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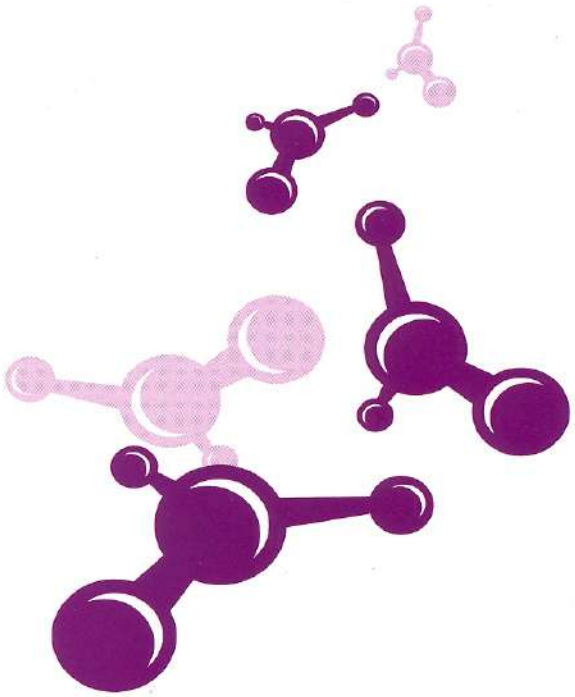
Health Technology Assessment

REPORT

POINT OF CARE TESTING (POCT)



HEALTH TECHNOLOGY ASSESSMENT UNIT
MEDICAL DEVELOPMENT DIVISION
MINISTRY OF HEALTH

DISCLAIMER

This Health Technology Assessment has been developed from analysis, interpretation and synthesis of scientific research and/or technology assessment conducted by other organizations. It also incorporates, where available, Malaysian data, and information provided by experts to the Ministry of Health Malaysia. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of the review.

Please contact: htamalaysia@moh.gov.my, if you would like further information.

Health Technology Assessment Unit,
Medical Development Division
Ministry of Health Malaysia
Level 4, Block E1, Precinct 1
Government Office Complex
62590 Putrajaya
Tel : 603 8883 1246
Fax : 603 8883 1230

Available at the following website: http://www.moh.gov.my

PROJECT EXPERT COMMITTEE

Dr Ng Siew Hian
Consultant Anaesthetist & Head of Department
Department of Anaesthesia and Intensive Care
Kuala Lumpur Hospital
(Chairperson)

Dr Angeline Yeoh Aing Chee
Consultant Paediatrician and Head of Department
Department of Paediatrics
Seberang Jaya Hospital
(Contributor of section on POCT for urine dipstick in UTI))

Dr Jamilah Baharom
Consultant Pathologist and Head of Department
Department of Pathology
Penang Hospital
(Contributor of section on POCT for Mg in critical care)

Dr Kauthaman Mahendran
Consultant Physician and Head of Department
Department of Medicine
Malacca Hospital
(Contributor of section on POCT for PT INR in primary care)

Dr Roshida Hassan
Consultant Haematologist
Department of Pathology
Kuala Lumpur Hospital
(Contributor of section on POCT for FBC in emergency department)

Dr R Sukumar
Family Medicine Specialist
Polyclinic Community Tanglin, Kuala Lumpur
(Contributor of section on POCT for HbA1c in primary care)

Dr Tai Li Ling
Consultant Intensivist
Department of Anaesthesia and Intensive Care
Kuala Lumpur Hospital
(Contributor of section on POCT for electrolytes in critical care)

Dr Vijayamalar B
Research Physician
Institute for Medical Research
Ministry of Health Malaysia
(Contributor of section on POCT for rapid dengue test in dengue infection)

PROJECT COORDINATORS

Y. Bhg Datin Dr Rugayah Bakri
Deputy Director & Head,
Health Technology Assessment Unit
Medical Development Division
Ministry of Health Malaysia

Mrs Mariammah Krishnasamy
Assistant Director (Science)
Health Technology Assessment Unit
Medical development Division
Ministry of Health Malaysia

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- Dr. Brian Cheong Mun Keong (Hospital Taiping), Mr. Sabab Bin Hashim (Taiping Hospital), Miss Lee Siew (Taiping Hospital), Mrs. Nurasyikin Bt Salim (Taiping Hospital), Mr. Mohd Faisal bin Razali (Taiping Hospital), Mr.Muhammad Nubli Bin Mohd Shuhaimi (Taiping Hospital).

EXECUTIVE SUMMARY

1. INTRODUCTION

Point of care testing (POCT) is defined as “clinical laboratory testing conducted close to the site of patient care, typically by clinical personnel whose primary training is not in the clinical laboratory sciences or by patients (self-testing). POCT refers to any testing performed outside of the traditional, core or central laboratory". Due to its simplicity and ease of use, POCT are increasingly being used in patient care especially in the critical and primary care settings.

2. OBJECTIVE

To determine the clinical effectiveness and reliability of selected point of care testing (POCT) in specific settings when compared to central laboratory tests.

3. METHODOLOGY

An electronic database search from 1990-2006 was carried out, using appropriate keywords and combinations of keywords. The literature retrieved was reviewed and critically appraised, then tabulated and graded the evidence according to the modified Catalonian Agency for Health Technology Assessment & Research Scale.

4. RESULTS & CONCLUSIONS

POCT for prothrombin time – INR in primary care

- Clinical outcomes (in terms of adverse event rates, changes in dosing advice and percentage of tests and percentage of time INR are within therapeutic range) from POCT for INR are comparable to central lab testing.
- Client satisfaction is higher with POCT INR.
- Reliability of POCT for INR varies with each device.

POCT for HbA1c in primary care

- Reliable POCT systems e.g. DCA 2000 for measuring HbA1c are currently available.
- Availability of HbA1c at the time of consultation has a positive impact by influencing the clinician to make appropriate management decision.
- This immediate availability of HbA1c also leads to better control of diabetes mellitus (reduction of HbA1c) on subsequent follow-up visits.

POCT for urine dipstick in urinary tract infection

- The use of urine dipstick may reduce laboratory workload for urine culture and increase the percentage of positive culture
- There are conflicting results on the accuracy of urine dipstick tests given the heterogeneity of studies
- In children, there is evidence that urine dipstick (combination of LE and nitrite) is useful in diagnosing or excluding UTI. Properly collected urine culture remains the gold standard
- In adults, negative urine dipstick (combination of LE and nitrite) does not exclude UTI
- In both adults and children, positive LE and nitrite tests in urine dipstick can aid in the initiation of therapy while awaiting urine culture results.

POCT for dengue rapid test in primary care

- There is no available evidence on the use of dengue rapid tests as POCT
- The rapid tests currently available are unable to detect early dengue infection especially cases of primary infection
- The result of dengue rapid test should be interpreted in the context of the overall clinical presentation of the patient

POCT for full blood count in emergency department

- There is no evidence available regarding the use of POCT for full blood count measurement in the emergency setting.
- Newer compact hematology analyzers have comparable results as conventional lab analyzers

POCT for electrolytes (Na, K, Cl) in critical care

- There is evidence that POCT for sodium, potassium and chloride in the critical care setting results in decreased turnaround time, increased staff satisfaction and reduced blood loss.
- When POCT for sodium, potassium and chloride is used in the critical care setting, there is conflicting evidence on its impact to cause change in clinical management.
- There is no evidence that POCT for sodium, potassium and chloride decreases length of stay or mortality in the critical care setting.
- Analytical performance studies that compare POCT systems to central laboratory for sodium, potassium and chloride vary between analyzers but the differences are not of clinical importance.

POCT for magnesium in critical care

- There is insufficient evidence that POCT of magnesium result leads to improved clinical outcomes in critical care settings
- There is fair evidence that more rapid turn-around time of magnesium result in critical care patient setting, leads to improved clinical outcomes.
- There is no evidence on the analytical performance of ion magnesium analyzers as POCT.

5. RECOMMENDATIONS

General Recommendations

- Before any POCT is considered, the clinical need should be clearly identified and evaluated at the specific setting bearing in mind that the desired rapid turnaround time may also be achieved by having an efficient mechanical transport system and bidirectional IT communication between the laboratory and end users
- Before implementation the POCT equipment should be evaluated for its analytical performance
- A POCT committee comprising of all stake holders should be established to coordinate and monitor all POCT activities
- Standard operating procedures must be strictly adhered, paying particular attention to training, quality assurance /control and safety policy
- Clear comprehensive record keeping and documentation of POCT results is mandatory

Specific Recommendations

POCT for prothrombin time – INR in primary care

- POCT for INR is recommended as the choice testing in the out-patient management of patients on Warfarin. Issues on quality control and costing need to be considered.

POCT for HbA1c in primary care

- It is recommended that HbA1c results be made available at the time of consultation.
- POCT for HbA1c is an alternative to central laboratory testing.

POCT for urine dipstick in urinary tract infection

- Urine culture remains the gold standard in the diagnosis of UTI.
- Urine dipstick as POCT may be used to initiate therapy in suspected UTI while awaiting urine culture results.
- Local studies to determine the prevalence of UTI in different populations, the accuracy of urine dipsticks available in the market and the dipsticks markers 'cut-off points' are recommended.

POCT for dengue rapid test in primary care

- There is a need for studies to be conducted on rapid dengue tests as POCT in health facilities without laboratory services with the objective of evaluating its impact on preventing an outbreak.

POCT for full blood count in emergency department

- Technical evaluation and feasibility studies for full blood count as POCT using the newer analysers should be conducted in the emergency departments.

POCT for electrolytes (Na, K, Cl) in critical care

- POCT for sodium, potassium and chloride is recommended as an alternative to central laboratory in the critical care setting where the turnaround time is not acceptable.
- POCT devices for electrolytes need to be evaluated for reliability at the local setting before implementation.

POCT for magnesium in critical care

- Studies on POCT Mg should be carried out and the performance of the analyser conducted before its implementation in the critical care setting.

TABLE OF CONTENTS

HEALTH TECHNOLOGY ASSESSMENT
POINT OF CARE TESTING

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1. INTRODUCTION

Point of care testing (POCT) is defined as “clinical laboratory testing conducted close to the site of patient care, typically by clinical personnel whose primary training is not in the clinical laboratory sciences or by patients (self-testing). POCT refers to any testing performed outside of the traditional, core or central laboratory". Other synonyms for POCT include *near patient testing*, *bedside testing* and *home testing*. In this report, tests done by the satellite or ancillary laboratory are not considered.

In the last decade, POCT is expanding at a market growth rate of 12-15% per annum, a rate several times larger than that of the central laboratories (Stephans 1999). POCT was initially introduced in the critical care setting i.e. intensive care units, operating theatre and emergency departments where the need for rapid turnaround times and early interventions are the main concerns. However, in recent years, POCT is increasingly being used in primary and home care settings e.g. in the management of diabetes mellitus and anti-coagulation therapy. The availability of test results at the time of consultation is convenient and appealing to both clinicians and patients. The increasing adoption of POCT in clinical practice is inevitable, however, its widespread use must be considered carefully to ensure that it is used safely, effectively and economically.

Technical Features

There is a wide range of point of care tests in the market. Examples of these tests are: electrolytes, blood gases, cholesterol (LDL, HDL and triglycerides), drugs of abuse (NIDA 5 and barbiturates, benzodiazepines), cardiac enzymes (CK, LDH, tropoinin, myoglobin), coagulation (PT), H. pylori (Helicobacter pylori), infectious diseases (HIV, Strep A, TB, Mycoplasma, C. difficile, E. coli, hepatitis, Chlamydia) and other quantitative assays (hCG, PSA, digoxin, pituitary gonadotropins).

Two broad types of technology support point of care testing: small bench top analyzer (for example blood gas analysis and electrolyte systems) and hand held, single use devices (such as urine albumin, blood glucose and coagulation tests). The bench top systems are smaller versions of laboratory analyzers in which vulnerable operator dependent steps have been automated – for example, automatic flushing of sample after analysis, calibration and quality control. Hand held devices have been developed using microfabrication techniques. They are outwardly simple but internally complex devices that do several tasks –for example, separate cells from plasma, add reagents and read colour or other end points. (Price, 2001)

The regulations on Clinical Laboratory Improvement Amendment (CLIA) in U.S. establish three categories of testing on the basis of the complexity of the testing. Waived tests are tests that employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible and pose no reasonable risk of harm to the patient if the test is performed incorrectly. Other tests methodologies are categorized as being of either moderate or high complexity according to the degree of knowledge needed to perform the test, training required, characteristics and availability of calibration, quality control and degree of interpretation and judgment in the testing process. POCT devices fall under the categories of waived or moderate complexity tests.

Advantages and Disadvantages

The main advantage of POCT is the rapid and effective analytic results with a decreased test turnaround time, which can allow a shorter therapeutic response interval or prompt therapy control. Problems with specimen identification and transportation do not arise. The analyzers require only small amounts of whole blood samples, utilize ready-to-use reagents and the operator's level of competence is not important, as a trained laboratory technician is not required. Another advantage is the substantially improved convenience for the patient and for the staff performing the test. (Mueller 1999, Kost 2001)

The main criticism of point of care testing has been the lack of analytical performance and quality control. There are concerns about the reliability of results obtained by non-laboratory personnel, who are often insufficiently or not at all familiar with the analyzers they are using. Essential calibration procedures may not be performed or may only be carried out rarely and /or inadequately. Insufficient documentation of the results affects data processing, data transfer and the data network, particularly with regard to data connection with the central laboratory. In addition, POCT makes additional time demands on clinicians and nurses. (Freedman 1998)

Cost-effectiveness

With the increasing popularity of POCT, there is a risk that such testing may expand in an uncritical and unjustified way. The need for more rapid results and the increasing emphasis on client convenience has resulted in a growing demand for such tests, and the manufacturing industry is steadily increasing the range of analytic tests available.

It is therefore not surprising that POCT has become controversial. In addition to differing opinion among clinicians and laboratory staff, there are many questions concerning the advantages, disadvantages, and economic and health-care aspects of POCT that have yet to be resolved.

Cost-effectiveness remains a major consideration when introducing a POCT to a clinical practice. However it is a difficult issue to address. When assessing cost effectiveness, it is necessary to explore more than the cost per test. It is necessary to perform a ‘total economics’ analysis that assesses the cost and benefits per encounter with laboratory testing.

The real costs are difficult to determine, as absolute comparison are extremely difficult to carry out, and there are wide variations in the costs associated with central laboratories and POCT. The expenses of training staff, and of obtaining supplies and personnel for POCT in comparison with laboratory testing are only a few of the key aspects involved in assessing cost, and different conditions apply in each hospital.

Published studies in the general medical literature are intrinsically subjective because, inevitably, values assigned to benefits such as extended life, quality of life, or decrease in projected expenditure are site and institute specific. Certain benefits such as patient satisfaction, reduction in total administrative time for clinicians and reduced number of clinic visits are difficult to be 'price-tagged'.

In order to effectively assess the cost-benefit ratio of POCT, each site therefore has to evaluate it in its own unique circumstances. (Price 2001) Findings of cost-effectiveness studies of POCT done in other countries may not be applicable to the Malaysian setting. To the best of our knowledge, there is no cost-effectiveness study on POCT done in Malaysia. For these reasons, we have excluded cost analysis from the scope of this report.

2. OBJECTIVE

The objectives are to answer the following two questions in each of the sections:

1. Does POCT of (test) in the (setting) improve clinical outcome when compared to central laboratory test?

2. Is POCT for (test) in the (setting) reliable compared to central laboratory test?

3. SCOPE OF STUDY

The committee brainstormed and prioritized the types of POCT which are currently in use or to be introduced to Ministry of Health hospitals. These tests were selected based on their perceived impact on clinical practice, cost implications and requests from health care managers. Tests which fulfilled the criteria but were dealt with in separate practice guidelines e.g. cardiac markers and HIV tests were excluded.

The following are the tests and settings selected for assessment:

- POCT for prothrombin time-INR in primary care
- POCT for HbA1c in primary care
- POCT for urine dipstick in urinary tract infection
- POCT for rapid dengue test in primary care
- POCT for full blood count in emergency department
- POCT for electrolytes (Na, K, Cl) in critical care
- POCT for magnesium in critical care

It is important to note that the assessment of a test using a specific point of care device must always be done in the specified setting where it is to be used. Findings obtained in such assessment cannot be inferred to other device or setting outside the study.

4. METHODOLOGY

The electronic database was searched; with the limitations of studies from 1995-2006.The following databases of PUBMED, Proquest, OVID and HTA databases and related links were used with the appropriate keywords and combinations of keywords, for each search on these databases. The keywords used were as follows: *point of care testing, point of care system, near patient testing, Point of care testing in prothrombin time, Point of care testing INR, Near patient testing INR, Point of care testing prothrombin time, POCT HbA1c, Near patient HbA1c, bedside testing HbA1c glycosylated ,haemoglobin, HbA1c,Point of care test dengue, Rapid diagnostic dengue test, NS1 Dengue , NS1 Dengue AND Point of care test urine dipstick, bacteri*uria and *urinary tract infection*, *full blood count , complete blood count', 'hemogram', 'rapid test', Haemoglobin POCT, POCT for electrolytes (sodium, potassium, chloride) in the critical care setting, critical care, blood gases, outcomes ,critical care , clinical outcomes ,sensitivity ,specificity, accuracy, reliability outcome, Point-of-care testing, bedside testing, near patient testing, intensive care, emergency room, operation room, electrolytes, and chemistry.* All the relevant studies retrieved were appraised, discussed and their level of evidence was graded by the committee.

5. RESULTS AND DISCUSSION

5.1 POCT FOR PROTHROMBIN TIME – INR IN PRIMARY CARE

Warfarin as an anticoagulant has been in use since the 1950's as prophylaxis against thrombosis and embolism. In some countries it is estimated that 1% of their population are on anticoagulants (Murray, *2003*). Among the common indications for long term Warfarin usage include atrial fibrillation, mechanical cardiac valves and recurrent deep vein thrombosis. The indications and number of patients using Warfarin are increasing. In the UK it is estimated to have a 10% year-on-year increase (Murray, *2004*).

The Prothrombin Time (PT), developed in 1935 (Quick, *1935*), is key to determining the therapeutic dose of Warfarin. This will avoid thrombo-embolic adverse events (eg stroke) from under-dosing or potentially lethal bleeding episodes from over-dosing. Standardization of the PT was achieved in the 1980s with the International Normalized Ratios (INR) system (Wood, *1998*).

Most government hospitals in Malaysia have dedicated Warfarin clinics to cope with the increasing pool of clients. Some centres provide the service as a part of the general out-patient service. They are served by a laboratory that measures the INR at the lab and transmits the results to the clinics. Venepuncture sampling may be done at the clinic, a separate bleeding area or at the laboratory. Timing between testing and dosing advice or therapeutic turn around times (TTOT) can vary from one hour to one week depending on the setting and system employed. In some systems, a patient may have to come for 2 separate visits before dosing advice can be given. (Personal communications with random clinicians running Warfarin services in government hospitals *2006*).

There are a number of private hospitals and clinics in Malaysia using the Roche Coaguchek XS INR Monitoring System as a POCT for INR (email from Lau, *2006*). No information is available on other brands or models in use locally for the out-patient setting. This system requires a drop of blood from a finger-prick placed on a strip and inserted into a meter. The result is available in less than a minute. The POCT system has the following features; ease of use, no need for a venepuncture, short test duration, and availability of result in a single visit for dosing decisions and patient convenience.

Health centres and polyclinics may in the future be expected to provide Warfarin services to cope with the increased burden in hospitals. Some of them do not have on-site laboratories providing an INR testing service. In the US and Britain, community clinic GPs, nurses and pharmacists run this service. Patient self monitoring (PSM) using home INR monitors have also been introduced, with FDA approval in the US, since 1997 (Nutesu, *2004*).

HTA for this test is warranted to justify and set directions for its use in our hospitals and clinics. This evaluation of INR POCT addresses its clinical effectiveness and reliability in the setting of out-patient Warfarin services. Patient self monitoring (PSM) is not addressed in this review.

5.1.1 Clinical Effectiveness

The articles selected were those that compared the outcomes between POCT and Central Lab in respect of:

i. Adverse events; thrombo-embolic (under-dosing) and hemorrhagic events(over- dosing).
ii. Clinical agreement on dosing advice or treatment decisions.
iii. Percentage of tests and percentage of times INR was within therapeutic ranges.
iv. Patient satisfaction

i. Adverse events

Two papers, (Fitzmaurice, *2000*; Chamberlain, *2001)* addressed adverse events. Both papers compared 2 models of anticoagulant care. One was a traditional care with testing in a central lab, review by a doctor and delayed dosing advice via telephone or the mail. Some were given dosing advice by the doctor on the same day. The other model was using a POCT, immediate advice by a trained nurse or pharmacist and using computerized decision support software (cdss). Fitzmaurice in his randomized controlled trial involving 367 patients over a one year period found no significant differences in overall death rates (3.44 vs. 3.6 per 100 patient years), serious thrombotic events (2.28 vs. 5.43 per 100 patient years) and serious hemorrhagic events (1.14 vs. 0 per 100 patient years) between the anticoagulant service using the POCT (Thrombotrak) and the service using a central lab. Unfortunately, the statistical tests for significance were not stated in this paper.

Chamberlain's observational study of 116 patients over a one year period found no statistically significant difference in the rates of emergency visits (9.5 vs. 14.8 per 100 patient years, p= 0.63) between patients in the 2 different models (POC based and lab based). The rates of admission were however noticeably lower in the POCT based service; 4.7 vs. 19.7 admissions per 100 patient years of therapy, p = 0.15.

The findings from these two papers could however have been attributed to other features of the anticoagulant clinic models; timing of advice at consultation instead of telephone/mail, use of trained nurse or pharmacist instead of doctor and use of a computerized decision support system. They were also not powered to show differences in adverse events.

ii. Dosing advice

Clinical agreement in dosing advice was addressed in 7 papers. Shiachi conducted a randomized cross over trial involving 46 patients. They were divided into 2 groups (Group 1 and 2); one with a POCT (CoaguCheck) and the other with a central lab testing (ACL Futura). The groups were crossed over after 6 months. All samples were tested by both the POCT and central lab. They defined clinically relevant standard agreement (Anderson *1993*) as a combination of the following criteria.

i. Both INR results within targeted therapeutic range
ii. Both INR results either above or below therapeutic range.
iii. Both INR results within 0.4 INR units of each other.

Clinically relevant standard agreement was found in 98% of the 465 tests.

This was the only trial that directly addressed the question of clinical effectiveness of POCT in comparison with central lab without confounders. It is impressive in its randomized cross over methodology but is limited by a low power and high withdrawal rate of 15%. (Schiachi, *2002*).

Five papers (Murray 1999, Shermock 2002, Reiss 2002, DeMiguel 2003 and McBane 2005) were observational studies comparing POCT with central lab results and their impact on dosing advice. The agreement in the dosing advice was found to be in the range of 66% to 90%.

Hobbs compared 3 different central labs (ACL, KC-10 and manual testing using Manchester reagent with a POC (Thrombotrak) and found that the 3 central labs results resulted in potentially differing dosing decisions in between 35% and 53% of the cases (Hobbs, *1999*)

The rigorous methodology employed in Schiachi's paper makes his results most acceptable. Hobbs paper questions which testing to be taken as the gold standard.

iii. Percentage of tests and percentage of time INR within therapeutic range

Schiaichi showed that the mean percentage of times INR was maintained within targets were identical for both systems. (60.9 vs. 59.3 for Gp 1 and 63.4 vs. 64.3 for Gp2, p= 0.2) (Schiachi, *2002*). Fitzmaurice and Chamberlain also showed in their papers that there were no statistically significant differences in the percentages of tests in range and percentages of time in range between the 2 systems. (Fitzmaurice *2000*, Chamberlain *2001*).

iv. Patient satisfaction

There were 2 papers that addressed patient satisfaction. Shiachi in his cross over design found that 98% of his surveyed patients preferred the community based clinic with POCT over the hospital clinic with central lab service. The sample size was only 46 with 15% drop out. They had shorter waiting times and shorter journey times to the clinics. Chaudry surveyed 187 patients after they switched from a 'venepuncture-delayed telephone advice' to a 'finger-prick face to face consultation' system. 79.1% preferred the new system and 74.8% claimed to experience less pain. Unfortunately the patients were not surveyed while they were on the old system and the 49% of patients who refused to switch to the new system were also not surveyed. (Chaudry, *2004*).

5.1.2 Reliability

Articles which addressed the correlation and precision of POC versus central lab were chosen.

Hobbs addressed the issue of reliability of trained nurses in performing the Thrombotrak POCT for INR after a one day training program. 196 samples were tested in parallel with a lab technician using the same testing instrument. He found a good correlation (r = 0.96). (Hobbs, *1999*). However, this paper addressed the reliability of the nurse performing the POCT, and not the instrument.

A total of 7 papers (Hobbs *1999,* McBane *2005*, Murray *1999*, Gosselin *2000*, Pollier *2003*, Pollier *2003* and Nutesu *2004*) addressed the reliability of POCT in comparison with a central lab instrument. Assessments were made comparing different POC models against different laboratory based gold standards.

Nutesu summarized these papers elegantly in his review article. The r values for the POCs varied between 0.7and 0.99. Precisions vary between 3 and 6%. He emphasized that devices cannot be used interchangeably and individual device performance cannot be generalized. (Nutesu *2004*).

Hobbs further showed that central labs were also not identical; 3 central labs differed in their r values when compared to a single POC device. (r = 0.89, 0.86 and 0.92) He highlighted the importance of quality assurance irrespective of the type of testing instrument (lab or POC) (Hobbs *1999*).

5.1.3 Conclusion

- Clinical outcomes (in terms of adverse event rates, changes in dosing advice and percentage of tests and percentage of time INR are within therapeutic range) from POCT for INR are comparable to central lab testing.
- Client satisfaction is higher with POCT INR.
- Reliability of POCT for INR varies with each device.

5.1.4 Recommendations

- POCT for INR is recommended as the choice testing in the out-patient management of patients on Warfarin. Issues on quality control and costing need to be considered.

5.2 POCT FOR HbA1c IN PRIMARY CARE

The prevalence of diabetes mellitus is increasing (Wild et al, 2004). The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that diabetes is associated with increased morbidity and mortality (Stratton et al, 2000).

The measurement of HbA1c is regarded as standard medical care for assessment of glycaemic control in patients with diabetes. HbA1c reflects the average blood glucose levels over the previous 2-3 months. The Malaysian Clinical Practice Guidelines for Type 2 diabetes (2004) recommends HbA1c to be measured every 3 to 6 months to ensure that glycaemic targets are being met. The UKPDS demonstrated that any reduction in HbA1c is likely to reduce the risk of diabetic complications (Stratton et al, 2000).

In Malaysia, hospitals have their HbA1c performed in central laboratories. In the primary care set up, bigger clinics have their own labs with lab technologists. The rest of the clinics send their blood specimens for HbA1c either to the hospital labs or have their own Point of Care System (POCT) for doing so. Some of the clinics are quite far from the central labs. Thus, having the blood tests performed according to recommendations may be an issue. In such cases having a POCT system for HbA1c would be beneficial in the management of patients with diabetes. However, it would be essential to know whether the POCT systems for measuring HbA1c are reliable. It would also be beneficial to know if having the HbA1c results rapidly available at the time of consultation would make an impact on the clinical outcome. This was the reason that led to HbA1c being included in this study.

5.2.1 Clinical Effectiveness

Studies on clinical outcome mainly covered 3 aspects – changes in management, effect on follow-up HbA1c and patient satisfaction.

i. Changes in management

In a technology assessment done by Matchar et al, evidence was reviewed regarding the influence of performing HbA1c at the point of care in patient management decisions. According to the author, POCT HbA1c is able to effect appropriate management decisions (Matchar et al 2005).

Grieve et al did a trial on 599 diabetic patients to evaluate whether the availability of HbA1c test result at the time of consultation would influence the number of management changes. They found that in patients with poor glycaemic control (HbA1c > 7.5%), more management changes were made if HbA1c results were available at the time of consultation compared to the control group where HbA1c was not available at the time of consultation (32% vs. 21%; OR 1.75; 95% CI 1.12-2.76). However the authors did not explain what the management changes were (Grieve et al, 1999).

Miller et al determined whether rapid availability of HbA1c results would improve appropriate intensification of diabetic therapy and reduce HbA1c levels in diabetic patients in an urban primary care clinic. Intensification of diabetes therapy was defined as the increase in the dosage of hypoglycaemic agents or the addition of a new agent. An HbA1c level of more than 7% was considered as to require intensification of therapy. Of the recruited 597 patients, rapid HbA1c availability resulted in more frequent appropriate intensification of therapy compared to the control group where HbA1c result was not rapidly available(51% vs. 32%; p=0.01) . If HbA1c was more than 9%, appropriate intensification was present in 65 % of the rapid group as against 46% of the routine group (p=0.006). The authors concluded that rapid HbA1c measurements increased the frequency of intensification of therapy (Miller et al, 2003).

In a randomized clinical trial in a diabetes specialty clinic by Thaler et al, the HbA1c results were made available on consultation for 575 patients whereas delayed by 24 hours in 563 patients. Adjustment of therapy was considered appropriate if therapy was intensified for HbA1c levels > 7% or not intensified for HbA1c levels ≤ 7%. The authors found that rapid HbA1c availability resulted in more appropriate management compared with conventional HbA1c availability (79 vs. 71%; p=0.003) (Thaler et al, 1999).

ii. Effect on follow-up HbA1c

Matchar et al in their technology assessment reviewed the evidence regarding impact of performing HbA1c at the point of care on clinical outcomes. Evidence shows an improvement in HbA1c ranging between 0.2 – 0.8%. However they find that there are few data available beyond 6 months and 12 months data from 1 study suggest a smaller effect on HbA1c of point of care at 12 months than at 6 months (Matchar et al, 2005).

Shepard et al studied a remote setting that introduced a one-stop shop, where, in a single appointment, the diabetic patients (n=54) met the local diabetic educator and podiatrist as well as the GP and had an on site POCT for HbA1c, urine albumin: creatinine ratio, lipids and glucose. The introduction of the one-stop shop led to the increase in the percentage of patients (from 33 to 63%) achieving optimal glycaemic control (HbA1c < 7%).

The number of patients exhibiting very poor control (HbA1c > 10%) was reduced (from 13 to 6%) (Shepard et al, 2005).

Miller et al in the study described in the earlier section studied the change in HbA1c in 275 patients with 2 follow-up visits. They found that HbA1c fell significantly in the rapid group (from 8.4 to 8.1%; p=0.04) but not in the routine group (from 8.1 – 8.0%; p=0.31).

The authors concluded that rapid HbA1c measurements lowered HbA1c levels in patients with diabetes (Miller et al, 2003).

A post-hoc analysis was performed by Thaler et al on patients who returned for follow-up 2-7 months later to ascertain the effect of rapid HbA1c availability on subsequent glycaemic control. During the 2-7 months follow-up, HbA1c increased more in patients with

conventional HbA1c results compared with rapid results (0.8 % vs. 0.4%; p=0.02) (Thaler et al, 1999).

Cagliero et al conducted a randomized control trial in 201 insulin treated diabetic patients. In the group of patients where HbA1c was done as a point of care test, HbA1c results decreased significantly at 6 and 12 months (0.57 ± 1.44%; p=0.001 at 6months and 0.40±0.65%; p=0.013 at 12 months). In the other group of patients, where HbA1c was done in the lab and the results were not rapidly available during consultation, HbA1c did not decrea(H.Taiping) se significantly on follow-up visits (Cagliero et al, 1999).

iii. Patient satisfaction

Patient satisfaction was assessed by Grieve et al in 2 hospitals. At both hospitals, patients were in strong agreement that immediate feedback of HbA1c is important, because it allows patients to discuss the results with the doctor (226/244). A majority of patients (216/244) considered that immediate feedback of HbA1c results helped them to understand their diabetes (Grieve et al 1999).

Shepard et al found that the proportion of patients with diabetes who were satisfied/very satisfied with the available diabetes services was significantly greater following the introduction of their one – stop shop project described in the previous section (from 64 to 91%). Most patients (97%) felt it as an advantage not having to return to the clinic for the result. (Shepard et al 2005)

In the studies mentioned above, the conventional way refers to that in which patients have their blood taken and sent on the day of appointment with the doctor. Hence the consultation proceeded without the HbA1c result available. However in Malaysia the blood is checked 1-3 weeks before the appointment with the doctor (personal communications with doctors managing diabetes). This results in the patient having to come separately for the blood tests. However on the day of the appointment, the blood test results including the HbA1c are available for review by the doctor and discussion with the patient.
Hence the results of the above mentioned studies may not be relevant in the Malaysian context apart from the immense value of availability of the HbA1c levels at the time of consultation.

5.2.2 Reliability

A technology assessment of POCT HbA1c by Matchar et al found that it was reasonable to say that devices which satisfy criteria for accuracy and precision disseminated by the National Glycohemoglobin Standardization Program (NGSP) certification protocol are functionally equivalent to conventional devices. Some of these devices are Clinical Laboratory Improvement Amendment (CLIA) waived as well, which means that these are simple tests having an insignificant risk of erroneous result. HbA1c devices that are approved by the FDA for point of care testing satisfy the NGSP Certification Protocol and CLIA waived are the DCA 2000, A1c Now, Bio-Rad MicroMat and Cholestech GDX (Matchar et al 2005). In another technology assessment for HbA1c as a POCT by Tice found that the most used device for this assessment in research studies was the DCA 2000 with 18 case series involving more than 3000 participants. (Tice, 2003).

Martin et al assessed the accuracy of point of care measurements of HbA1c levels in a remote Australian aboriginal community. They compared the DCA 2000 analyzer results with the laboratory results.
Median values by the 2 methods were identical (6%) as was the mean value (7.1%). Results by the two methods were significantly correlated ($r = 0.99$; $p < 0.001$). They concluded that POCT HbA1c testing using the Bayer DCA 2000 analyzer offers an accurate way of monitoring diabetes in rural and remote clinical settings (Martin et al, 2005).

Carter et al determined whether the DCA 2000 analyzer provided valid and reliable HbA1c results when used under field conditions and operated by non-medical personnel. Community members were trained to operate the DCA 2000 analyzer. Two study samples were taken, the first in 1994 and the second in 1995. Comparison of the mean results with those done by the standard laboratory method showed high validity with the absolute relative difference between the two methods being 4% for 1994 and 2% for 1995. Correlation coefficient between the two measures was 0.968 for 1994 and 0.996 for 1995 ($p < 0.0001$). The authors concluded that the DCA 2000 gave valid and reliable results when operated in a community setting by non-medical personnel (Carter et al, 1996).

Guerci et al compared the performance of the DCA 2000 system for HbA1c with that of the High Performance Liquid Chromatography (method used in laboratories to measure HbA1c). They found that the sensitivity of the DCA 2000 was 91% and the specificity 94%. The correlation coefficient was 0.95. The mean variation was -0.116 and the 95% confidence interval -1.23 to 0.998. The authors concluded that the DCA 2000 system was reliable for measuring glycated haemoglobin (Guerci et al, 1997).

In a study which compared four different POCT systems with the central lab deduced that the Diastat and the DCA 2000 system gave the best performance with acceptable imprecision and good agreement with both the central lab and each other (Hawkins, 2003).

5.2.3 *Conclusion*

- Reliable POCT systems e.g. DCA 2000 for measuring HbA1c are currently available.
- Availability of HbA1c at the time of consultation has a positive impact by influencing the clinician to make appropriate management decision.
- This immediate availability of HbA1c leads to better control of diabetes mellitus (reduction of HbA1c) on subsequent follow-up visits.

5.2.4 Recommendations

- It is recommended that HbA1c results be made available at time of consultation.
- POCT for HbA1c is an alternative to central laboratory testing.

5.3 POCT FOR URINE DIPSTICK IN URINARY TRACT INFECTION

Urinary tract infection (UTI) is a common bacterial infection in clinical practice. Urine culture is the gold standard for the diagnosis of UTI, but it is time consuming and labour intensive. It costs RM 22.00 per culture and an additional RM 6.00 for urine microscopy (Gribbles Laboratory, 2006).

Rapid method of diagnosing UTI is desirable as it facilitates early diagnosis and treatment; avoids patient's anxiety and unnecessary laboratory urinalysis. The most widely used rapid tests are urine dipsticks with the advantages of being cheap, easy to perform and interpret. Analytes commonly used in dipsticks include leukocyte esterase (LE), nitrite, protein and blood. Dipstick testing involves dipping the reactive section of a dry phase chemistry reagent strip briefly into urine and then comparing the colour change with a reference chart either manually or by a strip reader. Tighe recommended the use of electronic strip reader to reduce result errors. Common errors in dipstick testing are related to timing, misalignment, misunderstanding and transcription. (Tighe, 1999)

Detection of leukocyte esterase (LE) activity is an indirect measure of pyuria. False positive LE may happen if urine is contaminated with leukocyte containing vaginal fluid. (Wilson ML, 2004). Nitrite is an indirect measure of nitrate reducing bacteria (enterobacteriacae, non-fermenters, Gram negative cocci) and it is present provided the urine contains sufficient dietary nitrate and has been retained in the bladder for more than four hours. Gram positive uropathogens (S. saprophyticus, enterococci) and Pseudomonas spp do not produce this biochemical reaction.

Urine dipsticks have been used widely as point of care tests in diagnosing UTI. This assessment is a review on the use of POCT urine dipsticks in the following aspects:

1. Clinical outcome – reduction of laboratory workload, over or under-treatment
2. Analytical performance as compared to conventional microbiology methods

The diagnostic accuracy of microscopic urinalysis and urine dipstick for suspected UTI has been studied extensively, but the results of these investigations vary depending on patient population, definition for UTI, test cutoffs, and laboratory techniques.

5.3.1 Clinical Effectiveness

Patel studied the implementation of urinary dipstick algorithm in the diagnosis of UTI in inpatients as compared to the conventional laboratory technique (semiquantitative counts of RBC, leukocytes, epithelial cells and culture). Using the combination of four markers (LE, nitrite, protein and blood) in patients suspected of UTI, he concluded that if the four markers are negative, there is a high probability that the patient does not have UTI with the exceptions of neutropenic and immunosuppressed patients and therefore no further urine test is necessary. However if the dipsticks display any amount of leukocyte, nitrite, blood or protein, midstream urine is to be sent to the laboratory for culture and sensitivity and empirical treatment may be considered while awaiting culture results. Two years after the implementation, there was a reduction in the urine specimens for microscopy, however there was an overall increase in specimens for urine culture. This has also resulted in an increase in the positivity rates of urine culture. (Patel, 2005)

More than 300 adult women with UTI symptoms in the emergency department or intermediate care center were studied by Lammers et al. Using stringent cut off points for urine dipsticks (LE > 2 and nitrite positive) the over treatment rate ranges from 13% (positive culture, 10^5 CFU ml) to 0% (positive culture, 10^4 CFU /ml), whereas the corresponding under treatment rates increase to unacceptable level (48% for both).

He concluded that test cut-offs for urine dipstick can be set at points to provide over treatment and under treatment rates that are equivalent to those for urinalysis.With this, urine dipstick can be substituted for urinalysis for adult women with symptoms suggestive of UTI. (Lammers, 2001)

5.3.2 Reliability

i). Urine dipstick in children

In a systematic review by Whiting et al on the rapid tests for the diagnosis of UTI in children under 5 years, he reviewed 39 studies with 107 data sets evaluating dipstick tests. These studies assessed nitrite, LE, protein, glucose, blood; either individually or in combinations. Considerable heterogeneity exists between studies in terms of methods, samples, populations and therefore the results need to be interpreted with caution.

The systematic review showed that best performance is obtained with a combination of nitrite and LE results. Dipstick tests positive for both nitrite and LE has the highest likelihood ratio (LR) (+28.2, 95% CI: 17.3-46.0) while dipstick negative for both nitrite and LE has the best negative LR (0.20, 95%CI: 0.16-0.26). If either one is positive, further test is required. There is insufficient information on the value of protein, blood, glucose or their combinations. The 9 studies on the combination of microscopy and dipstick tests were inconclusive. However, microscopy was found to be superior to urine dipstick in diagnosing UTI in eight of the studies. To exclude UTI, 4 out of the 5 studies found that negative microscopy was superior to negative urine dipsticks. He concluded that negative dipstick both for LE and nitrite or negative microscopic analysis for pyuria and bacteriuria may reasonably rule out UTI. Similarly, combinations of positive tests can be used to diagnose UTI and trigger further investigations (Whiting 2005). The above data was also published in the Health Technology Assessment Report 2006 (Whiting, 2006) and used in the algorithm for the diagnosis of UTI in children under 5 years.

Systematic review and Meta analysis regarding performance of rapid diagnostic tests for UTI in children less than 12 years was also studied by Gorelick et al. He took into consideration the definition of UTI based on colony count and the age of the patients noting the heterogeneity among the studies. The presence of bacteria on Gram stain in an uncentrifuged urine specimen had the best combination of sensitivity (0.93) and false positive rate (0.05). Urine dipstick tests performed nearly as well, with a sensitivity of 0.88 for the presence of either LE or nitrite and a false positive rate of 0.04 for the presence of both LE and nitrite. Pyuria had lower true positive rate and higher false positive rate.

The conclusion was that both Gram stain and dipstick analysis for nitrite and LE perform similarly in detecting UTI in children less than 12 years of age and are superior to microscopic analysis for pyuria. (Gorelick 1999)

According to the American Academy of Pediatrics Committee on Quality Improvement (1999), the three most useful components in urinalysis in the evaluation of possible UTI in children of two months to two years of age are LE test, nitrite test, and microscopy. The standard test for diagnosis of UTI is urine culture. No element or combinations of elements in urinalysis is as sensitive and specific. Urinalysis of either positive LE or nitrite test, presence of > 5 WBC per HPF in a properly spun specimen, or presence of bacteria in an unspun Gram-stained specimen is valuable in selecting individuals for prompt initiation of treatment while awaiting urine culture results.

Sharief et al in a study concluded that both negative LE and nitrite dipstick method is the most likely useful screening test to exclude UTI in children older than a year. However, positive dipstick tests for nitrite and/or LE are not specific indicators of UTI. In infants, a negative combination of dipstick has a higher false negative rate. The limitations in this study were the lack of stringent method of urine collection and the wide range of age in the study population. (Sharief, 1998)

Shaw et al conducted a cross-sectional study on various rapid screening tests in children below 2 years in the emergency department setting. In her study, a positive urine culture is defined as $\geq 10^4$CFU/ml, which is a lower threshold compared to most studies. She concluded that no rapid test can detect all children below 2 years with UTI and recommended that urine culture should be done and presumptive treatment started only on those with significantly positive dipstick result (moderate LE or nitrite). The sensitivity, specificity and positive predictive value are 73%, 99% and 61% respectively. (Shaw, 1998)

A retrospective review of medical records of febrile patients under 2 years attending the emergency department was studied by Bachur in 2001. The overall sensitivity for dipstick analysis alone was 79% (95%CI, 76-82%), and the sensitivity of combined dipstick and microscopy (standard urinalysis in this laboratory) was 82% (95%CI, 79-84%). The specificity of combined dipstick and microscopy was 92% (95% CI, 91-92%).

The likelihood ratios for positive and negative UA results were 10.6 (95% CI, 10.0-11.2) and 0.19 (95%CI, 0.18-.0.20). He concluded that urine culture should be obtained in all boys younger than 6 months and girls younger than 12 months with fever of unknown source. It is worth noting that in this study the detected prevalence of UTI represents a minimum estimate of true prevalence because not all patients had urine culture but all febrile patients were used as denominator regardless whether a urine culture is obtained or patient had other source of infection. (Bachur, 2001)

Doley concluded that overall urinalysis has poor specificity (39.4%) and very poor positive predictive value and therefore not useful in the diagnosis of UTI in a retrospective review of children in the emergency department setting. In the 0-2 years age group, the prevalence of UTI is higher (15%) while the sensitivity (87.5%) and negative predictive value (94.7%) are reduced. Therefore dipstick urinalysis is inadequate to exclude UTI. In children of 2-10 years age group, UTI can be adequately excluded with a negative dipstick urinalysis (for all of blood, protein, leukocytes and nitrite) as sensitivity and negative predictive value were 100%. The limitation of this study is that it had a high rejection rate of cases with inadequate data and a high rate of urine contamination from urine bag samples. (Doley, 2003)

*ii)***.** *Urine dipstick in adults*

The only retrievable meta-analysis in the adult population is by Hurlbut et al in 1991. However, the full text of this article is not available for review.

Ohly et al did a short cut review of Medline search form 1966-2004 to answer the clinical question if a negative dipstick analysis is sensitive enough to rule out UTI in adults with urinary symptoms. From the two papers with the best evidence, he concluded that dipstick urine analysis (nitrite and LE) is of insufficient sensitivity to be used to rule out UTI in patients with one or more symptoms. (Ohly, 2003).

Semeniuk et al reviewed 479 ambulatory women with symptoms of uncomplicated UTI. Using a colony count of ≥ 10^3 CFU/ml, a positive dipstick (combined LE and nitrite) had a sensitivity 81.1%, specificity 59.4%, positive predictive value 31.6% and negative predictive value 93.2%. At higher colony count of ≥10^5 CFU/ml, the sensitivity is higher at 84% and the specificity 98.3%.

The author did not recommend the use of positive dipstick results to screen for UTI or to determine the need for urine culture in this population as many women with UTI symptoms had lower bacterial counts (≤ 10^5 CFU/ml) as reported by Stamm and Kunin. (Semeniuk, 1999)

In a study by Rehmani, he concluded that dipstick alone cannot accurately predict UTI in the emergency department setting as a significant number of positive urinalysis for leukocytes were missed by dipstick examination. The sensitivity for LE and nitrite is 94%, specificity 50%, positive predictive value 45% and negative predictive value 95%. (Rehmani, 1998)

In a study conducted by Preston comparing urine dipstick and microbiological laboratory testing, he found that the combined use of nitrite and LE provides a valid method for mass screening for UTI in the gynecological patients. The sensitivity, specificity, positive predictive values and negative predictive values were 96.4%, 88.5%, 54% and 99.4% respectively. (Preston 1999)

Similar findings were noted by Medina where a positive nitrite test and pyuria increases the probability of UTI by more than seven times in women with urinary tract symptoms. (Medina, 2003)

In symptomatic female patients, a urine sample with a positive nitrite test (positive predictive value 96% and specificity 94%) or with a negative nitrite test with a positive LE test (positive predictive value 79% and sensitivity 82%) should be considered indicative of UTI and the patient should be treated accordingly. However, when both nitrite and LE tests are negative, a UTI cannot be excluded and sample should be further investigated by culture. (Nyrs 2006)

5.3.3 Conclusion

- The use of urine dipstick may reduce laboratory workload for urine culture and increase the percentage of positive culture
- There are conflicting results on the accuracy of urine dipstick tests given the heterogeneity of studies
- In children, there is evidence that urine dipstick (combination of LE and nitrite) is useful in diagnosing or excluding UTI. Properly collected urine culture remains the gold standard
- In adults, negative urine dipstick (combination of LE and nitrite) does not exclude UTI
- In both adults and children, positive LE and nitrite tests in urine dipstick can aid in the initiation of therapy while awaiting urine culture results.

5.3.4 Recommendations

- Urine culture remains the gold standard in the diagnosis of UTI
- Urine dipstick as POCT may be used to initiate therapy in suspected UTI while awaiting urine culture results
- Local studies to determine the prevalence of UTI in different populations, the accuracy of urine dipsticks available in the market and the dipsticks markers 'cut-off points' are recommended

5.4 POCT FOR RAPID DENGUE TEST IN PRIMARY CARE

Dengue infections ranging from asymptomatic infection to dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS) continue to be a public health problem in many parts of the world, including Malaysia. Since the 1990's the incidence of dengue in Malaysia has been on the increase from a few thousand cases to more than 30,000 cases in 2005. DHF has also increased from a few hundreds to 2,800 in 2005.

Early laboratory confirmation of dengue infection is important for clinical diagnosis and essential for cost-effective public health control measures. Laboratory diagnosis of dengue can be done by

1) serological diagnosis by detection of rising IgG or IgM from body fluids e.g. blood, cerebrospinal fluid 2) isolation of virus from body fluids or biopsy specimens or 3) detection of viral genome from body fluids or biopsy specimens.

Currently, serological detection of dengue IgM is the most practical method for laboratory confirmation of dengue infection. In primary infections, detectable dengue IgM usually appears by the 5^{th} day of illness. For patients who present early, their dengue IgM test may still be negative. In these cases, dengue IgM should preferably be repeated daily if the patent is admitted or 3 to 4 days later for those who are not admitted.

In secondary infections, the currently used serology test kit can detect high levels of IgG, giving a presumptive positive result. IgM may not be detected in these cases because of the very high levels of IgG.

Dengue IgM detection by ELISA is done in batches in the central laboratory and it may take up to 3 to 4 days to run the batch depending on the number of specimens received. This causes delay in confirming or ruling out of dengue infection especially in patients who present in the later stage of the disease. Early confirmation of dengue infection will assist in public health control measures by instituting timely or avoiding unnecessary fogging activities. With the advent of rapid diagnostic assays using lateral flow tests for dengue antibodies, POCT for dengue may become possible. This may then overcome the above issues.

5.4.1 Clinical Effectiveness

In the literature review, there are several evaluations of these rapid test kits that have the potential of being used as POCT. However, all these evaluations are carried out in central laboratory settings and there is no publication found on its use in the actual POCT setting.

In the meta-analysis conducted by Blacksell, the author concluded that the rapid test in dengue is useful in the diagnosis, bearing in mind its limitations. The main limitation is its poor sensitivity in the early phase of the disease.

The test evaluated has acceptable sensitivity and specificity after day 7 of onset of illness. A negative result does not rule out dengue infection and the test has to be repeated. (Stuart D. Blacksell, 2004)

5.4.2 Conclusion

- There is no available evidence on the use of dengue rapid tests as POCT
- The rapid tests currently available are unable to detect early dengue infection especially in cases of primary infection
- The results of dengue rapid test should be interpreted in the context of overall clinical presentation of the patient

5.4.3 Recommendations

- There is a need for studies to be conducted on rapid dengue tests as POCT in health facilities without laboratory services with the objective of evaluating its impact on preventing an outbreak.

5.5 POCT FOR FULL BLOOD COUNT IN EMERGENCY DEPARTMENT

A full blood count (FBC) or complete blood count (CBC) is one of the most commonly requested tests for the detection of anaemia and other blood disorders. This “profile” test is performed using an automated haematology analyser which counts the red cells, white cells and platelets, measures the haemoglobin(Hb) content, packed cell volume (Hct) and also generate other associated parameters depending on the type of analyzer used. In 1999, Barbara J. Bain noted that (Blood cells, Blackwell Science) “the latest blood counters are able to determine 8 to 23 variables”. Since then, some of the newer, high end haematology analysers are capable of generating more parameters (Product information leaflet).

In the Malaysian hospitals, the FBC test services are provided by the laboratories, either within the central pathology laboratory or as part of the satellite laboratory service. It is a known fact that the FBC results may not always be available rapidly to the clinicians in the critical care areas such as the emergency department.

This may be due to local constraints such as lack of efficient transport of specimen and delivery of results and other intra-laboratory factors e.g. frequent breakdowns of the equipments and the inefficiency of personnel. To overcome this problem of delayed result availability, several emergency physicians in the government hospitals have requested that FBC test be made available as POCT.

In the emergency department, the availability of the FBC aids in clinical management and facilitates rapid turn over of patients. Hb and Hct confirm anaemia and guides blood transfusion. Raised TWBC with increased neutrophil count supports an infective cause of an acute abdomen e.g. acute appendicitis while platelet count is used as a criterion for hospital admission in dengue infections. (Personal communication)

The automated haematology analysers in general are more complex than the usual POCT instruments. As stated by Kratz et al (2004), “the size and the complexity of the modern cell counters is often an impediment to their use as point of care.” The staff operating and maintaining the analyzer has to be well trained to ensure that the results generated are reliable. Even in the updated list on 9 January 2007, Clinical Laboratory Improvement Amendments, USA has not included any haematology analyzer in the waived list which is normally assigned to POCT devices.

5.5.1 Clinical Effectiveness

The search found 7 titles of which one was relevant and a full text was obtained. The article was a report on the performance evaluation of a new compact haematology analyzer, Sysmex pocH-100i. The authors (C. Briggs et al, 2003) concluded that its performance was comparable to the established small haematology analyzer Sysmex KX-21, commonly used in low volume laboratories. They were of the opinion that due to the simplicity of operation and other technical features, this analyzer is highly recommended for point of care services. However, it should be noted that this evaluation was carried out in the laboratory setting by competent technical personnel.

There has been no retrievable article on the use of FBC POCT in the emergency departments. This could be due to the fact that there is currently no established suitable hematology analyzer used as POCT except for Sysmex pocH-100i as mentioned above.

The paucity of study on this topic could also be due to the fact that delayed FBC result in the emergency department does not arise in the developed countries as most of them have efficient transport and communication systems for both sample and result delivery. In a survey by Gray on the use of the laboratory for urgent tests and clinician's attitude to POCT, FBC was not one of the tests performed via POCT (TA Gray, 1996)

In a recent review of literature on POCT, Kratz et al (2004) wrote that by decreasing patient wait times and avoiding additional visits , shorter turnaround times for CBC can significantly improve patient satisfaction .

5.5.2 *Conclusion*

- There is no evidence available on the use of POCT for full blood count in the emergency departments
- Newer compact hematology analyzers have comparable results as conventional lab analyzers

5.5.3 Recommendations

- Technical evaluation and feasibility studies for full blood count as POCT using the newer analysers should be conducted in the emergency departments

5.6 POCT FOR ELECTROLYTES (Na, K, Cl) IN CRITICAL CARE

The definition used for "critical care setting" in this section is any clinical setting in which patients who have major organ dysfunction, severe trauma, undergoing or post major surgery, severe sepsis, or other high severity disorders that require life-sustaining care are managed. These settings include intensive care units (ICU), coronary care units (CCU), neonatal intensive care units (NICU), operation theatres (OT) and emergency departments (ED).

The provision of critical care to these patients is a complex process that utilizes many resources and various physiologic data. Clinical laboratory evaluation is an important part of the overall diagnostic and treatment process. Another important characteristic of critical care settings is the potential for rapid (i.e., seconds to minutes) and clinically significant changes in a patient's status that may require prompt intervention. Rapid results are often needed for effective monitoring and treatment in the above settings.

Electrolyte and metabolic disturbances are common in the critically ill patient. Turnaround time (TAT) is crucial for a patient in an unstable condition, such as a cardiac arrest or a sudden deterioration in status for which the cause is unclear. For the clinician managing these patients, test results made available in minutes can often be used to make the diagnosis, and results of serial testing can be used to direct management until the patient's condition is stabilized. The expected turnaround time for these tests in the critical care settings varies, but it is generally in the range of five to fifteen minutes (Harvey, 1999). The German working group on "Medical laboratory testing for POCT in hospitals" recommends that the acceptable TAT for electrolytes in the critical care settings to be less than 30 minutes. (Briedigkeit, 1999).

The chemistry profile (Na^+, K^+, Cl^-, TCO_2, glucose, urea nitrogen, and creatinine) provided by the whole-blood analyzer is the "basic metabolic panel" (without calcium) in current procedural terminology (CPT) defined by the American Medical Association. These tests are classified as moderately complex under the Clinical Laboratory Improvements Amendments of 1988. (MMWR)

In Malaysia, most intensive care units, coronary care units and emergency departments are equipped with blood gas analyzers and arterial blood gases are usually analyzed as point-of-care. Currently, many of the whole-blood analyzers available in the market as point-of-care are able to perform other tests (e.g. electrolytes, haemoglobin, glucose, lactate) simultaneously with blood gases analysis.

The relevant clinical outcomes in the critical care settings include:

- Turnaround time
- Change in patient management
- waiting time in emergency department
- Length of stay
- Morbidity and mortality
- Blood loss
- Staff satisfaction

5.6.1 Clinical Effectiveness

Therapeutic turnaround time (from initiating order to implementation of any indicated change in treatment) for arterial blood gases, electrolytes and glucose in ICUs between a central laboratory, a satellite laboratory, and POCT was compared in a study by Kilgore and colleagues. The article showed that therapeutic turnaround time was 1-2 min shorter for bedside testing in the emergency department compared with a satellite laboratory and 9-14 min shorter in the satellite laboratory compared with centralized testing. POCT results prompted treatment changes 38% of the time and central laboratory tests were acted on 21% of the time. Glucose and electrolyte testing produced a change in treatment far more often than did blood gas testing. (Kilgore et. al, 1998).

Heyningen studied the laboratory turnaround time (from blood sampling to result availability) and waiting time in an emergency department for electrolyte tests done by POCT, central laboratory with porter system and central laboratory with pneumatic tube system. Although TAT was significantly shorter for POCT (5 min for POCT, 58 min for central laboratory with porter system, 49 min for central laboratory with pneumatic tube system), there were no significant differences in the waiting time in the emergency department (219 min, 212 min and 258 min respectively). (Heyningen, 1999).

In a randomized controlled study of 1728 patients in an emergency department, Kendall and co-workers (1998) found that, although point-of-care testing resulted in reduced turnaround times and earlier therapeutic interventions (86 min earlier when POCT was used for biochemical tests as compared to central laboratory testing), it did not lead either to differences in the length of stay in the emergency department (188 vs. 193 min., p=0.30) and length of stay in hospital (7.8 vs. 8.3 days, p=0.37), or to a reduced mortality rate (6.4% vs. 5.5%, p=0.45) (Kendall, 1998).Similar results were obtained by Parvin and co-workers (1996).

In a prospective study of 200 patients with major trauma, physicians were queried using a standardized set of questions as to their diagnostic and therapeutic management plan before and after a battery of POC tests (haemoglobin, electrolytes, glucose, blood gases and pH, base deficit, and lactate) became available. Management plan changes were deemed emergently appropriate, if they were influenced by the results and, within the ensuing 30 minutes the change in management was likely to reduce morbidity. Na^+, K^+ or blood urea nitrogen did not influence the management of these patients with blunt trauma when compared to other analytes (Hb, blood gases, glucose, lactate) where emergently appropriate changes were made in 0.5% to 3.5% of cases. (Asimos, 2000)

Blood transfusions administered to neonates can by reduced by using a POCT device, an in-line, ex vivo, bedside monitor that withdraws blood through an umbilical artery catheter, analyses blood gases and sodium, potassium, and haematocrit levels, and returns the sample to the patient. The POCT group had 33% lower cumulative blood transfusion and 25% less cumulative blood loss throughout the study period. However, there was no difference between groups in neonatal mortality, morbidity, and neurodevelopmental outcome rates at 18 to 24 months (Wildness et. al., 2005).

Staff satisfaction, comparing a central laboratory, a satellite laboratory, and point-of-care testing devices, was evaluated by Kilgore and colleagues. On a satisfaction score of 0 – 4, he showed that staff satisfaction was highest with satellite laboratory (mean score 3.49), followed by point-of-care testing (3.37) and lowest with central laboratory (2.21). ANOVA showed the differences in scores to be significant ($p<0.0001$). (Kilgore et. al., 1998).

5.6.2 Reliability

Accurate and precise laboratory data on which immediate and often critical decisions can be made are important for managing the patients in the critical care setting.

Electrolyte concentrations can also be analysed at the bedside with good precision across a range of concentrations for each electrolyte analyte. In a recent comparison trial, precision studies performed at three different concentrations for each electrolyte demonstrated an intra-assay coefficient of variation of 2.5% or less and an interassay precision of 4% or less in all tests (Chance et. al., 2000).

Other studies showed that bias and precision vary depending on the specific analysers compared but the differences were clinically not significant. In one study, paired blood samples were taken from 88 patients undergoing cardiopulmonary bypass for elective cardiac surgery for analysis of electrolytes. One sample was analysed in the operating room using GEM Premier 3000 while the other sent to the laboratory via internal transfer system for analysis using Ciba Corning865 analyser.

There is a linear trend in the deviation of the measurement of K^+ in the lower or upper reference range of the GEM Premier 3000 from the Ciba Corning 865 but from a clinical and therapeutical perspective, the deviation ($\leq$ 0.3) is not relevant.(Steinfelder-Visscher et. al., 2006)

ABL 70 analyser used as POCT to measure electrolytes showed a small positive bias for Na^+ but not for K^+ when compared to reference ABL625 in central laboratory. However, these differences are not clinically significant. (St. Louis, 2001)

Na^+ and K^+ done via POCT using i-STAT compared well with results by the central laboratory but not for Cl^- where there were 11 samples of outliers with absolute differences of 6 mmol/L among a total of 379 samples analysed in a large emergency department (Parvin, 1996).

5.6.3 Conclusion

- There is evidence that POCT for sodium, potassium and chloride in the critical care setting results in decreased turnaround time, increased staff satisfaction and reduced blood loss.
- When POCT for sodium, potassium and chloride is used in the critical care setting, there is conflicting evidence on its impact to cause change in clinical management.
- There is no evidence that POCT for sodium, potassium and chloride decreases length of stay or mortality in the critical setting.
- Analytical performance studies that compare POCT systems to central laboratory for sodium, potassium and chloride vary between analyzers but the differences are not of clinical importance.

5.6.4 Recommendations

- POCT for sodium, potassium and chloride is recommended as an alternative to central laboratory in the critical care setting where the turnaround time is not acceptable.
- POCT devices for electrolytes need to be evaluated for reliability at the local setting before implementation.

5.7 POCT FOR MAGNESIUM IN CRITICAL CARE

Magnesium is the fourth most abundant cation in human body and the second most abundant intracellular cation after potassium. 99% of the total body magnesium is intracellular. The remaining 1% in the plasma is divided into three fractions: magnesium bound to protein (27-34%), ionized magnesium (50-70%) and magnesium complex with anions (8-12%). Ionized magnesium is the physiologic active form. Until recently, most laboratory tests measure total magnesium in plasma or serum. Currently three different analyzers are available for the measurement of ionized magnesium i.e. AVL 988/4 (Austria), KONE (Finland) and NOVA (USA).

Hypomagnesaemia has been reported in the critically ill patients in the intensive care units (Soliman et al 2003, Henk J et al 2000, Adam Malon et al 2004, and Sakamoto T et al 2005). In eclampsia, infusion of magnesium has been shown to reduce recurrence of fits, time taken to regain consciousness and mortality (Shamsuddin L et al 2005) the use of prophylactic magnesium in cardiothoracic surgery reduces the incidence of post-operative atrial fibrillation and the length of hospital stay (Henyan NN 2005). Although magnesium is widely used in the management of arrhythmias in acute myocardial infarction, its benefit is still controversial. (ISIS Group 1995).

5.7.1 Clinical Effectiveness

From our search strategy, we did not find any study on the clinical impact of the availability of magnesium result via POCT compared to that from the central laboratory. This is also evidenced in the systemic review by the U.S. National Academy of Clinical Biochemistry with the conclusion that there is insufficient evidence that POCT of magnesium leads to improved clinical outcome.

In the same review, there were sixty citations on turnaround time and magnesium in the critical care setting. Based on these citations, the authors concluded that there is fair evidence that more rapid turnaround time of magnesium result in critical care setting leads to improved patient outcome. (NACB, Laboratory Medicine Practice Guideline 2006)

5.7.2. Reliability

Search results showed that currently three models of analyzers are being used in the measurement of ionized magnesium. These models are: AVL 988/4 (Austria), KONE (Finland) and NOVA (USA). There was no retrievable article on the analytical performance of these analyzers being used as POCT devices. All the analytical performance studies by the authors listed below were conducted in cental laboratory settings. (J.Thode et al 1998, Ronald J et al 1996, Elena N 1995, Z. Coa et al 2001, Christoph Ritter et al 1996, Francesco Zoppi et al 1996).

5.7.3 Conclusion

- There is insufficient evidence that POCT for magnesium leads to improved clinical outcome in the critical setting.
- There is fair evidence that more rapid turn- around time of magnesium result in the critical care setting, leads to improved clinical outcome.
- There is no evidence on the analytical performance of ion magnesium analyzers as POCT.

5.7.4 Recommendations

- Studies on POCT Mg should be carried out and the performance of the analyser conducted before its implementation in the critical care setting.

6. CONCLUSIONS

6.1 POCT for prothrombin time – INR in primary care

- Clinical outcomes (in terms of adverse event rates, changes in dosing advice and percentage of tests and percentage of time INR are within therapeutic range) from POCT for INR are comparable to central lab testing.
- Client satisfaction is higher with POCT INR.
- Reliability of POCT for INR varies with each device.

6.2 POCT for HbA1c in primary care

- Reliable POCT systems e.g. DCA 2000 for measuring HbA1c are currently available.
- Availability of HbA1c at the time of consultation has a positive impact by influencing the clinician to make appropriate management decision.
- This immediate availability of HbA1c also leads to better control of diabetes mellitus (reduction of HbA1c) on subsequent follow-up visits.

6.3 POCT for urine dipstick in urinary tract infection

- The use of urine dipstick may reduce laboratory workload for urine culture and increase the percentage of positive culture.
- There are conflicting results on the accuracy of urine dipstick tests given the heterogeneity of studies.
- In children, there is evidence that urine dipstick (combination of LE and nitrite) is useful in diagnosing or excluding UTI. Properly collected urine culture remains the gold standard.
- In adults, negative urine dipstick (combination of LE and nitrite) does not exclude UTI.
- In both adults and children, positive LE and nitrite tests in urine dipstick can aid in the initiation of therapy while awaiting urine culture results.

6.4 POCT for rapid dengue test in primary care

- There is no available evidence on the use of dengue rapid tests as POCT.
- The rapid tests currently available are unable to detect early dengue infection especially cases of primary infection.
- The result of dengue rapid test should be interpreted in the context of the overall clinical presentation of the patient.

6.5 POCT for full blood count in emergency department

- There is no evidence available regarding the use of POCT for full blood count measurement in the emergency setting.
- Newer compact haematology analysers have comparable results as conventional lab analysers.

6.6 POCT for electrolytes (Na, K, Cl) in critical care

- There is evidence that POCT for sodium, potassium and chloride in the critical care setting results in decreased turnaround time, increased staff satisfaction and reduced blood loss.
- When POCT for sodium, potassium and chloride is used in the critical care setting, there is conflicting evidence on its impact to cause change in clinical management.
- There is no evidence that POCT for sodium, potassium and chloride decreases length of stay or mortality in the critical care setting.
- Analytical performance studies that compare POCT systems to central laboratory for sodium, potassium and chloride vary between analyzers but the differences are not of clinical importance.

6.7 POCT for magnesium in critical care

- There is insufficient evidence that POCT of magnesium result leads to improved clinical outcomes in critical care settings.
- There is fair evidence that more rapid turn-around time of magnesium result in critical care patient setting, leads to improved clinical outcomes.
- There is no evidence on the analytical performance of ion magnesium analyzers as POCT.

7. RECOMMENDATIONS

7.1 General Recommendations

- Before any POCT is considered, the clinical need should be clearly identified and evaluated at the specific setting bearing in mind that the desired rapid turnaround time may also be achieved by having an efficient mechanical transport system and bidirectional IT communication between the laboratory and end users.

- Before implementation the POCT equipment should be evaluated for its analytical performance.

- A POCT committee comprising of all stake holders should be established to coordinate and monitor all POCT activities.

- Standard operating procedures must be strictly adhered, paying particular attention to training, quality assurance /control and safety policy.

- Clear comprehensive record keeping and documentation of POCT results is mandatory.

7.2. Specific Recommendations

7.2.1 POCT for prothrombin time INR in primary care

- POCT for INR is recommended as the choice testing in the out-patient management of patients on Warfarin. Issues on quality control and costing need to be considered.

7.2.2 POCT for HbA1c in primary care

- It is recommended that HbA1c results be made available at the time of consultation.
- POCT for HbA1c is an alternative to central laboratory testing.

7.2.3 POCT for urine dipstick in urinary tract infection

- Urine culture remains the gold standard in the diagnosis of UTI.
- Urine dipstick as POCT may be used to initiate therapy in suspected UTI while awaiting urine culture results.
- Local studies to determine the prevalence of UTI in different populations, the accuracy of urine dipsticks available in the market and the dipsticks markers 'cut-off points' are recommended.

7.2.4 POCT for rapid dengue test in primary care

- There is a need for studies to be conducted on rapid dengue tests as POCT in health facilities without laboratory services with the objective of evaluating its impact on preventing an outbreak.

7.2.5 POCT for full blood count in emergency department

- Technical evaluation and feasibility studies for full blood count as POCT using the newer analysers should be conducted in the emergency departments.

7.2.6 POCT for electrolytes (Na, K, Cl) in critical care

- POCT for sodium, potassium and chloride is recommended as an alternative to central laboratory in the critical care setting where the turnaround time is not acceptable.
- POCT devices for electrolytes need to be evaluated for reliability at the local setting before implementation.

7.3.7 POCT for magnesium in critical care

- Studies on POCT Mg should be carried out and the performance of the analyser conducted before its implementation in the critical care setting.

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Appendix 1

LEVELS OF EVIDENCE

Level	Strength of evidence	Study Design
1	Good	Meta-analysis of RCT, Systematic Review
2	Good	Large sample RCT
3	Good to Fair	Small sample RCT
4	Good to Fair	Non- randomized controlled prospective trial
5	Fair	Non- randomized controlled prospective trial with historical control
6	Fair	Cohort studies
7	Fair	Case- control studies
8	Poor	Non- controlled clinical series, descriptive studies multi-centre
9	Poor	Expert committees, consensus, case reports anecdotes

SOURCE : ADAPTED FROM CATALONIAN AGENCY FOR HEALTH TECHNOLOGY ASSESSMENT, (CAHTA) SPAIN

Appendix 2

Search Strategy

a) POCT for prothrombin time- INR in Primary Care

Date	Database	Keywords	Year Publications	Other limit	No of search	No of relevant title	No of relevant abstract	No of full article obtained
25 May 2006	Medline	Point of care Coagulation	2000-2005	Lang: english Study: Age: Sex: Journal: Publication Type:	74	15	12	4
6 June 2006	Medline	Point of care testing in prothromin time	2000-2005	Lang: english Study: Age: Sex: Journal: Publication Type:	50	12	9	3
11th June 2006	Medline	Cross referenced earlier articles	1995-2006	Lang: English Study: Age: Sex: Journal: Publication Type:	33	10	5	2
13th June	Medline	Cross referenced earlier articles	1995-2006		15	5	5	1
12th October	Medline	Point of care testing INR	2004-2006		60	23	12	2
12th October	Medline	Near patient testing INR	2004-2006		40	5	5	1
12th October	Medline	Point of care testing prothrombin time	2004-2006		48	1	1	1

b) POCT for Hb A1c in primary care

Date	Database	Keywords	Year Publications	Other limit	No of search	No of relevant title	No of relevant abstract	No of full article used	Notes
				Lang: english Study: Age: Sex: Journal: Publication Type:					
10.10.06	pubmed	POCT AND HbA1c			8	2	2	1	
10.10.06	pubmed	Point of care testing AND HbA1c			43	8	5	3	
10.10.06	pubmed	Near patient testing AND HbA1c			13	1	1	0	
10.10.06	pubmed	Bedside testing AND HbA1c			25	2	2	1	

c) POCT for urine dipstick in urinary tract infection

Date	Database	Keywords	Year Publications	Other limit	No of search	No of relevant title	No of relevant abstract	No of full article used	Notes
				Lang: Study: Age: Sex: Journal: Publication Type:					
3/1/07	pubmed	[point of care testing]OR [rapid testing]OR [bedside testing]OR poct AND [urine dipsticks]	Last 10 years		10	2	2	0	
21/7/06	pubmed	[point of care testing]OR [rapid testing]OR [bedside testing]OR poct AND bacteriuria	Last 10 years	Human English Exclude letter and editorials	2	2	2		
21/7/06	Related links		Last 10years			22	22	17	
21/7/06 3/1/07(update)	pubmed	[point of care testing]OR [near patient testing] OR [bedside testing] AND [urinary tract infection]	Last 10 years		28	6	3	1	

d) POCT for rapid dengue test in primary care

Date	Database	Keywords	Year Publication	Other limit	No of search	No of relevant title	No of relevant abstract	No of full article used	Notes
	Pubmed	Point of care test dengue	1995-2006	Lang: English Study: Age: Sex: Journal: Publication Type:	114	4	3	3	
	Pubmed	Rapid diagnostic test	1995-2006	Lang: English Study: Age: Sex: Journal: Publication Type	38	2	1	1	
	DARE/NHS/EED/HTA	Point of care test dengue	1995-2006	-	6	-	-	-	
	Cochrane systematic review	Point of care test dengue	-	-	-	-	-	-	

e) POCT for full blood count in emergency department

Medline ,Googles and OVID searches were carried out between the 12th of June 2006 and 12th of October 2006 using the following key words; 'point of care testing', 'near patient testing', 'bedside testing ', ' Full blood count' , 'complete blood count', 'hemogram', 'rapid test', 'emergency department ' , casualty and HTA . Limits applied were for articles in English, abstracts available and published between 1995 and 2006. The search found seven titles of which only 1 was the most relevant. The search for any HTA reports on POCT in ED was also assisted by the secretariat at the HTA division of the Ministry of Health.

f) POCT electrolytes (Na, K, CL) in critical care.

Literature searches were conducted through on-line Medline database for articles published in English from year 1996-2006. The search strategy included the following terms: point-of-care testing, bedside testing, near patient testing, critical care, intensive care, emergency room, operation room, electrolytes, chemistry, accuracy, reliability, outcome. The search revealed 35 relevant titles. There were 16 relevant articles used in this assessment: 13 full text articles and 3 abstracts.

g) POCT magnesium in critical care

Literature searches were conducted through on-line PubMed database from 1996-2006 and some link articles and through on-line MedLine database. The search strategy includes Point of Care Testing or Near patient testing, bedside testing , Ancillary Testing, NPT, POCT, Decentralized Testing, STAT Laboratory, Satellite Laboratory and Magnesium, Magnesium in critical care testing, Intensive Care, Critical Care and Magnesium Rapid Laboratory Result, Rapid Test, Turnaround time and Magnesium.

EVIDENCE TABLE

Appendix 3

POCT prothrombin time INR in primary care
Clinical Effectiveness

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade
1.	Fitzmaurice DA, Hobbs FD, Murray ET, Holder RL, Allan TF, Rose PE (2000) Oral anticoagulation management in primary care with the use of computerized decision support system (CDSS) and near-patient testing: a randomized, controlled trial. *Arch Intern Med. Aug 14-28; 160(15):2343-8.*	RCT involving 367 patients from 12 primary care practices in the UK. Intervention was a nurse led; POCT and CDSS based service over a period of 12 months. 3 control practices, inter-practice controls, (n=143) used lab based testing and dosing advice given by hospital doctors or through the mail. The 9 intervention practices' patients were further randomized to the ntervention (practice-based anticoagulation clinic) n=122 or control (hospital clinic) n= 102 group. This was called the intra-practice control to estimate the Hawthorn effect. The POCT used was the Thrombotrak. Central labs used ACL, KC-10 or Manchester reagent. Primary outcomes were 1. Proportion of tests in range. 2. % time within target range Secondary outcomes were adverse events	RESULTS: 1. No sig difference in proportion of tests in range between intervention, intra-practice control and inter-practice control. (62 vs. 53 vs. 62%) 2. No sig difference in % time in target range (69 vs. 62%) 3. Overall death rate 3.44 vs. 3.6 per 100 patient years. 4. Serious thrombotic rate 2.28 vs. 5.43 per 100 patient years. 5. Serious hemorrhage 1.14 vs. 0 per 100 patient years Compares favorably to previously published data; major bleeding 1.1 to 2.7 per 100 patient years and stroke and TIA rate of 8 per 100 patient years in a homogenous population on Warfarin Health economic analysis showed an average increase of £100 per patient per year in the intervention arm; £169 vs. £69. Limitation: Confounders of trained nurse and CDSS Costing not applicable to local setting.	3

2.	Shiachi CR, (2002). Reliability of POC PT in a comm. *Clinic, Br. J Hematology Nv;119(2):370-5*	Prospective 6 month randomized cross over study over 1 year, 46 patients, and mean age 65. CoaguCheck (POC) vs. ACL Futura. (Central lab). 2 groups studied (n=23 each group) Parallel INR testing done and dosage basis made from either one system in each group for the first period of 6 months. This was followed with a cross over in the second 6 month period. Questionnaire to patients comparing hospital based clinic to community care clinic.	Success in therapeutic control assessed as % of times INR maintained within INR targets. Mean % of times were identical for both systems. (60.9 vs. 59.3 for Gp 1 and 63.4 vs. 64.3 for Gp2) No sig difference in mean INR; 2.48 vs. 2.5, p=0.08. Mean relative deviation of 9%. Success taken as less than 10% Levels above 4 had higher MRD of 12.6%, but smaller number of samples, n= 40 Clinically relevant standard agreement in 98% Defined as iii. Both tests within target therapeutic range iv. Both tests either above or below therapeutic range. v. Results within 0.4 INR units of each other. Narrow agreement in 97%, defined as… i. Both tests within target therapeutic range (ttr) ii. Both tests above ttr and between 0.8units iii. Both tests below and between 0.4units iv. One was within range and other was within 0.5units 98% patients preferred the community clinic to hospital Journey time by bus was shorter (35 vs. 70min) Journey time by car was shorter (13 vs. 33min) Waiting time in clinic was shorter (9 vs. 33 min) Limitations: 15% withdrawals., Low Power	3
3.	Chamberlain MA, Sageser NA, Ruiz D.(2001) Comparison of anticoagulation clinic patient outcomes with outcomes from traditional care in a family medicine clinic. *J Am Board Fam Pract. Jan-Feb; 14(1):16-21.*	Observational study between 2 anticoagulation management services. The anticoagulant clinic (n=41) used a POCT for INR with immediate dosing advice by a trained pharmacist. The traditional care (n=75) used venepuncture collection by a central laboratory with reports sent to physicians within 24 hrs and dosing advice given through the telephone.	1. The Ac-C group had fewer INR values outside the target range, +/- 0.1, than the traditional care group (40.4% vs. 47.3% P = .022). 2. There was no statistically significant difference in emergency department visit rates caused by adverse events (9.5 vs. 14.8 per 100 patient years.) 3. Inpatient admission rates for the anticoagulation clinic and traditional care groups were not statistically different; however, they were clinically different (4.7 vs. 19.7 admissions per 100 patient years of therapy P = .15) Limitations: Confounders include timing of advice and Person giving the advice.	8

4.	Hobbs FD,(1999) Is the INR reliable? A trial of comparative measurements in hospital laboratory and primary care settings, *J.Clin. Pathol,52;494-497*	Prospective comparative trial. 1. Parallel testing compared between a trained nurse and a lab technician using the same POC (Thrombotrak) on 196 samples 2. Parallel testing compared between POC and 3 different central labs. ACL/IL, KC-10, manual using Manchester reagent. 405 samples from 296 patients tested	1. Satisfactory correlation between nurse and technician on same POC, correlation coefficient (*r*) of 0.96 2. Poor correlation between different central labs, r=0.89, 0.86 and 0.92. 3. Clinically different dosing advices potentially given to 35, 50 and 53% of samples Conclusions 1. Trained nurse as good as technician in performing POC 2. Poor inter-laboratory clinical agreement for INR testing 3. Importance of rigorous Quality Assurance programs at all levels of testing.	8
5.	Shermock Km,(2002) Diff in Warfarin dosing decision based on INR with 2 POC and reference lab, *Pharmacotherapy, Nov;2(11):1397-1404*	Prospective trial, 202 patients and 10 controls. 2 kits; AvoSure and ProTime. Samples taken from patients tested on both POC and compared to lab	AvoSure 78% dosing agreement with lab, mean bias 0.4units ProTime 66% dosing agreement, mean bias 0.5units	8
6.	Reiss RA, (2002) POC vs. Lab monitoring of diff anticoagulation therapies, *Pharmacotherapy, Jun; 22(6):677-85.*	150 patients tested by both POC and lab	Clinical decision agreement varied based on type of anticoagulation used; Warfarin only73%, Warfarin + Hep 47%, War + enox 93%	8

7.	McBane RD,(2005) Imp of device evaluation for POC PT INR testing programs, *Feb Mayo Clin Proc; 80(2);181-6*	CoaguCheck and ProTime 3 evaluated against lab, 94 patients Correlation (r2), relative differences (r) and inappropriate treatment decisions(ITD) were calculated	CoaguCheck: r2=0.9, mean SD 0.2+/-0.31 units, ITD 10% ProTime 3; r2=0.73, mean SD 0.8+/-0.68 units, ITD 22% Reliability of data generated can vary with device used.	8
8.	Murray ET,(1999) A primary care evaluation of 3 near patient coagulometers. J *Clin Patho, 52, 842-845*	Protime, Coagucheck, TAS done by nurses. Gold standard ACL2000 hospital machine. 19 patients and 62 INR results compared	r values varied between 0.908 and 0.96 76-81% clinical decision agreement Claims that inter-laboratory clinical decision agreement can be only 50% (Hobbs FDR, Is the INR reliable? A trial of comparative measurements in hospital and primary care settings. J Clin Pathology 1999;52:494-7	8
9.	DeMiguel D, (2003) Evaluation of the AvoSurePT PRO ad Thrombotrack Nycomed PT monitors, *Am J Clin Pathol.;120:28-33*	62 patients Evaluated to a standard laboratory.	11% clinically significant different results, needing change in medication	8

10.	Chaudhry R,,(2004) Patients satisfy with POC and counseling in community into med practice, *Manag Care InterfaceMar;17(3):44-6*	Questionnaire satisfaction survey of 187 pts after one month of switching to finger-prick POC INR with face to face consultation, from traditional venepucture and delayed telephone dosing instructions. Patients could choose to switch and survey was conveniently done on the first 216 who switched. 87% of them responded. 49% of the 762 patients chose not to switch.	Theory here is that increased patient satisfaction will lead to increased adherence 79.1% prefer the new system. 88.2% higher overall satisfaction. 93% happier with time to receive result. 80.4% happier with time spent at appointment. 74.8% less pain Limitations The 49% who opted against switching to the POC were not surveyed. No survey was done whilst patients were on old system. The results may have been similar. Major variable was opportunity for face to face counseling. That may have been the main reason for increased satisfaction and not necessarily the POC system itself.	8

POCT for prothrombin time- INR in primary care
Reliability

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade	Comment
1.	Hobbs FD,(1999) Is the INR reliable? A trial of comparative measurements in hospital laboratory and primary care settings, *J.Clin. Pathol.;52;494-497*	Prospective comparative trial. 3. Parallel testing compared between a trained nurse and a lab technician using the same POC (Thrombotrak) on 196 samples 4. Parallel testing compared between POC and 3 different central labs. ACL/IL, KC-10, manual using Manchester reagent. 405 samples from 296 patients tested	1. Satisfactory correlation between nurse and technician on same POC, correlation coefficient (*r*) of 0.96 2. Poor correlation between different central labs, r=0.89, 0.86 and 0.92. 3. Clinically different dosing advices potentially given to 35, 50 and 53% of samples Conclusions 1. Trained nurse as good as technician in performing POC 2. Poor inter-laboratory clinical agreement for INR testing 3. Importance of rigorous Quality Assurance programs at all levels of testing.	8	
2.	McBane RD,(2005) Imp of device evaluation for POC PT INR testing programs, *Feb Mayo Clin Proc; 80(2);181-6*	CoaguCheck and ProTime 3 evaluated against lab, 94 patients Correlation (r2), relative differences (r) and inappropriate treatment decisions(ITD) were calculated	CoaguCheck: r2=0.9, mean SD 0.2+/-0.31 units, ITD 10% ProTime 3; r2=0.73, mean SD 0.8+/-0.68 units, ITD 22% Reliability of data generated can vary with device used.	8	
3.	Murray ET, (1999) A primary care evaluation of 3 near patient coagulometers. *J Clin Patho, 52, 842-845*	Protime, Coagucheck, TAS done by nurses. Gold standard ACL2000 hospital machine. 19 patients and 62 INR results compared	r values varied between 0.908 and 0.96 76-81% clinical decision agreement Claims that inter-laboratory clinical decision agreement can be only 50% (Hobbs FDR, Is the INR reliable? A trial of comparative measurements in hospital and primary care settings. J Clin Pathology 1999;52:494-7	8	

4.	Gosselin R,(2000) A comparison of POC instruments for oral anticoag with standard laboratory, *Thromb Hamostat May; 83(5):698-703.*	9 kits tested against ref lab.Coumatrak, CoaguCheck, TAS PT-One, TAS PTNC,TAS PT, HemachronJr Sig, Protime Microcoag system, Medtronics ACT II	r for all POC compared with lab >0.9. Most tests demonstrate sig diff in INR mean values. Suggesting biases. Clinicians must be aware of diff between POC and lab.	8	
5.	Pollier L, (2003) Reliability of INR from 2 POC systems comparison with conventional method, *BMJ, Jul 5;327(7405):30*	600pts, 10 centres Evaluation study CoagueCheckMini and TAS PT-NC (RapidpointCoag)	21.3% difference. Better QC needed Gives suggestions on improving the accuracy and precision of POC monitors.	8	
6.	Poller L, ECAA (2003). Correction of displayed INR on 2 POC by independent ISI calibration, *Brit J of Haem, (122), 944-949*	Coagucheck Mini and TAS PT-NC7 of the previous 10 centres were independently	Differences reduced from 21 to 3.5%. Syst A from 19-9.5% and B from 6.8 to 0.3% Recommends external quality control of individual POCTs	8	
7.	Nutesu EA,(2004) POC for oral anticoag therapy, *Sem Thromb Hemost, Dec;30(6):697-702*	Review article of 12 different monitors looking at their accuracy and precision	Advantages of POC over lab Ease of use, perceived positively by patients, short test duration, faster TOT for decision making, greater provider patent interaction Accuracy (r) ranges from 0.7 to 0.99 and precision vary (3-6%) between devices. Devices cannot be used interchangeably. Individual device performance cannot be generalised	9	

POCT for HbA1c in primary care
Clinical Effectiveness

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade	Comment
1	Christopher D. Miller, Catherine S. Barnes, Lawrence S. Phillips, David C. Ziemer, Daniel L. Gallina, Curtiss B. Cook, Sandra D. Maryman and Imad M. El-Kebbi. (2003) Rapid HbA1c Availability Improves Clinical Decision-Making in an Urban Primary Care Clinic *Diabetes Care*; 26:1158-1163	Prospective randomized controlled trial N=597	Rapid A1c availability resulted in more frequent intensification of therapy when A1c was ≥7.0% at the baseline visit (51 vs. 32% of patients, *P* = 0.01), particularly when A1c was >8.0% and/or random glucose was in the 8.4–14.4 mmol/l range (151–250 mg/dl). In 275 patients with two follow-up visits, A1c fell significantly in the rapid group (from 8.4 to 8.1%, *P* = 0.04) but not in the routine group (from 8.1 to 8.0%, *P* = 0.31). CONCLUSIONS—Availability of rapid A1c measurements increased the frequency of intensification of therapy and lowered A1c levels in patients with type 2 diabetes in an urban neighborhood health center.	good	

2	Cagliero E, EV Levina and DM Nathan (1999) Immediate feedback of HbA1c levels improves glycemic control in type 1 and insulin-treated type 2 diabetic patients Diabetes Care; Vol 22, Issue 11; pages: 1785-1789	Randomised controlled trial N = 201	HbA1c levels decreased significantly at 6 and 12 months in the immediate assay group (-0.57 +/- 1.44 and -0.40 +/- 1.65%, respectively; P < 0.01) but did not change in the control group (-0.11 +/- 0.79 and -0.19 +/- 1.16%, respectively; NS). The changes were similar for both type 1 and type 2 diabetic patients. There were no differences in the rates of hypoglycemic events or use of health care resources. CONCLUSIONS: In the setting of a controlled randomized trial, the immediate feedback of HbA1c results at the time of patient encounters resulted in a significant improvement of glycemic control at 6-month follow-up and persisted for the 12-month study. The introduction of this assay was positively received by both patients and physicians.	good	Insulin treated patients

3	Thaler LM, DC Ziemer, DL Gallina, CB Cook, VG Dunbar, LS Phillips and IM El-Kebbi. (1999) Diabetes in urban African-Americans. XVII. Availability of rapid HbA1c measurements enhances clinical decision-making Diabetes Care; Vol 22, Issue 9 1415-1421	The research design was a randomized clinical trial in which rapid HbA1c results were made available to providers on even days of the month (rapid, n = 575), but delayed by 24 h on odd days (conventional, n = 563). Adjustment of therapy for patients with type 2 diabetes was considered appropriate if therapy was intensified for HbA1c values >7% or not intensified for HbA1c values < or =7%. A post-hoc analysis was also performed using patients (n = 574) who returned for follow-up 2-7 months later to ascertain the effect of rapid HbA1c availability on subsequent glycemic control. Participants studied - 57	Rapid HbA1c availability resulted in more appropriate management compared with conventional HbA1c availability (79 vs. 71%, P = 0.003). This difference was due mainly to less frequent intensification when HbA1c levels were < or =7% (10 vs. 22%, P < 0.0001) and slightly to more frequent intensification for patients with HbA1c values >7% (67 vs. 63%, P = 0.33). Over 2-7 months of follow-up, HbA1c rose more in patients with conventional HbA1c compared with rapid results (0.8 vs 0.4% p=0.02). In patients with initial HbA1c >7%, rapid HbA1c results had a favorable impact on follow up HbA1c independent of the decision to intensify therapy (p=0.03) CONCLUSIONS: Availability of rapid HbA1c determinations appears to facilitate diabetes management. The more favorable follow-up HbA1c profile in the rapid HbA1c group occurs independently of the decision to intensify therapy, suggesting the involvement of other factors such as enhanced provider and/or patient motivation.	good	Speciality diabetes clinic

4	Grieve R Beech J Vincent J.Mazurkiewicz Near patient testing in diabetes clinics: appraising the costs and outcomes. (1999) Health Technology Assessment; Vol. 3: No. 15	A controlled trial compared the effect of the testing method on the process of care. A total of 599 patients were alternately allocated to either nurse NPT or conventional testing. The number of management changes to the patients' diet, insulin or tablet therapy was recorded for all the patients	Patients were more likely to have a change in management related to their glycaemic control if they had been in the NPT rather than the conventional testing group Subgroup analysis showed that patients with poor glycaemic control were more likely to have management changes in the NPT than in the conventional group This suggested that the process of care may be improved if results related to glycaemic control (HbA_{1C}) are provided by NPT	fair	

5	Shephard MD, Mazzachi BC, Shephard AK, McLaughlin KJ, Denner B, Barnes G.(2005) The impact of point of care testing on diabetes services along Victoria's Mallee Track: results of a community-based diabetes risk assessment and management program. Rural Remote Health. Jul-Sep; 5(3):371.	54 diabetes patients The multidisciplinary 'one-stop' service for the management of people with diabetes involved having a single appointment with their local GP, during which time they met the local diabetes educator and podiatrist as well as the GP, and on-site POC testing (POCT) performed for haemoglobin A1c (HbA1c), urine albumin : creatinine ratio (ACR), lipids and glucose. A written survey was conducted among patients with diabetes, local GPs and local health professionals to assess the level of satisfaction with the project and the use of POCT, and to assist policy development for the future planning and development of diabetes services along the Mallee Track region.	Since the introduction of the 'one-stop shop', the percentage of persons achieving optimal glycaemic control (HbA1c <7%) has increased by 30% (from 33% to 63%), the percentage achieving controlled glycaemia (HbA1c < 8%) has increased by 32% (59% to 91%), while the number exhibiting poor control has reduced by 7% (13% to 6%).Falls in cholesterol and blood pressure were also observed There was overwhelming support within this group for the use of POCT as part of their management, because it was convenient, encouraged self-management and enhanced doctor-patient relationships. The proportion of patients with diabetes who were satisfied/very satisfied with the available diabetes services was significantly greater following the introduction of the project Health professionals felt confident in using the POC analysers and believed the program had raised community awareness about diabetes and enhanced community ownership. Most patients felt it as an advantage not having to return to the clinic for result	fair	

6	Matchar DB, McCrory DC, Samsa GP, Patwardhan M, Lobaugh B, Liu K. (2005) Point of care Testing of Hemoglobin A1c Agency for Healthcare Research and Quality	Influence of performing HbA1c at the point of care on patient management decisions compared to performing in lab2005 setting	Evidence suggests POCT HbA1c can effect management decisions, such as appropriate intensification of therapy for patients with substantial elevation of HbA1c, intensification of therapy for patients who have mild hyperglycaemia if they also have an elevated HbA1c level; and diminished inappropriate intensification of therapy for patients under good control by HbA1c but who have a high POC glucose result	good	Technology assessment
7	Matchar DB, McCrory DC, Samsa GP, Patwardhan M, Lobaugh B, Liu K (2005) Point of care Testing of Hemoglobin A1c Agency for Healthcare Research and Quality	Impact of performing HbA1c at the point of care on clinical outcomes compared to performing the test in lab setting	Improvement in HbA1c between 0.2-0.8%. However available data indicate that these results may not necessarily be durable or generalizable. Few data are available beyond six months and twelve month data from one study suggest a smaller effect on HbA1c of point of care at twelve than at six months	good	Technology assessment

POCT for HbA1c in primary care
Reliability

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade	Comment
1	David D Martin, Mark D S Shephard, Hayley Freeman, Max K Bulsara, Timothy W Jones, Elizabeth A Davis and Graeme P Maguire (2005) Point-of-care testing of HbA1c and blood glucose in a remote Aboriginal Australian community MJA; 182 (10): 524-527	Cross- sectional study comparing POC HbAIc results with those from corresponding venous samples measured in a reference laboratory N=88	Values for POC capillary HbA1c and laboratory HbA1c were identical: mean 7.06%; and median, 6.0%. The correlation coefficient *r* for POC and laboratory results was 0.99 for HbA1c The mean difference in results was <0.01% for HBA1c (95% CI,-0.07% to 0.07%; LOA, - 0.66% to 0.66%; p=0.95), respectively. Conclusions: POC capillary HBA1c testing offers an accurate, practical, community-friendly way of monitoring diabetes in rural and remote clinical settings	fair	Rural setting DCA 2000+

2	Carter JS, CA Houston, SS Gilliland, GE Perez, CL Owen, DR Pathak and RR Little Rapid HbA1c testing in a community setting Diabetes Care, Vol19, Issue 7 764-767,	Seven community members in 1994 and six new community members in 1995 were trained over 2 days, using standard protocol, to operate the DCA 2000 HbA1c analyzer and to collect two capillary blood samples from participants in the Native American Diabetes Project. Duplicate DCA 2000 HbA1c measurements performed by the community workers were compared with measurements from a high-performance liquid chromatography (HPLC) system.	Comparison of the mean DCA 2000 results with those of HPLC showed high validity, with the absolute relative difference between the mean DCA 2000 and the external reference of HPLC (magnitude of mean DCA 2000-HPLC magnitude of /HPLC) as 4.0 and 2.0% for 1994 and 1995, respectively. The Pearson correlation coefficients (r) between these two measures were 0.968 and 0.996 for 1994 and 1995, respectively. The within-run reliability was excellent, with an intraclass correlation coefficient of reliability of 0.959 and 0.975 for paired samples, for 1994 and 1995 respectively. The mean coefficient of variation for these paired measures was 3.0% in 1994 and 2.8% in 1995. All correlation coefficients were statistically significant ($P < 0.0001$). CONCLUSIONS: The DCA 2000 gave valid and reliable HbA1c results when operated in a community setting by non-medical personnel.	fair	Community setting Non-medical personnel
3	Guerci B, Durain D, Leblanc H, Rouland JC, Passa P, Godeau T, Charbonnel B, Mathieu Daude JC, Boniface H, Monnier L, Dauchy F, Slama G, Drouin .(1997) Multicentre evaluation of the DCA 2000 system for measuring glycated haemoglobin. DCA 2000 Study Group Diabetes Metab. Jun;23(3):195-201	This study compared the performance of the DCA 2000 system for HblAc measurement with that of high-performance liquid chromatography (HPLC). A total of 1.016 insulin-dependent and non-insulin-dependent diabetic patients from 5 outpatient clinics took part.	The correlation coefficient assayed by the two methods was 0.95. The mean variation was -0.116 and the 95% confidence interval -1.23 to 0.998. The sensitivity of DCA 2000 was 91%, and the specificity 94% This study confirms the reliability of DCA 2000 for measuring glycated Hb. The system is easy to use and provides valuable information for the care of the diabetic patients.	fair	

4	Hawkins RC (2003) Comparison of Four Point-of-Care HbA1c Analytical Systems against Central Laboratory Analysis Singapore Med J , Vol 44(1) : 008-011	Methods: Analytical inaccuracy was assessed by analysis of 110 patient samples on all five analytical platforms (Biorad Diastat, Drew DS5, Bayer DCA 2000, Nycomed Nycocard And Roche Tinaquant (used in central lab). Analytical imprecision was assessed by analysis of two levels of patient sample four times daily for six days, as well as analysis of two levels of commercial control	The Diastat and DCA2000 systems gave the best performance with acceptable imprecision and good agreement with both The central lab and each other.	fair	
5	Matchar DB, McCrory DC, Samsa GP, Patwardhan M, Lobaugh B, Liu K (2005) Point of care Testing of Hemoglobin A1c Agency for Healthcare Research and Quality	Performance of tests measuring HbA1c in the point of care setting and the lab setting	Reasonable to say that devices which satisfy criteria for accuracy and precision disseminated by NGSP certification protocol are functionally equivalent to conventional devices Axis- Shield Nycocard, Bayer DCA 2000. Bio-Rad D-10, Bio-Rad Dia-STAT, Drew Scientific DS5, Metrika A1c Now, Provalis Glycosal (Bio-Rad MicroMat and Cholestech GDX) – NGSP protocol DCA 2000, A1c Now, Provalis Glycosal – CLIA waived as well	fair	Technology assessment

POCT for urine dipstick in urinary tract infection
Clinical Effectiveness

<table>
<tr><th>No</th><th>Author, title, Journal, Year, Volume, Page Number</th><th>Study Design, Sample Size, Follow up</th><th>Outcomes & Characteristics</th><th>Grade</th><th>Comment</th></tr>
<tr>
<td></td>
<td>Patel HD, Livsey SA, Swann RA, Bukhari SS. (2005)

Can urine dipstick testing for urinary tract infection at point of care reduce laboratory workload?

J Clin Pathol. Sep; 58(9):951-4.</td>
<td>Descriptive study
Urinary dipstick testing algorithm for infection associated markers to screen out negative urine workload among inpatients of University Hospitals of Leicester NHS Trust (Leicester Royal infirmary (LRI), Leicester General Hospital (LGH and Glenfield General Hospital (GGH)</td>
<td>Results of screening using different marker combinations:
<table>
<tr><th>Marker</th><th>Culture missed</th><th>%screened out</th><th>NPV%</th><th>Sensitivity%</th><th>Specificity%</th></tr>
<tr><td>L/N/B/P</td><td>3</td><td>16.3</td><td>98.3</td><td>98.3</td><td>19.2</td></tr>
<tr><td>L/B/P</td><td>4</td><td>16.8</td><td>97.8</td><td>97.8</td><td>19.8</td></tr>
<tr><td>L/N/B</td><td>5</td><td>25.7</td><td>98.2</td><td>97.2</td><td>30.2</td></tr>
<tr><td>L/N/P</td><td>6</td><td>28.2</td><td>98.0</td><td>96.7</td><td>33.1</td></tr>
<tr><td>N/B/P</td><td>18</td><td>27.9</td><td>94.0</td><td>90.0</td><td>31.5</td></tr>
<tr><td>L/N</td><td>17</td><td>48.0</td><td>96.7</td><td>90.6</td><td>55.8</td></tr>
</table>
Based on basis that 4 markers offered the best sensitivity and negative predictive value, and the lowest missed out true infections, an algorithm using negative 4 markers to reduce number of negative urines was introduced.
CONCLUSIONS: Two years after the algorithm and promoting reagent strips and strip readers, a reduction in the urine workload against increasing specimen load.
<table>
<tr><th>Hospital</th><th>One year before algorithm</th><th>One year after algorithm distribution(% change)</th><th>2 years after algorithm distribution(%change)</th></tr>
<tr><td>LRI</td><td>21267</td><td>-237(-1.1)</td><td>-997(-4.7)</td></tr>
<tr><td>LGH</td><td>22065</td><td>-2333(-10.6)</td><td>-1917(-8.7)</td></tr>
<tr><td>GGH</td><td>6571</td><td>+557(+8.8)</td><td>+2311(+35.2)</td></tr>
<tr><td>Total</td><td>49903</td><td>-1993(-4.0)</td><td>-603(-1.2)</td></tr>
</table>
Impact of dipstick algorithm on %of positive urines for 2 years
LRI:+1.7 (1yr);+2.7(2yr)
LGH:+3.5(1yr);+4.5(2yr)
GGH:+2.6(1yr);+1.2(2yr)</td>
<td></td>
<td></td>
</tr>
</table>

	Lammers Kovacs RL,Gibson S, D,Sears W,Strachan G (2001) Comparison of test characteristics of urine dipstick and urinalysis at various test cutoff points. Ann Emerg Med. Nov; 38(5):505-12.	Prospective, observational study Multistix 9 SG reagent strip 343 adult female ≥18 years old with UTI symptoms. Setting emergency department or intermediate care center Urine collection – midstream clean catch or catheterized 12 withdrawn because missing results	Prevalence 46% (152/331) If urine dipstick results are defined as positive when leukocyte esterase or nitrite is positive or blood is more than trace, the over treatment rate is 47% (156/331) and the under treatment rate is 13% (43/331). If urinalysis results are defined as positive when WBCs are more than 3 per high-power field or RBCs are more than 5 per high-power field, the overtreatment rate is 44% (146/331) and the undertreatment rate is 11% (36/331). CONCLUSION: In this patient population, similar over treatment and under treatment rates were identified for various test cutoff points for urine dipstick tests and urinalysis. Although a urine dipstick may be equivalent to a urinalysis for the diagnosis of UTI, the limitations in the diagnostic accuracy of both tests should be incorporated into medical decision making. *(Table 1*)	Good	Full text Limitations: 1.only women 2.no sample size analysis Positive culture ≥100000 colonies 1 or 2 uropathogen per ml urine Negative culture < 100000 colonies per ml 1 or 2 species Over treatment = 1 minus the PPV Under treatment = the probability of an erroneous decision to withhold treatment on the basis of a negative result or 1 minus NPV

Test characteristics for dipstick performance when positive culture is defined as 10^4 cfu/ml (Lammers)
T *(Table 1)*

Models paired	LE		Nitrite		Blood	Sensitivity %	Specificity %	PPV %	NPV %	Over treatment rate%	Under treatment rate%
A	>0	or	+	Or	>0	99	19	51	94	49	6
B	>0	or	+	or	trace	96	27	53	87	47	13
C	>0	or	+			92	39	56	83	44	17
	>0		NA			91	41	56	82	44	18
D	>trace	Or	+			85	53	60	78	40	22
E	>1	Or	+			77	66	66	74	34	26
	>2	Or	+			53	83	72	64	28	36
	>0	&	+			30	91	74	57	26	43
	>trace	&	+			27	93	77	56	23	44
	>1	&	+			21	96	82	55	18	45
	>2	&	+			9	99	88	52	13	48

NA-not applicable

POCT for urine dipstick in urinary tract infection
Reliability

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade	Comment
1.	Sharief N, Hameed M , Petts D (1998) Use of rapid dipstick tests to exclude urinary tract infection in children. Br J Biomed Sci.Dec;55(4):242-6	Descriptive study To evaluate the use of rapid dipstick tests to exclude UTI in children. 375 children (229 males, 146 females) age 2 days to 16 years old inpatients with possible UTI. 124 ‹ one year old. Comparing Urine dipstick for nitrite and leucocyte esterase, urine culture and microscopy. Clean catch collection- 158 (83 male,75 female) and sterile bag collection- 167 (111 male,56 female)	Nitrite alone – sensitivity 54.6,specificity 96.8, PPV 37.5, NPV 98.4 LE alone- sensitivity 100,specificity 78.1, PPV 13.9, NPV – 100 Nitrite and LE- sensitivity-54.6, specificity 98.7, PPV 60.0 , NPV 96.9 In children < 1 year old, NPV and specificity of nitrite and LE were 96.7% and 99.2% respectively. The LE test - NPV for pyuria of 94.3% ,sensitivity 75.9%, specificity of 86.9% and PPV 55.7% In children < 1 year, these values were 93.1% and 84.4% respectively. The use of dipsticks to detect of urinary nitrate and LE is recommended. The absence of both nitrite and LE in urine indicates that UTI is unlikely; however, positive dipstick tests for nitrite and/or LE are not specific indicators of UTI, and should not replace lab examination. The dipstick method is most likely useful as a screening test to exclude UTI in children, but may be less suitable for infants. It should not be used to diagnose UTI.	poor	Full text Definition of : 1. UTI:Pure growth≥10^5 organisms /ml and pyuria 2.Pyuria :≥20 WBC/mm 3 3.inconclusive culture: 10^{4-}-10^5 organisms/ml and pyuria 4.Negative: No growth; pure growth≥10^5organisms without pyuria; 10^{4-}-10^5organisms /ml without pyuria;, <10^4 organisms/ml and mixed growth Limitation: Possible High contamination rate in urine bag and clean catch samples especially young children

<table>
<tr>
<td>2.</td>
<td>Zaman Z, Borremans A, Verhaegen J,Verbist L, Blanckaert N(1998)

Disappointing dipstick screening for urinary tract infection in hospital inpatients.

J Clin Pathol. Jun;51(6):471-2.</td>
<td>Descriptive study
AIM: To compare the performance of 1)LE and nitrite dipstick tests 2)direct microscopic counting WBC and bacteria per ul of urine 3)spun urine sediment microsopy for bacteria and WBC per HPF
420 inpatients over 3 weeks.
(4 paediatrics, 5 oncology, 39 O&G, 51 surgery, 57 geriatrics, 68 ambulant consultation, 93 internal medicine and 103 postoperative intensive care.

234 females and 186 males
Age 17 days to 97 years</td>
<td>72 (17%) patients' urines had positive culture (≥10^5 CFU/ml)

RESULTS:

<table>
<tr><th>+</th><th>n</th><th>FN %</th><th>FP %</th><th>Sen %</th><th>Spe %</th><th>PPV %</th><th>NP V%</th></tr>
<tr><td>LE alone</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>>10WBC/ul</td><td>204</td><td>43</td><td>6</td><td>57</td><td>94</td><td>91</td><td>68</td></tr>
<tr><td>>20 WBC/ul</td><td>136</td><td>23</td><td>9</td><td>77</td><td>91</td><td>81</td><td>88</td></tr>
<tr><td>>5WBC/HPF</td><td>126</td><td>16</td><td>11</td><td>84</td><td>90</td><td>77</td><td>93</td></tr>
<tr><td>≥5x10 4 CFU/ml</td><td>90</td><td>31</td><td>23</td><td>69</td><td>77</td><td>45</td><td>90</td></tr>
<tr><td>≥10 5</td><td>72</td><td>26</td><td>24</td><td>74</td><td>76</td><td>39</td><td>93</td></tr>
<tr><td>Reference cutoff ≥5x10 4CFU/ml</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Nitrite</td><td>90</td><td>73</td><td>7</td><td>27</td><td>93</td><td>51</td><td>82</td></tr>
<tr><td>Nitrite/LE</td><td>90</td><td>28</td><td>23</td><td>72</td><td>77</td><td>46</td><td>91</td></tr>
<tr><td>Nitrite+LE</td><td>90</td><td>77</td><td>6</td><td>23</td><td>94</td><td>51</td><td>82</td></tr>
<tr><td>Significant Bacteria/HPF</td><td>90</td><td>17</td><td>40</td><td>83</td><td>60</td><td>36</td><td>93</td></tr>
<tr><td>Reference cutoff ≥10 5 CFU/ml</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Nitrite</td><td>72</td><td>67</td><td>6</td><td>33</td><td>94</td><td>52</td><td>87</td></tr>
<tr><td>Nitrite/LE</td><td>72</td><td>22</td><td>25</td><td>78</td><td>75</td><td>39</td><td>94</td></tr>
<tr><td>Nitrite+LE</td><td>72</td><td>71</td><td>6</td><td>29</td><td>94</td><td>51</td><td>87</td></tr>
<tr><td>Significant (>50) Bacteria/HPF</td><td>72</td><td>8</td><td>40</td><td>92</td><td>60</td><td>32</td><td>97</td></tr>
</table>

CONCLUSIONS: LE and nitrite dipstick tests are not suitable for screening for UTI in inpatient setting because of high negative rates.</td>
<td>Poor</td>
<td>Full text

Bayer Multistix 8 SG read by Clinitek 200+

Abbreviations
FN=false negative
FP=false positive
Sen=sensitivity
Spe=specificity

Limitations- no consideration of possibility of contamination by method of urine collection

Positive culture≥10^5CFU/ml</td>
</tr>
</table>

3.	Al-Daghistani HI, Abdel-Dayem M. (2002) Diagnostic value of various urine tests in the Jordanian population with urinary tract infection Clin Chem Lab Med. Oct; 40(10):1048-51.	Comparing the performance of leukocyte esterase and nitrite reductase dipstick tests with microscopic examination and uroculture in cases with clinically suspected urinary tract infection (UTI). 504 Jordanian patients.	Significant bacteriuria in 117 cases (23.2%) with positivity of 59% and 68.5% for the presence of nitrite reductase and LE, respectively. The dipstick LE and nitrite testing - sensitivity of 68.5% and 59% to detect bacteriuria in UTI cases and specificity of 73.5% and 78%, respectively. The PPV of the tests was 44% and 60%, and the NPV 88.5% and 86.2%, respectively. Microscopic WBC - 86.5% specificity but low sensitivity. Urine dipstick results and pyuria significantly correlated with the results of urine culture but more false-positive results, (13.4-26.6%). The probability of growing a urinary pathogen correlated with urinary WBC counts. A combination of pyuria and urine dipstick testing appears to be a very useful marker of UTI. Urine C&S can be omitted if both tests negative.		Abstract

4.	Gorelick MH, Shaw KN.(1999) Screening tests for urinary tract infection in children: A meta-analysis Pediatrics. Nov;104(5):e54	Systematic review and meta analysis regarding performance of rapid diagnostic tests for UTI in children. Published articles from MEDLINE search from 1966 to 1998 reporting the performance of urine dipstick tests (leukocyte esterase [LE] and/or nitrite), Gram stain, or microscopic analysis of spun or unspun urine in the diagnosis of UTI in children ≤12 years old.	1489 titles; 26 articles met all criteria for inclusion. Significant heterogeneity among studies for nearly all tests for both TPR and FPR. Dipstick – Any nitrite only- 13 studies, summary estimate of FPR 0.02, TPR 0.50 Any LE only-7 studies, FPR 0.16, TPR 0.83 Any nitrite or LE-9 studies, FPR 0.07, TPR 0.88 Both nitrite and LE-5 studies, FPR 0.04, TPR 0.72 Gram stain (any organism) – 5 studies, FPR 0.05, TPR 0.93 Microscopic centrifuged urine≥5 WBC/hpf - 5 studies, FPR 0.21, TPR 0.67 Microscopic uncentrifuged urine ≥ 10 WBC/mm³ – 9 studies, FPR 0.11, TPR 0.77 The presence of bacteria on Gram stain on an uncentrifuged urine specimen had the best combination of sensitivity (0.93) and FPR (0.05). Urine dipstick tests performed nearly as well, with a sensitivity of 0.88 for the presence of either LE or nitrite and an FPR of 0.04 for the presence of both LE and nitrite. Pyuria had lower TPR and higher FPR: for presence of >5 WBC/HPF in a centrifuged urine sample, the TPR was 0.67 and the FPR was 0.21, whereas for >10 white blood cells per mm(3) in uncentrifuged urine, the TPR was 0.77 and the FPR was 0.11. CONCLUSIONS: Both Gram stain and dipstick analysis for nitrite and LE perform similarly in detecting UTI in children and are superior to microscopic analysis for pyuria. (Table 2)	Good	Full text

Diagnostic test characteristics from published studies (Table 2)

Test criterion for positivity	Number of studies	FPR Range	TPR Range	Summary Estimate of FPR†	Summary Estimate of TPR‡
Dipstick					
Any nitrite only	13	0, 0.05§	0.16, 0.72§	0.02	0.50
Any LE only	7	0.05, 0.29§	0.64, 0.89§	0.16	0.83
Any nitrite or LE	9	0.02, 0.24§	0.71, 1.0§	0.07	0.88
Both nitrite and LE	5	0, 0.05§	0.14, 0.83§	0.04	0.72
Gram stain,any organisms	5	0, 0.13§	0.80, 0.98§	0.05	0.93
Microscopic of centrifuged urine≥ 5WBC/hpf	5	0.16, 0.23§	0.55, 0.88§	0.21	0.67†
Microscopic of uncentrifuged urine≥10 WBC/mm³	9	0.05, 0.63§	0.57, 0.92§	0.11	0.77

†pooled estimate from combining all studies with more stringent definition of UTI

‡Estimated TPR at summary FPR, derived from summary ROC curve based on studies with more stringent definition of UTI

§$P<0.05$ for x^2 test of heterogeneity.

5.	Shaw KN,McGowan KL, Gorelick MH, Schwartz JS. (1998) Screening for urinary tract infection in infants in the emergency department: which test is best? Pediatrics. Jun;101(6):E1	Prospective, Cross-sectional study. 3873 infants <2 years of age in hospital emergency department Period 12/12 1994-2/2/1996 Method urethral catheterization 1.Compare urine dipstick tests for leukocyte esterase or nitrites, enhanced urinalysis (UA) (urine WBC count/mḿ plus Gram stain), Gram stain alone, and dipstick plus microscopic UA (WBC and bacteria per high-powered field) with urine culture results 2.Compare cost and outcomes of the 3 possible screening strategies (bedside dipstick and culture for all ; enhanced UA for all ,culture positive results only ; and urine cell count for all, culture +/- Gram stain positive results only) based upon a cohort of 1000 children	3873 cultures, 105 (2.7%) positive and 454 (11.7%) contaminated. RESULTS: The enhanced UA most sensitive (94%), but more false-positive results (16%) than the dipstick or Gram stain (3%). Sensitivity for dipstick 79%, cell count 82%, Gram stains 82% and positive dipstick plus UA 83%. False positive for cell count and positive dipstick plus UA were 13%.All tests had high NPV (≥ 99%). At more specific definitions, the sensitivity of all tests reduced but specificity improved especially UA and combination dipstick and microscopy (,1% false positive results) CONCLUSION: No rapid test can detect UTI in all infants. Urine C&S for all infants & presumptive treatment only if significant positive dipstick results. The enhanced UA is most sensitive, but is less specific. (Table 3)	good	Full text Positive urine culture ≥ 10^4 (CFU/ml) of urinary tract pathogens. Contamination – growth ≥500 CFU/ml of mixed organisms or nonpathogens Negative – no growth (<100 CFU/ml) or growth of < 500 CFU/ml Urine dipstick test Multistix 10 SG 228 Bayer The cost of the tests are calculated using Labtrack cost analysis software

Comparison of rapid screening tests for UTI (Table 3)

Test	N	Positive cultures	Sensitivity %	Specificity%	PPV
Most sensitive definitions					
Dipstick (≥trace LE or + nitrite)	3394	95	79(69,86)	97(97,98)	46(38,54)
Enhanced UA (≥10 WBC/mm³ or + Gram stain)	2016	52	94(83,99)	84(82,86)	13(10,17)
Cell count(≥10WBC/mm3)	2193	57	82(70,91)	87(86,89)	15(11,19)
Gram stain(any bacteria)	2305	62	81(68,89)	97(96,98)	43(34,52)
Dipstick plus UA* Dipstick+ or UA(≥5 WBC/HPF or any bacteria/HPF)	3394	95	83(74,90)	87(86,88)	16(12,19)
Most specific definitions					
Dipstick(≥moderate LE or nitrite)	3394	95	73(62,81)	99(98,99)	61(52,70)
Enhanced UA(≥10WBC/mm³ plus +Gram stain)	2016	52	75(61,86)	99(99,100)	80(66,90)
Gram stain(single organism on Gram stain)	2305	62	79(67,88)	98(97,98)	49(39,59)
Dipstick plus UA* Dipstick+ plus UA +(≥5WBC plus bacteremia/HPF)	3394	95	73(62,81)	98(98,99)	57(47,65)

*UA performed only if any component of protein, blood, glucose, LE, nitrite, ketones is positive on dipstick.
+positive

<table>
<tr>
<td>6.</td>
<td>Preston A,O'Donnell T, Phillips CA. (1999)

Screening for urinary tract infections in a gynaecological setting: validity and cost-effectiveness of reagent strips.

Br J Biomed Sci.;56(4):253-7</td>
<td>Prospective study
To test the validity and cost-effectiveness of reagent-strip analysis (LE & nitrite) compared with microbiological laboratory testing for mass screening of urine for UTI in a gynaecological setting.
Over a six-month period, 228 women in a gynaecological ward.</td>
<td>Comparison of LE, nitrite and combination to diagnose UTI
<table>
<tr><td>Results</td><td>LE</td><td>nitrite</td><td>LE & nitrite</td></tr>
<tr><td>True -</td><td>177</td><td>198</td><td>177</td></tr>
<tr><td>False-</td><td>7</td><td>10</td><td>1</td></tr>
<tr><td>True+</td><td>21</td><td>18</td><td>27</td></tr>
<tr><td>False+</td><td>23</td><td>2</td><td>23</td></tr>
<tr><td>Total</td><td>228</td><td>228</td><td>228</td></tr>
</table>
Comparison of sensitivity, specificity, PPV and NPV of LE, nitrite and combined LE/nitrite
<table>
<tr><td></td><td>nitrite</td><td>LE</td><td>combined</td></tr>
<tr><td>sensitivity</td><td>64.3</td><td>75.0</td><td>96.4</td></tr>
<tr><td>Specificity</td><td>99.0</td><td>88.5</td><td>88.5</td></tr>
<tr><td>PPV</td><td>90.0</td><td>47.7</td><td>54.0</td></tr>
<tr><td>NPV</td><td>95.3</td><td>96.2</td><td>99.4</td></tr>
</table>
The use of combined LE and nitrite reagent strips in a mass-screening programme in a gynaecological setting proved both valid and cost-effective.</td>
<td>fair</td>
<td>Full text

Multistix 8SG strip

Positive culture≥10^5</td>
</tr>
<tr>
<td>7.</td>
<td>Little P, Turner S, Rumsby K, Warner G, Moore M, Lowes JA, Smith H, Hawke C, Mullee M.
(2006)

Developing clinical rules to predict urinary tract infection in primary care settings: sensitivity and specificity of near patient tests (dipsticks) and clinical scores.

Br J Gen Pract.
Aug;56(529):606-12</td>
<td>Aim: To estimate independent clinical and dipstick predictors of infection and to develop clinical decision rules.
Validation study of clinical and dipstick findings compared with laboratory testing.
General practices in the south of England.427 women with suspected UTI</td>
<td>UTI was confirmed in 62.5% of women with suspected UTI. Only nitrite, LE (+ or greater), and blood (haemolysed trace or greater) independently predicted diagnosis (adjusted odds ratios 6.36, 4.52, 2.23 respectively). A dipstick decision rule, based on having nitrite, or both leucocytes and blood, was moderately sensitive (77%) and specific (70%); positive predictive value (PPV) was 81% and negative predictive value (NPV) was 65%. Predictive values were improved by varying the cut-off point: NPV was 73% for all three dipstick results being negative, and PPV was 92% for having nitrite and either blood or LE. A clinical decision rule, was less sensitive (65%) (Specificity 69%; PPV 77%, NPV 54%.
Conclusion: Strategies need to take into account limited negative predictive value, which is lower than expected from previous research.</td>
<td></td>
<td>abstract</td>
</tr>
</table>

8.	Wammanda RD, Aikhionbare HA, Ogala WN. (2000) Use of nitrite dipstick test in the screening for urinary tract infection in children West Afr J Med. Jul-Sep;19(3):206-8	Prospective study 185 children attending the paediatric units of Ahmadu Bello University Teaching Hospital, Zaria were evaluated for UTI by culture, microscopy and nitrite dipstick test. 118 males and 67 females	Positive urine culture with significant bacteria - 45 samples (24.3%). Urine microscopy for leukocyturia - significant in 55 urine samples. Significant leukocyturia identified 23 of the 45 culture positive urine samples (sensitivity 51.1%). Nitrite dipstick test identified 13 of the 45 urine samples with proven UTI (28.9% sensitivity). The positive and negative values were 72.2% and 80.8% respectively. The nitrite dipstick test < sensitive than significant leukocyturia in detecting UTI. Nitrite dipstick test -excellent specificity, but not sensitive enough as a routine screening test for UTI in children.		abstract

9.	Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. American Academy of Pediatrics. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection. Pediatrics. 1999 Apr; 103(4 Pt 1):843-52.	Systematic review. Literature review from 1966 to 1996 supplemented with consensus opinion of subcommittee member To formulate recommendations about the diagnosis, treatment, and evaluation of an initial UTI in febrile infants and young children (ages 2 months to 2 years	The three most useful components in urinalysis in the evaluation of possible UTI are leukocyte esterase test, nitrite test, and microscopy. Sensitivity and specificity Leucocyte esterase 83% and 78%respectively Nitrite 53% and 98% respectively Leucocyte esterase or nitrite positive 93% and 72%respectively Microscopy : WBCs 73% and 81% respectively Microscopy: bacteria 81% and 83% Leukocyte esterase or nitrite or microscopy positive 99% and 70% respectively The wide range of reported test characteristics for microscopy indicates the difficulty in ensuring quality performance; the best results are achieved with skilled technicians processing fresh urine specimens. Standard test for UTI is urine culture but the urinalysis can be valuable in selecting individuals for prompt initiation of treatment while waiting for the results of the urine culture. Any of the following are suggestive (although not diagnostic) of UTI: positive result of a leukocyte esterase or nitrite test, more than 5 white blood cells per high-power field of a properly spun specimen, or bacteria present on an unspun Gram-stained specimen. Test — Sensitivity% (range) — Specificity % (range) LE — 83(67-94) — 78(64-92) Nitrite — 53(15-82) — 98 (90-100) LE or Nitrite positive — 93 (90-100) — 72 (58-91) Microscopy : WBCs — 73(32-100) — 81(45-98) Microscopy : bacteria — 81(16-99) — 83(11-100) LE or nitrite or Microscopy positive — 99.8 (99-100) — 70(60-92)	fair	Full text

10.	Doley A, Nelligan M. (2003) Is a negative dipstick urinalysis good enough to exclude urinary tract infection in paediatric emergency department patients? Emerg Med (Fremantle). Feb;15(1):77-80.	Retrospective case note review Period 8 months (May to December 2000) AIMS: To determine if a negative dipstick urinalysis is adequate to exclude UTI in children aged 0-10 years. Urine collection –bag or clean catch.	2482 case note reviews – 720 had urinalysis record and 375 had full culture result. 375 cases – Overall prevalence 10.7%, sensitivity 92.5%, specificity 39.4% and a NPV 97.8%. In the 0-2-year-old group, prevalence 15%, sensitivity 87.5%, specificity 39.7% and a NPV 94.7%. Older group (2-10 years) - prevalence 7.0%, sensitivity 100%, specificity 39.7% and a NPV of 100%. Urinalysis-poor specificity and very poor PPV---not useful to diagnose UTI Higher prevalence in the 0-2 year's age group. The lower NPV and the higher clinical importance in this age group means that dipstick urinalysis is inadequate to exclude UTI. Children in the 2-10 years age group can adequately have UTI excluded with a negative dipstick urinalysis.	poor	Full text Multistix 10 SG dipstick Definition: Negative dipstick-negative for all of blood, protein, leucocytes and nitrites Positive culture:≥ 10^5organism/mm³ Limitations: 1.possible of contamination with urine bag sample 2.Many cases rejected due to lack of data (retrospective review)

<table>
<tr>
<td>11.</td>
<td>Rehmani R. (2004)

Accuracy of urine dipstick to predict urinary tract infections in an emergency department

J Ayub Med Coll Abbottabad. Jan-Mar; 16(1):4-7.</td>
<td>Descriptive study

984 Adult patient > 15 years old with urinary symptoms attending Section of Emergency section (SEM) of the Aga Khan University Hospital, from March to May 1998 Urine collection by MSSU or catheterization

Study the performance of dipsticks (LE alone, nitrite alone and combination of both) with automated urinalysis (including automatic dipstick reading) in laboratory, leucocyte counts on microscopy and urine culture.</td>
<td>Results:
Sensitivity of LE for detecting pyuria on microscopy
<table>
<tr><td>LE</td><td>WBC 5-9</td><td>WBC 10-20</td><td>WBC>20</td></tr>
<tr><td>True +</td><td>112</td><td>90</td><td>119</td></tr>
<tr><td>False -</td><td>325</td><td>72</td><td>20</td></tr>
<tr><td>Sensitivity %</td><td>25</td><td>56</td><td>86</td></tr>
</table>
Characteristic of nitrite and LE test for positive culture
<table>
<tr><td>Positive test</td><td>Culture positive n=404</td><td>Sensitivity%</td><td>Specificity%</td><td>PPV %</td><td>NPV %</td></tr>
<tr><td>LE</td><td>95</td><td>77</td><td>54</td><td>43</td><td>85</td></tr>
<tr><td>nitrite</td><td>99</td><td>81</td><td>87</td><td>73</td><td>91</td></tr>
<tr><td>LE and nitrite</td><td>115</td><td>94</td><td>50</td><td>45</td><td>95</td></tr>
</table>
Sensitivity and PPV of pyuria on clinical microscopy for urine culture
<table>
<tr><td>microsopy</td><td>Culture true +</td><td>Culture false +</td><td>PPV%</td></tr>
<tr><td>WBC 5-9</td><td>11</td><td>326</td><td>3</td></tr>
<tr><td>WBC10-20</td><td>25</td><td>137</td><td>15</td></tr>
<tr><td>WBC>20</td><td>87</td><td>50</td><td>63</td></tr>
</table>
Out of 404 cultures, 123 grew organisms.8 (5%) patients had negative urine dipsticks for LE and nitrite.</td>
<td>fair</td>
<td>Full text

Urine dipstick Multistix 10SG

Positive culture: 10^5CFU/ml 1 or 2 species

Negative : sterile or < 10^5 CFU/ml or contaminated</td>
</tr>
</table>

12.	Whiting P,Westwood M, Watt I, Cooper J, Kleijnen J.(2005) Rapid tests and urine sampling techniques for the diagnosis of urinary tract infection (UTI) in children under five years: a systematic review. BMC Pediatr. Apr 5; 5(1):4.	Systematic review to determine the diagnostic accuracy of rapid tests for detecting UTI in children less than five years of age.	39 studies report 107 data sets on dipsticks tests for UTI (nitrite,LE, protein, glucose and blood, alone and in combination) Positive nitrite and LE- LR+ 28.2, 95% CI: 17.3, 46.0 (highest LR) Negative nitrite and LE – LR- 0.20, 95%CI: 0.16, 0.26 Positive or negative either LE or nitrite less informative/indeterminate Insufficient information about protein, blood, or for combinations of 3 different dipstick tests. Glucose tests better than other tests to rule in/out UTI but too few and old studies. Combinations of microscopy and dipstick tests (9 studies) but unable for conclusion. Comparison of dipstick and microscopy by pooled LR suggest microscopy more accurate. One study found positive dipstick combination was best for ruling in disease (LR+18.9 vs. 11.6) compared to microscopy. 4 out of 5 studies compare negative dipstick vs. negative microscopy found microscopy better in ruling out UTI. CONCLUSION: Dipstick negative for both LE and nitrite or microscopic analysis negative for both pyuria and bacteriuria of a clean voided urine, bag, or nappy/pad specimen may reasonably be used to rule out UTI. These patients can then reasonably be excluded from further investigation, without the need for confirmatory culture. Similarly, combinations of positive tests could be used to rule in UTI, and trigger further investigation.	good	Full text

13.	Medina-Bombardo D, Segui-Diaz M, Roca-Fusalba C, Llobera J; dysuria team. (2003) What is the predictive value of urinary symptoms for diagnosing urinary tract infection in women? : Fam Pract. Apr;20(2):103-7.	Descriptive study Primary health care setting. 343 women > or =14 years of age who consulted their family physician for incident urinary tract symptoms. Age ranges 15 -90 years old 35 physicians from 18PHC in Spain	Positive cultures in 166 cases (39.8%) and negative in 177 (42.4%). Probability of UTI in this women with UTI symptoms were 0.484(95%CI 0.431-0.536) CONCLUSIONS: In women with urinary symptoms, a thorough clinical examination, together with performance of a reactive strip test during the office visit, improves the chances of detecting UTI. (Table 4)	fair	Full text Ames Multistix Positive culture $\geq 10^5$ CFU/ul Pyuria≥70 leukocytes/ml Abbreviations: PLR=positive likelihood ratio, NLR=negative likelihood ratio

Positive Nitrites increases the probability of UTI by >5 times, moderate pyuria increases it by >1.5 times, and the presence of both finding increases it by 7 times. (Table 4)

Reactive strip	Relative frequency	Sensitivity 95%CI	Specificity 95%CI	PLR 95%CI	NLR 95%CI
Pyuria	58%	0.72 (0.36-0.46)	0.57 (0.52-0.62)	1.67 (1.37-2.01)	0.50 (0.41-0.60)
+ nitrite	22.0%	0.41 (0.36-0.47)	0.92 (0.90-0.95)	5.41 (3.19-9.18)	0.64 (0.38-1.08)
Pyuria and + nitrite	17%	0.60 (0.53-0.67)	0.92 (0.88-0.96)	7.52 (3,84-14.73)	0.44 (0.22-0.86)

14.	Ohly N, Teece S. (2003) Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Accuracy of negative dipstick urine analysis in ruling out urinary tract infection in adults. Emerg Med J. Jul;20(4):362-3	Short cut review to establish whether negative dipstick urine analysis is sensitive enough to rule out urinary tract infection (UTI) in adults with urinary symptoms.	Medline search 1966-04/03. Two papers out of 75 search with the best evidence to answer the clinical question. Lammers RL et,2001 and Bent S et al, 2002 were reviewed. Dipstick urine analysis is of insufficient sensitivity to be used to rule out UTI in adults patients with one or more symptoms.	good	Full text

15.	Nys S, van Merode T,Bartelds AI, Stobberingh EE. (2006) Urinary tract infections in general practice patients: diagnostic tests versus bacteriological culture 1: J Antimicrob Chemother. May;57(5):955-8. Epub 2006 Mar 22.	Descriptive study 1993 non pregnant female patients (11-70 years) complaints of an acute uncomplicated UTI. 21 general practices from the Sentinel Station of The Netherlands Institute for Health Services Research (NIVEL) Period – January 2003-December 2004 Urine nitrite dipstick and/or LE test vs. dipslide (Uriline)	161/1993 (8%) - no growth. 249/1993 (13%) - contaminated/ mixed growth. Nitrite test – 1892 out of 1993. PPV (96%), specificity high (94%).NPV-30%, sensitivity 44%. A negative nitrite with a positive LE test showed a high PPV (79%) and sensitivity (82%). When both nitrite and LE tests were negative approximately 50% of the samples were culture positive. For female patients with symptoms of an acute uncomplicated UTI a positive nitrite test or a negative nitrite test with a positive LE test confirmed UTI whereas a negative nitrite together with a negative LE test did not rule out infection.	fair	Full text 1. Positive urine≥10^3cfu/ml (low cut off value) 2.False positive nitrite 4% as certain pathogen cannot grow in urislide 4. False positive LE + negative nitrite 21% cause by leukocyte of vaginal fluid in the urine or eosinophils

16.	Diagnosing UTI in the under fives Effective health care Vol 8 Number 6 2004 Bulletin produced by Center for Reviews and Dissemination, University of York.	Summary of research evidence for diagnosis and evaluation of UTI in children< 5 years old.	39 studies evaluated dipsticks tests for diagnosis UTI. (Nitrite, LE, protein, glucose and blood, alone and in combination). Combination of nitrite and LE test - the best performance in ruling disease both in and out. Dipstick positive for both nitrite and LE , a high chance of UTI (pooled LR=28.2, 95% CI: 17.3, 46.0). Negative both LE and nitrite, small likelihood of UTI. (pooled LR = 0.20, 95% CI: 0.16,0.26)Another combination that showed promise in ruling out UTI was for nitrite, LE and protein. Insufficient information protein, blood, or for combinations of 3 different tests. 39 studies evaluated microscopy for UTI (bacteriuria, pyuria or both).If positive for both pyuria and bacteriuria, good in ruling disease. (pooled LR=37.0, 95% CI:11.0, 125.9) If negative for both pyuria and bacteriuria good in ruling out disease. (Pooled LR = 0.11, 95% CI 0.05, 0.23). Microscopy- more accurate tests for UTI than dipstick. This is balanced by trade-offs in time, skill and cost requirements. An algorithm for diagnosis of UTI was derived, based on the conclusions of the review in terms of practice	Fair	Full text

17.	Tighe P. Taunton and Somerset NHS Trust, Musgrove Park Hospital, England, UK.(1999) Laboratory-based quality assurance programme for near-patient urine dipstick testing, 1990-1997: development, management and results. Br J Biomed Sci.; 56(1):6-15.	A quality assurance programme on dipsticks for urinalysis in the wards and clinics of a district general hospital, and in some of the general practitioner surgeries.	From preparation of an aqueous 'urine' sample, the design of a report form, the dispatch of the sample and report forms to the ward/clinic/health centre, the receipt and scoring of the returned results, and the assessment of the results, both in terms of management information and sources of error. Samples were spiked to give a target value midway between two colour blocks for each analyte. Results were scored as +/- 1 if adjacent colour block to the target, +/- 2 for results two colour blocks (error) and +/- 3 (gross error) for results three or more colour blocks from the target value. Results of each analytes based on error and gross error rate: glucose (14.7%, 2.6%); bilirubin (1.0%, 3.3%); ketone (4.3%, 0.3%); specific gravity (13.4%, 3.1%); pH (11.2%, 6.5%); blood (7.7%, 2.9%); protein (9.7%, 2.3%); and nitrite (gross errors 4.9%). 4 types of error in dipstick testing-timing, misalignment, misunderstanding and transcription. Error rates decreased when an electronic reader was used (errors 2.0%, gross errors 0.75%), compared to reading against the colour blocks on the side of the bottle (7.7%, 1.6%) or using the colour blocks on a flat card reader (7.4%, 1.7%).		Abstract

18.	Van Nostrand JD, Junkins AD, Bartholdi RK (2000) Poor predictive ability of urinalysis and microscopic examination to detect urinary tract infection Am J Clin Pathol. May; 113(5):709-13.		Urine culture results (n = 225) were obtained from the clinical microbiology laboratory. Stepwise binary logistic regression was used to derive a model using presence of infection as determined by culture as the dependent variable and urinalysis results as independent variables. A second set of data (n = 128) then was obtained to test the model. Statistical significance and the ability to predict infection based on urinalysis results were determined. Conclusion: a lack of sensitivity for LE, nitrite, and presence of bacteria in the microscopic examination as indicators of UTI.		abstract
19	Sultana RV,Zalstein S, Cameron P, Campbell D. (2001) Dipstick urinalysis and the accuracy of the clinical diagnosis of urinary tract infection J Emerg Med. 2001 Jan;20(1):13-9	Prospective study Dipstick urinalysis (DU) augmented the accuracy of clinical assessment in the diagnosis of UTI. 627 adult patients in emergency department (ED) with possibility of UTI .227 patients excluded.	The assigned clinical probabilities of UTI based on an ordinal and continuous scale by treating doctor were compared to the results of formal urine culture. The areas under receiver-operating characteristic curves (AUC) were calculated. Clinical assessment alone was effective in detecting those patients with a UTI from those without (AUC 0.75; $p < 0.0001$). A statistically significant difference in the accuracy of diagnosing UTI after DU (AUC 0.87; $p < 0.0001$). Proportionately more patients with a moderate pre-test probability of UTI were re-assigned to a different probability rating following DU, compared to the low or high pre-test probability groups ($p < 0.001$). DU in combination with clinical assessment is a superior method for diagnosing UTI than clinical assessment alone		abstract

<table>
<tr>
<td>20</td>
<td>Semeniuk H, Church D. (1999).

Evaluation of the leukocyte esterase and nitrite dipstick screening tests for detection of bacteriuria in women with suspected uncomplicated urinary tract infections.

J Clin Microbiol;37:3051-3052</td>
<td>Prospective study

479 ambulatory women with suspected uncomplicated UTI

age 15-65 years</td>
<td>Performance of LE and NIT in screening for significant bacteriuria
<table>
<tr><td></td><td colspan="3">Sensitivity % at colony counts of</td><td colspan="3">Specificity% at colony counts of</td></tr>
<tr><td></td><td>10^3</td><td>10^4</td><td>10^5</td><td>10^3</td><td>10^4</td><td>10^5</td></tr>
<tr><td>LE</td><td>71.4</td><td>76.9</td><td>84.4</td><td>59.4</td><td>59.4</td><td>59.4</td></tr>
<tr><td>NIT</td><td>0</td><td>7.9</td><td>43.6</td><td>96.6</td><td>96.6</td><td>96.6</td></tr>
<tr><td>LE& NIT</td><td>0</td><td>25</td><td>84</td><td>98.3</td><td>98.3</td><td>98.3</td></tr>
<tr><td></td><td colspan="3">PPV(%) at colony counts of</td><td colspan="3">NPV% at colony counts of</td></tr>
<tr><td></td><td>10^3</td><td>10^4</td><td>10^5</td><td>10^3</td><td>10^4</td><td>10^5</td></tr>
<tr><td>LE</td><td>3.1</td><td>16.0</td><td>19.4</td><td>99.1</td><td>96.3</td><td>97.1</td></tr>
<tr><td>NIT</td><td>0</td><td>27.3</td><td>75.0</td><td>99.1</td><td>86.8</td><td>88.2</td></tr>
<tr><td>LE& NIT</td><td>0</td><td>42.9</td><td>84</td><td>99.1</td><td>96.3</td><td>98.3</td></tr>
</table>
A positive dipstick (LE and/or nitrite) –unreliable to detect significant bacteriuria in women with uncomplicated UTI.</td>
<td>good</td>
<td>Full text

Chemstrip-10 dipsticks (Roche Diagnostics)

NIT=nitrite
Significant bacteriuria≥10^3 CFU/ml</td>
</tr>
</table>

21	Bachur R, Harper MB. (2001) Reliability of the urinalysis for predicting urinary tract infections in young febrile children. Arch. Pediatr. Adolesc. Med; 155:60-5	Retrospective review of medical record for 65 months (January 1993 to June 1999) Children≤ 2 years old, fever ≥38.0˚C attended ED.	37,450 patients. Urinalysis (UA) - 17679 patients (47%). Urine cultures – 11089 patients (30%). Paired UA and culture – 8815. Positive culture – 785.Prevalence of UTI 2.1% overall. (2.9% in girls and 1.5% in boys). . Dipsticks were positive for LE and nitrite in 78% and 10% of those with culture-proven UTI. The overall sensitivity for dipstick analysis - 79% (95%CI, 76-82%), sensitivity of combined dipstick and microscopy (standard UA in this laboratory) - 82% (95%CI, 79-84%) and did not vary by age subgroups. Specificity of combined dipstick and microscopy 92% (95% CI, 91-92%). The likelihood ratios for positive and negative UA results were 10.6 (95% CI, 10.0-11.2) and 0.19 (95%CI, 0.18-.0.20).	Fair	Full text Multistix (Bayer) Positive dipstick- Presence of LE or nitrite or both. Pyuria ≥ 5 WBC/HPF. Positive UA – positive dipstick test result and/ or pyuria Urine culture is considered positive if ≥ 10^3 CFU/ml form suprapubic aspiration, ≥10^4 CFU/ml on catheterized specimens and ≥10^5 CFU/ml on clean voided samples. Contamination – more than 1 organism or nonpathogens.

22	P Whiting, M Westwood, L Bojke, S Palmer, G Richardson, J Cooper, I Watt, J Glanvile, M Sculpher, and J Kleijnen.(2006) Clinical effectiveness and cost effectiveness of tests for the diagnosis and investigation of UTI in children: a systematic review and economic model Health Technology Assessment Vol 10: No 36	HTA report AIM: 1. Determine accuracy of tests for detecting UTI in children< 5 years old. 2.Evaluate the effectiveness of further investigations in confirmed UTI 3.Evaluate the effectiveness of follow up 4.Evaluate cost effectiveness of diagnostic and imaging tests 5.Develop preliminary diagnostic algorithm for healthcare professional	Dipsticks- 38 studies,106 evaluations Difficult to draw conclusions about the overall accuracy of dipstick tests given the heterogeneity between studies in some areas, and lack of data in others. Combination of LE and nitrite best in ruling in disease (Both positive) and ruling out disease (both negative) Insufficient information about accuracy of dipstick test for protein or blood.	good	Executive summary

POCT for rapid dengue test in primary care

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade	Comment
1.	Stuart D. Blacksell (2004) Diagnostic accuracy of rapid immunochromatographic assays for the detection of IgM antibodies to dengue virus during the acute phase of infection: A systematic review and meta-analysis. Dengue diagnostics: Proceedings of an international workshop / 4-6 Oct / WHO/TDR/ Geneva, Switzerland. p32-38	Systematic review and meta-analysis. 11 studies used for the meta-analysis.	All studies used the PanBio ICT as the index test. Significant heterogeneity between the studies seen in sensitivity, specificity, *DOR (diagnostic odd ratio), +LR (positive likelihood ratio) and -LR (negative likelihood ratio*)* chi-squared statistical results reduces the validity of statistical pooling of individual study results. Subgroup analysis by pooling 4 studies using the PanBio Duo ELISA as the reference assay has evidently shown that the dengue ICT has acceptable diagnostic accuracy. Pooled diagnostic accuracy results of the dengue ICT compared with the PanBio Duo ELISA gave high sensitivity, specificity and DOR results. The +LR has shown that a sample from a dengue patient had an eightfold higher chance of giving positive result in a dengue ICT ('ruling in') compared with samples from patients without dengue infection. The -LR demonstrated that the ICT was also acceptable at 'ruling out' negative dengue samples. This study's finding has shown that diagnostic accuracy is improved by using 'late acute' samples (7-10 days after onset of symptoms) with higher sensitivity, DOR, +LR, and lower –LR results when compared to 'early acute' (hospital admission) samples. The dengue ICT demonstrated low sensitivity for detecting primary and secondary dengue infections. However, diagnostic capacity for detection of primary infections by the dengue was improved compared to the secondary infections. Conclusions: It was demonstrated that the dengue ICT is a useful diagnostic test, but with limitations. The timing of sample collection is probably the most important aspect in the diagnosis of dengue infection when using the ICT, whereby significantly higher results are recorded for samples collected 7-10 days after the onset of symptoms.		

POCT for full blood count in emergency department

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade	Comment
1	Lab Hematol. 2003; 9(4):225-33. Performance evaluation of a new compact hematology analyzer, the Sysmex pocH-100i. Briggs C, Kunka S, Pennaneach C, Forbes L, Machin SJ. Department of Haematology, University College London Hospital, London, United Kingdom. carolbriggs@hotmail.com	The technical evaluation was made in accordance with International Council for Standardization in Haematology (ICSH) guidelines for precision, linearity, carryover, and effects of sample aging.	The pocH-100i analyzer was compared with the existing small analyzer Sysmex KX-21N. The results for all parameters tested were almost identical. When samples including blast cells, immature granulocytes, and nucleated red blood cells were excluded, the pocH-100i automated differential compared well with a 400-cell manual differential. Results for neutrophils (r2 = 0.996), lymphocytes (r2 = 0.999), and the "mixed" population of cells (r2 = 0.611) indicated the pocH-100i analyzer would be highly suitable for low-volume laboratories and near-patient services.	Fair	-

POCT for electrolytes (Na, K, CL) in critical care
Clinical Effectiveness

No	Author, title, journal, year, volume, page number	Study design, sample size, follow up	Outcomes & characteristics	Grade	Comment
1	Widness JA, Madan A, Grindeanu LA (2005) Reduction in red blood cell transfusions among preterm infants: results of a randomized trial with an in-line blood gas and chemistry monitor Pediatrics. May;115(5):1299-306	Prospective, randomized, controlled, clinical trial N= 93 extremely low birth weight infants in ICU	Use of an in-line, ex vivo, bedside monitor that withdraws blood through an umbilical artery catheter, analyzes blood gases and sodium, potassium, and hematocrit levels, and returns the sample to the patient. In the first 2 weeks of life, there was a non-significant 17% lower cumulative RBC transfusion volume in the monitor group (n = 46), compared with the control group (n = 47). However, data from the first week only (the period of greater catheter use) demonstrated a significant 33% lower cumulative RBC transfusion volume in the monitor group. Cumulative phlebotomy loss was approximately 25% less in the monitor group throughout the 2-week study period. There was no difference between groups in neonatal mortality, morbidity, and neurodevelopmental outcome rates at 18 to 24 months.	good	Full-text
2	Asimos AW, Gibbs MA, Marx JA (2000) Value of point-of-care blood testing in emergent trauma management. *J Trauma. Jun; 48(6):1101-8.*	Prospective, non-interventional, study N= 200 major trauma patients with blunt trauma in ED	Na^+, Cl^-, K^+, and blood urea nitrogen levels do not influence the initial management of major trauma patients.	fair	Full-text

3	Murray RP, Leroux M, Sabga E, Palatnick W, Ludwig L. (1999) Effect of point of care testing on length of stay in an adult emergency department. *J Emerg Med.*, 17(5), Sep-Oct, pp 811-4.	RCT N= 180 patients in ED	Tests done were creatinine, sodium, potassium, chloride total CO2, glucose, BUN, hematocrit, CK-MB and myoglobin either PCT vs. central laboratory. Patients randomized to PCT (n = 93) had a median stay of 3 h, 28 min (interquartile range [IR] 2:28 to 5:30), while those allocated to the central laboratory (n = 87) had a median stay of 4 h, 22 min (IR 3:04 to 5:47). Among patients who were destined to be discharged home, there was also a significantly shorter stay, but not among those who were destined to be admitted.	Fair	Full-text
4	Heyningen C, Watson ID, Morrice AE (1999) Point-of-care testing outcomes in an emergency department Clin Chem; 45: 437-438	N=? In ED	TAT and waiting time in ED for tests done by POCT vs central lab with porter vs. central lab with pneumatic tube. TAT , median (range) in min : 5(4-6) vs. 58 (47-77) vs. 49 (37-65) Median, (range)waiting time in min 219, (171-277) vs. 212 (170-275) vs. 258 (189-364)	Fair	Full-text

5	Kilgore ML, Steindel SJ, Smith JA (1998) Evaluating stat testing options in an academic health center: therapeutic turnaround time and staff satisfaction *Clinical Chemistry,* 44 pp 1597 - 1603	Evaluation study N= 11284 satellite lab = 5394 POCT and central lab (blood gas, glucose and electrolytes) sites: CICU, neuro ICU, Heart Transplant ICU	Therapeutic TAT was 1-2 min shorter for bedside testing compared to satellite laboratory and 9-14min shorter in satellite laboratory compared to centralize testing. Satellite laboratories received highest staff satisfaction, followed by bedside testing and lowest with central laboratory.	fair	Full-text
6	Kendall J, Reeves, Clancy M (1999) *Point of care testing: randomized controlled trial of clinical outcome* BMJ ;316:1052-1057	Randomized control study N=1728 pts in ED	Changes in management in which timing was considered to be critical occurred in 6.9% Decisions were made 86 min earlier (80-92 min, p<0.0001) when POCT was used for biochemical tests vs. central lab testing. No differences between the groups POCT vs. Lab - time spent in the dept 188 min (181 to 194) vs. 193 (186 to 200) p=0.30 - LOS in hospital 7.8days (6.9 to 8.6) vs. 8.3 (7.5 to 9.1) p=0.37 - admission rates 85.2% vs. 83.5%, p= 0.33 - mortality rates 6.4% vs. 5.5%, p=0.45	good	full-text
7	Parvin CA, Lo SF, Deuser SM (1996) Impact of point-of-care testing on patients' length of stay in a large emergency department Clin Chem ; 42(5):711- 717	Prospective study N= 4985 pts (2067 during 5 weeks of experimental period, 2918 during control period-5 weeks before and 3 weeks after) In ED	No decrease in ED LOS was observed in pts tested with POCT for Na, K, Cl, glucose and blood urea; Median LOS was 209 min for POCT and 201 min for combined control periods.	fair	Full-text

POCT for electrolytes (Na, K, CL) in critical care
Reliability

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade	Comment
1	Steinfelder-Visscher J, Weerwind PW, Teerenstra S, Brouwer MHJ (2006) Reliability of point-of-care hematocrit, blood gas, electrolyte, lactate and glucose measurement during cardiopulmonary bypass Perfusion; 21: 33-37	Evaluation study 127 blood samples from 88 patients undergoing cardiopulmonary bypass for elective cardiac surgery. Paired samples taken – one sent for laboratory analysis via internal transfer system and another analysed in the operating room using GEM Premier 3000	GEM Premier 3000 was compared with laboratory testing using Ciba Corning 865 analyser for electrolytes. For Na^+, the SD of difference (random deviation) between GEM Premier and laboratory analyser is 1.71 and is therapeutically acceptable. For K^+ measurement, a clear linear trend (r=/0.79, p</0.001) in the deviation of the GEM Premier 3000 from the Ciba Corning was noticed, i.e., in the lower or upper K^+ reference range, the GEM Premier 3000 measured systematically too low or too high, respectively. From a clinical and therapeutical perspective, the deviation (< 0.3) is not relevant.	Fair	Full-text

2	St-Louis P (2001) Point-of-care blood gas analysers: a performance evaluation Clin Chim Acta 307;.139–144	Evaluation study 28 patients in OR or ICU(68 specimens); ages: 3 weeks to 19 years; includes 4 liver transplants, 1 kidney transplant and 4 cardiac surgeries	POCT analyser ABL70 (Radiometer, Copenhagen) vs. reference ABL625 in central laboratory For Na measurement , Bland–Altman analysis using the ABL625 as reference showed a mean of differences (S.D. of differences)= 5.15 (2.1150) mmol/l; the mean bias was calculated at - 4%. ABL 70 tends to underestimate Na. For K measurement, the calculated mean (S.D) of differences =0.0369 (0.1922) mmol/l with differences in the range - 5.1 to 20.9% of reference.	Fair	Full-text
3	Schlebusch H, Paffenholz I, Zerback R, Leinberger R (2001) Analytical performance of a portable critical care blood gas analyzer Clin Chim Acta 307;107–112	Evaluation study Electrolytes n=81	Portable analyzer OPTI Critical Care Analyzer was evaluated in comparison to routine laboratory assays using OPTICheck Multianalyt Control (Roche Diagnostics) The coefficients of variation were below 1.1% for Na and below 6% for K.	Fair	Full-text

4	Chance JJ, Li DJ, Sokoll LJ (2000) Multiple site analytical evaluation of a portable blood gas/electrolyte analyzer for point of care testing *Crit Care Med*, 28:2081-2085	N=20 for 20 days in critical care unit and operating rooms	Analytical performance of the SenDx 100 portable blood gas and electrolyte analyzer (SenDx Medical,Carlsbad, CA) compared with Nova Stat Profile 5 (Nova Biomedical, Waltham, MA) and the Ciba Corning 865 (Chiron Diagnostics, Medford, MA). Precision studies performed at three different concentration levels for each analyte demonstrated intra-assay precision of <0.3% and < 1.1%CV for Na^+ and K^+ respectively; And interassay precision of < 0.75% and < 1.1% CV for Na^+ and K^+ respectively. Analysis of patient specimens in general showed good to excellent correlation to reference analyzers.	Fair	Full-text
5	Kost GJ, Vu HT, Inn M (2000) Multicenter study of whole-blood creatinine, total carbon dioxide content, and chemistry profiling for laboratory and point-of-care testing in critical care in the United States. Crit Care Med. Jul; 28(7):2379-89.	N = 191 patients in Emergency room and operating room.	The NOVA 16 whole-blood analyzer (NOVA Biomedical, Waltham, MA) was used on paired sample tested by non-lab trained and medical technologists. Mean paired differences (result for point-of-care personnel vs. medical technologist result) for Na, K, and Cl in the emergency room setting were not statistically significant. The mean paired differences for Na and Cl in the operating room were statistically significant (Na^+ - 0.39mmol/L; Cl^- 0.37 mmol/L) but were not clinically significant	Fair	Full-text

6	Parvin CA., Lo SF, Deuser SM (1996) Impact of point-of-care testing on patients' length of stay in a large emergency department ClinChem :42(5): 711-717	N=380	Comparison of POCT electrolytes using i-STAT vs. central laboratory using Ektachem 750analyzer (Clinical Diagnostics Division of Johnson & Johnson, Rochester, NY). Na and K compared extremely well, with results by the central lab, with only 2 and 3 samples producing outliers of absolute differences for the same sample as much as 7 and *0.5* mmol/L, respectively. For Cl there were 11 samples of outliers with absolute differences of 6 mmol/L.	Fair	Full-text
7	Flegar-Mestric Z, Perkov S. (2006) Comparability of point-of-care whole-blood electrolyte and substrate testing using a Stat Profile Critical Care Xpress analyzer and standard laboratory methods. Clin Chem Lab Med. 44(7):898-903	N=70 ICU patients	Measurement of electrolytes using a Stat Profile Critical Care Xpress (Nova Bio-medical, Waltham, MA, USA) multiprofile analyzer and compare with standard laboratory methods Olympus AU 600 analyzer (Olympus Mishima, Shizuoka, Japan). Imprecision, expressed as CV% was less than 5.7% for Na, K, Cl at both high and low concentrations The inaccuracy of electrolyte measurements met the analytical quality specification required for near patient testing, with observed bias within the range -4.5% to 5.3%.	Fair	Abstract

8	Walton HG, Boucher DM, Marroquin R. (2003) Comparison of blood gas and electrolyte test results from the Gem-Premier and the ABL-70 versus a conventional laboratory analyzer. J Extra Corpor Technol. Mar;35(1):24-7.	N=30	To evaluate the accuracy, reliability, consistency, and bias of the Radiometer ABL-70 point of care blood gas analyzer. When comparing the ABL-70 with the hospital blood gas machine and electrolyte analyzer (Corning 278/270 blood gas machine/ Co-Ox, the AVL-9180, and the Dimension XL) there was statistical significance seen between the pH, pC0 [2,] pO [2], sodium, calcium, hematocrit, and base excess. Although this statistical significance was observed between the ABL-70 and the other analyzers, the significance was not of clinical importance. The ABL-70 demonstrated acceptable accuracy, reliability, consistency, and bias.	fair	Abstract
9	Bingham D, Kendall J, Clancy M. (1999) The portable laboratory: an evaluation of the accuracy and reproducibility of i-STAT. Ann Clin Biochem. Jan; 36 (Pt 1):66-71.	N=?	Two cartridges were assessed: the 6+ and the G3+, which provide results for urea, glucose, sodium, potassium, chloride, haematocrit, pH, PCO2, PO2 and various calculated parameters. The results for all analytes agreed well with the analysers in routine use in the laboratory. The reproducibility was comparable even when analysis was carried out by a nurse with only 5 min training. The system was found to be reliable, easy to use and required no maintenance (only a 2-min daily check of the electronics). These features, together with portability and the storage capacity for results, make the i-STAT suitable for point-of-care use, particularly in critical care units.	fair	Abstract

POCT for magnesium in critical care

No	Author, title, Journal, Year, Volume, Page Number	Study Design, Sample Size, Follow up	Outcomes & Characteristics	Grade	
1.	Henk J et al. (2000) Magnesium level in critically ill patient. What should we measure?, Am J Clin. Pathol,;114: 688-695	Prospective multiucenter study N=115, 1 month mortality recorded	Analyzer KONE instrument for Mg2+ and AAS for total Mg Cut off value iMg is 0.46mmol/l, Using APACHE 11 for bad clinical outcome Based on tMg (Cut 0ff 0.75 mmol/l) 51.3% of ICU had hypoMg, only 14.4% had hypoMg based on serum iMg (Cut off 0.47mmol/l) , None of ICU patient detected hypoMg if based on intracellular Mg concentration (total) The normal or high tMg is accompanied by normal or high iMg, Predictive value of low tMg for low iMg is only 29%. In situation wher low Mg is suspected iMg measurement is preferred to tMg. HypoMg based on iMg or intracellular measurement did not correlate with an increased mortality rate or increased APACHEE 11 Score	3	Full Article
2.	J Thode and B. Juul-Jorgensen, M. Seibeak, H. Elming. (1998) Evaluation of an ionized magnesium-pH analyzer- NOVA 8. Scand J Lab Invest ; 58: 127133	Evaluation Study: Linearity measuring cMg2+ in different weighed in Mg2+(0,0.5, 1.0, 1.5, 2.0,2.5,3.0) in aqueous solution Stability: IQC 3 level cMg2+ 1.24, 0.48, 0.25) Manufacturer and human serum 0.54mmo/l Reference interval: n=70 healthy individuals Equipment NOVA 8 (NOVA CRT, NOVA biomedical)	Result: Linearity, direct measurement of Mg+ compared to actual weight were linear in Mg+ range from 0.1 - .0 mmol/l Day-to-day Precision at 1.24, 0.48,0.25 were 2.2%, 3.1% and 3.2% using control materials and 1.7% when using human external serum control.. Reference range : 0.51 + 0.08 mmol/l Relationship between Mg+ and TMg: Only weak but significant relationship found between cMg+ and cTMg. The linear regression were y (Mg+)= 0.47x + 0.12, r=0.75, Sy/x=0.03mmol/l		

3.	Christoph Ritter, Massoud Ghahramani & Hermann J. Marsoner. (1996) More on the measurement of ionized magnesium in whole blood. Scan J Clin Lab Inveast;56, Suppl:224: 275-280	Evaluation Study AVL 988/4 Reproducibility Using Quality Control solution, human serum, whole blood within run n=30, between run n= 20 Whole blood measurement against plasma samples	AVL 988/4 gave a reasonable performance with CV 1.25%,0.48% and 0.93% at level 0.32, 0.62 and 1.18 mmol/l respectively when using protein based QC, CV of 1.29% at level of 0.54 mmol/l when using Serum and 1.27% at level 0.55 when using whole blood.. The result of whole blood showed excellent correlation 0.987) to that of plasma result. Up to 6% Haematocrit give very little influence on iMg result The study also showed some influences when using different type of heparine during sample collection		

4.	Francesco Zoppi, Andrea De Gasperi, Emma Guagnellini et al. (1996) Measurement of ionized magnesium with AVL 988/4 electrolyte analyzer: Preliminary analytical and clinical result. Scand J Clin Lab Invest; 56, Suppl 224: 259-274	Evaluation Study Tmg utilizing enzymatic method (Sera-Pak it) on H717 (Boehringer Mannheim Itali SpA Milan) other chemistry test on Kodak Ektachem Precision: ISE-trol Protein based QC material n=20 Effect on type of tube (n=10 healthy person sample) a) BD tube with gel separation silicone oil lubricated stopper (7783) b) with silicone lubricated stopper(7634) c) with glycerol lubricated stopper(7626) Effect of pH a) Using 3 pool Sera b) Using 20 non Haemodialyzed patient's sample (7783) c) Using 20 Haemodilyzed patient's samples tube 7626) Effect of Heparine and/or ionic strength	Result: Precision n=20 cMg+ mmol/l 1.29 0.76 0.23 CV% (within run) 0.67 0.67 3.00 CV% (between run) 4.06 3.91 5.89 Clinical significant was not able to assess as the biological variation is not known Sample collected from silicone coated tube or syringe displayed higher iMg result. Linearity iMg 0.25- 1.6mmol/l Effect of Heparin Heparin effect on Mg measurement becomes appreciable at heparin concentration higher than 20IU/ml of serum. Effect of pH pH dependence of ciMg is present t a lower extend with respect to ciCa Correlation with total Mg (n=100 both in healthy and ill patient) Tmg range 0.45 to 2.10 mmol/l ciMg=0.73TMg + 0.008 mmol/l, Sy/x=0.05mmol/l r=0.987, n=100 Serum iMg fraction is about 72% of TMg Reference range (n=103 healthy volunteers , 53 men, 50 women age 20-58 yr, median 36 yrs old) is 0.60 + 0.05 mmol/l fractioned of iMg 0.71 + 0.05 mmol/l (mean + SD)		

5.	NACB, Laboratory Medicine Practice Guideline, Evidence Based Practice for POCT	Systematic review	Guideline- there is fair evidence that more rapid TTAT of Mg result in critical care patient setting leads to improved clinical outcomes. Recommended that more rapid TTAT of M result to be considered as a way to improve out comes in critical care patient setting (24 literature) Guideline – There is insufficient evidence that POCT of Mg result leads to improved clinical outcomes, in critical patient settings. Recommended that prospective randomized controlled studies be performed (25 literature)		