutes; p<0.001) and in overall length of stay (38.5 minutes, p<0.001).

Gilkar et al (2013)	This article reported a project that implemented POCT to test the hypothesis that interfacing 'on-line' POCT devices to a clinical electronic order communications system reduces patient waiting times in an NHS A&E in 2012. The devices selected for evaluation initially comprised the Sysmex XS 1000i haematology analyser and the i-STAT chemistry analyser (i-STAT cartridges were unspecified but the manufacturer claims it was the CHEM8+ cartridge). Patient waiting time (presumably, it was defined as from time of arrival to time of discharge) and the time to produce test results (turnaround time, i.e. from requesting a test and receiving the results) were assessed in total of 217 cases associated with POCT tests only, and were compared with that in 229 controls who were randomly selected from the clinical laboratory database. Study period was not specified. No further details on sampling process for both groups. The time to produce test results was 23 minutes for the POCT tests and 60 minutes for the laboratory tests. The patient waiting time was 167 minutes for the POCT group and 208 minutes for the clinical laboratory group, a difference of 31 minutes.
Webb and Campbell (2014)	This article described a project setting up an Emergency Multidisciplinary Unit in the Oxford region in the UK. The i-STAT was used but cartridges were unspecified (although specified that it would give a full biochemical profile).

Giles et al (2015)	A press-release published on an online in-house journal by Step Communication. It reported a project that integrated POCT and evidence-based lean service redesign at an NHS hospital (year unclear) to provide emergency medical patients with efficient and high quality care. The i-STAT analyser (cartridges unspecified) and Emerald CEL-DYN full blood count analyser were used for a 3-month pilot period, coupled with service redesign. Performance data were reported for each of the 3 months, including total patients, average patients per day, mean length of stay, median length of stay, and same-day discharge rate. The authors stated that for the patient cohort the length of stay reduced from 1.04 to 0.8 bed-days (reduced by 40.8% from an established baseline of 250 minutes). There was an 8.22% increase (188 patients) in the number of same-day discharges (zero length of stay admission), with an associated decrease of 8.93% in "1, 2 and 3 day length of stay patient admissions – equating to 59 saved bed days during the pilot period."
Abbreviations: A&E, accident and emergency department; ED, emergency department; POCT, point-of-care testing.	

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

Changes after publication

September 2015: Minor maintenance.

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This briefing was developed for NICE by Birmingham and Brunel University Consortium. The Interim process & methods statement sets out the process NICE uses to select topics,

and how the briefings are developed, quality-assured and approved for publication.

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Declarations of interest

No relevant interests declared.

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