Developing a sustainable framework for managing the implementation and assessing the effectiveness of Point-of-Care Testing in remote settings

by

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ABSTRACT

Introduction:

Point-of-care testing (POCT) is pathology testing performed at the site of patient care with results immediately available to inform clinical decisions. POCT is different from traditional laboratory-based pathology testing which requires patient specimens to be transported to a laboratory with test results later reported to the treating practitioner; this can cause delays to the initiation of, or changes in, clinical management. POCT has a particular niche in rural and remote locations where the increased distance from the nearest laboratory lengthens transport times, extends delays in receiving pathology results and can result in loss to patient follow-up. However, the evidence base to support the use of POCT in rural and remote settings is limited as most POCT studies have occurred in urban general practice or metropolitan tertiary hospital settings. In particular, very little evidence exists for the use of POCT for acute care in rural or remote primary health care settings.

Methods:

This thesis documents ten years of quantitative and qualitative research into the effectiveness of POCT in rural and remote settings. Most of this work was facilitated by the author's role as the Coordinator of POCT services in the Northern Territory (NT) of Australia; one of the most remote and challenging environments for POCT delivery. Thirteen peer-reviewed studies provide a large evidence-base supporting the use of POCT in these settings. The studies focus on the implementation and assessment of key outcomes of POCT and represent the most comprehensive research assessment conducted to date on the effectiveness of POCT in remote Australia.

Results:

In the NT remote primary care setting, POCT was determined to be analytically sound with results of quality control testing performed by remote operators being consistently of equivalent quality to laboratory benchmarks.

Operational effectiveness was demonstrated through the increased uptake of POCT in the NT (with volume of testing increasing 600% since initial implementation), and significant increases in satisfaction with pathology services post introduction of POCT. More than 1,500 health professionals have now been trained as POCT operators contributing to significant workforce capacity building and increased community resilience. The improved timeliness of pathology results by POCT has enabled more rapid initiation and changes to treatment.

Clinical effectiveness of POCT is highlighted through case studies documenting clinical benefits to patients, including improvements in glycaemic control and increased time in therapeutic range. For acute care, POCT has made significant improvements to patient safety through enabling informed stabilisation of patients on-site, and enhanced decision-making regarding the triage and prioritisation of patients requiring emergency medical retrievals.

An economic evaluation of POCT identified savings to the NT health sector estimated to be upwards of $21 million per annum for three common acute presentations.

The robustness of the methods developed for the NT POCT model were also verified through translation to an international setting and with different POC tests.

Impact:

Collectively, this body of evidence-based research has significantly shaped government policy on pathology service provision in the NT, with POCT now embedded in mainstream service delivery in every remote health facility.

DECLARATION OF ORIGINAL WORK

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that, to the best of my knowledge and belief, it does not contain any material previously published or written by another person except where due reference is made in the text.

Signed:___B A SPAETH_____ On:_03_/_08_/_2018_

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GLOSSARY OF TERMS

Aboriginal: A person of Aboriginal descent in Australia who identifies as an Aboriginal and is accepted as such by the community in which he or she lives.

Aboriginal Heath Worker/Practitioner: Aboriginal people who live and work in the community and have training in primary health care.

Aboriginal Community Controlled Health Service (ACCHS): A primary health care service initiated and operated by the local Aboriginal community to deliver holistic, comprehensive, and culturally appropriate health care to the community which controls it (through a locally elected Board of Management).

Accuracy: Closeness of agreement between the result of a measurement and the true value of the measurand.

Aeromedical evacuation/retrieval: Use of rotary or fixed winged aircraft staffed by suitably qualified practitioners of aviation medicine to facilitate the retrieval of the critically injured or acutely unwell patients.

Bias: The difference between the expectation of the test results and an accepted reference value.

Coefficient of Variation: Standard deviation expressed as a fraction of the mean.

External Quality Assurance (EQA): Also referred to as Proficiency Testing (PT), EQA is a program in which multiple specimens are periodically sent to a service provider in the program for analysis, and the results are reported to the participants and others. Such a program may therefore compare the analytical performance of an individual device (POCT or laboratory-based device) with a peer group measuring the same analyte.

Gold Standard method: A term used to describe the primary reference method for a particular analyte.

Indigenous: Used interchangeably with Aboriginal and/or Torres Strait Islander.

Imprecision: The standard deviation of coefficient of variation of the results in a set of replicate measurements.

Precision: The closeness of agreement between independent test results obtained under stipulated conditions.

Rapid Diagnostic Tests (RDTs): A simple, single-use test that captures a marker for the disease or infection on a nitrocellulose strip with varied sensitivity and specificity.

Reference Method: An analytical procedure sufficiently free of ransom or systematic error to make it useful for validating a new analytic procedure for the same analyte

Remote Area Nurse (RAN): A primary health care worker (nurse) in a remote area of Australia where population density and remoteness precludes the provision of permanent doctors.

Rural Medical Practitioner (RMP): A medical practitioner employed by the Department of Health to provide a medical telephone consultation service to remote communities in the Northern Territory on a 24-hour duty roster.

Sensitivity: The proportion of people with the disease who test positive.

Specificity: The proportion of people without the disease who test negative.

Torres Strait Islander: A person from any of the Torres Strait Islands between northern Australia and Papua New Guinea.

ACRONYMS AND ABBREVIATIONS

Abbreviation	Explanation
ACCHS	Aboriginal Community Controlled Health Service
ACR	Albumin creatinine ratio
ACS	Acute Coronary Syndrome
AHP	Aboriginal Health Practitioner
AHW	Aboriginal Health Worker
BV	Biological Variation
CI	Confidence Interval
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CT	Chlamydia Trachomatis
CI	Confidence Interval
cTnI	Cardiac Troponin I
CV%	Coefficient of Variation
DoH	Department of Health
DoHa	Department of Health and Aging
eGFR	Estimated Glomerular Filtration Rate
EOS	Eosinophil
EQA	External Quality Assurance
INR	International Normalized Ratio
FBE	Full Blood Examination
GP	General Practice
HbA1c	Haemoglobin A1c

HDL-C	High-density Lipoprotein Cholesterol
ICPOCT	International Centre for Point-of-Care Testing
INR	International Normalised Ratio
LYM	Lymphocyte
MON	Monocyte
NAAT	Nucleic Acid Amplification Testing
NEU	Neutrophil
NG	Neisseria Gonorrhoeae
Non-STEMI	Non-ST Elevation Myocardial Infarction
NT	Northern Territory
POC	Point-of-Care
POCT	Point-of-Care Testing
PPT	Parallel Patient Testing
p-value	Probability value
QAAMS	Quality Assurance for Aboriginal and Torres Strait Islander Medical Services
QC	Quality Control
QLD	Queensland (Australia)
r	Correlation coefficient
RAN	Remote Area Nurse
RDT	Rapid Diagnostic Test
RMP	Rural Medical Practitioner
SA	South Australia
STI	Sexually Transmitted Infection
TAT	Turnaround Time

TAS	Tasmania (Australia)
TTANGO	Test, Treat and Go
TTR	Time in Therapeutic Range
TV	Trichomonas Vaginalis
WBC	White Blood Cell
WCC	Total White Cell Count
WCC Diff	5-part differential White Cell Count
WHO	World Health Organization

CHAPTER 1 INTRODUCTION

This thesis by published works represents the culmination of ten years of research, and comprises seven first-authored and five co-authored peer-reviewed publications and one peer-reviewed and co-authored book chapter. Also included as research outputs are three book chapters and one editorial, with the author being invited to contribute as a direct result of her experience and the research studies presented in this thesis. These published works are linked by a common theme - the implementation and evaluation of Point-of-Care Pathology Testing (POCT) in rural and remote locations in Australia. The overarching aim of these studies was to determine the effectiveness of POCT in rural and remote locations, with specific focus on the Australian setting. While each of the studies individually contributes to new knowledge in the field of POCT, the studies also systematically build upon one another to establish a significant body of evidence supporting the use of POCT in rural and remote locations in Australia. The final published work in the thesis demonstrates how the methods developed through the Australian-based studies were translatable to an international setting. A list of these studies is provided below in chronological order.

1. Shephard, M, Peake, M, Corso, O, Shephard, A, Mazzachi, B, **Spaeth, B**, Barbara, J & Mathew, T 2010, 'Assessment of the Nova StatSensor whole blood point-of-care creatinine analyzer for the measurement of kidney function in screening for chronic kidney disease', Clinical Chemistry and Laboratory Medicine, vol. 48, no. 8, pp. 1113-119.

2. Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Loudon, J, Rigby, J & Daniel, V 2012, 'Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program', *Australian Journal of Rural Health*, vol. 20, no. 1, pp. 16-21.

3. Shephard, M, Halls, H, McAteer, B, Mazzachi, B, Motta, L, **Spaeth, B** & Shephard, A 2013, 'Management challenges for point-of-care coordinators in delivering training and competency programs', *Point of Care*, vol. 12, no. 2, pp. 84-5.

4. Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Lingwood, A, Loudon, J, Rigby, J & Daniel, V 2014, 'Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program', *Point of Care*, vol. 13, no. 1, pp.

6-11.

5. Shephard, M, **Spaeth, B**, Motta, L & Shephard, A 2014, 'Point-of-care testing in Australia: Practical advantages and benefits of community resiliency for improving outcomes.', in G Kost & C Curtis (eds), Global Point-of-Care - Strategies for Disasters, Complex Emergencies, and Public Health Resilience., American Association of Clinical Chemistry Press, Washington DC, pp. 527-35.

6. **Spaeth, B**, Shephard, M & Schatz, S 2014, 'Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care', *Rural and Remote Health*, vol. 14, no. 4, p. 2849.

7. **Spaeth, B**, Shephard, A, Shephard, M & Mathew, T 2015, 'Assessment of a point-of-care device for measuring creatinine in a community screening program for chronic kidney disease', *Medical Research Archives*, no. 3, pp. 1-6.

8. **Spaeth, B**, Shephard, M, McCormack, B & Sinclair, G 2015, 'Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory', *Pathology*, vol. 47, no. 1, pp. 91-5.

9. **Spaeth, B** & Shephard, M 2016, 'Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's Northern Territory', *Point of Care*, vol. 15, no. 1, pp. 30-4.

10. **Spaeth, B**, Shephard, M, Auld, M & Omond, R 2017, 'Immediate pathology results now available for all remote Northern Territorians', paper presented to 14th National Rural Health Conference, Cairns, Queensland, 26-29th March 2017.

11. **Spaeth, B**, Shephard, M & Omond, R 2017, 'Clinical Application of Point-of-Care Testing in the Remote Primary Health Care Setting', *Quality in Primary Care*, vol. 25, no. 3, pp. 164-75

12. McCormack, T, Ayub, R, Aziz, F, Motta, L, **Spaeth, B** & Shephard, M 2017, 'Point-of-care testing facilitates screening and treatment for anaemia in women and children in rural

Pakistan', *Australian Journal of Rural Health*, vol. 10.1111/ajr.12395, DOI 10.1111/ajr.12395.

13. **Spaeth, B**, Kaambwa, B, Omond, R & Shephard, M 2018, 'Economic Evaluation of Point-of-Care Testing in the Remote Primary Health Care Setting of Australia's Northern Territory', *ClinicoEconomics and Outcomes Research,* (accepted 12 March 2018).

The body of work conducted by this author describes, and adds new knowledge to, each of phase of POCT implementation, management and evaluation, particularly in the context of rural and remote primary health care settings. A summary of the 13 studies and the phases of POCT implementation or evaluation they relate to is provided in Figure 1.

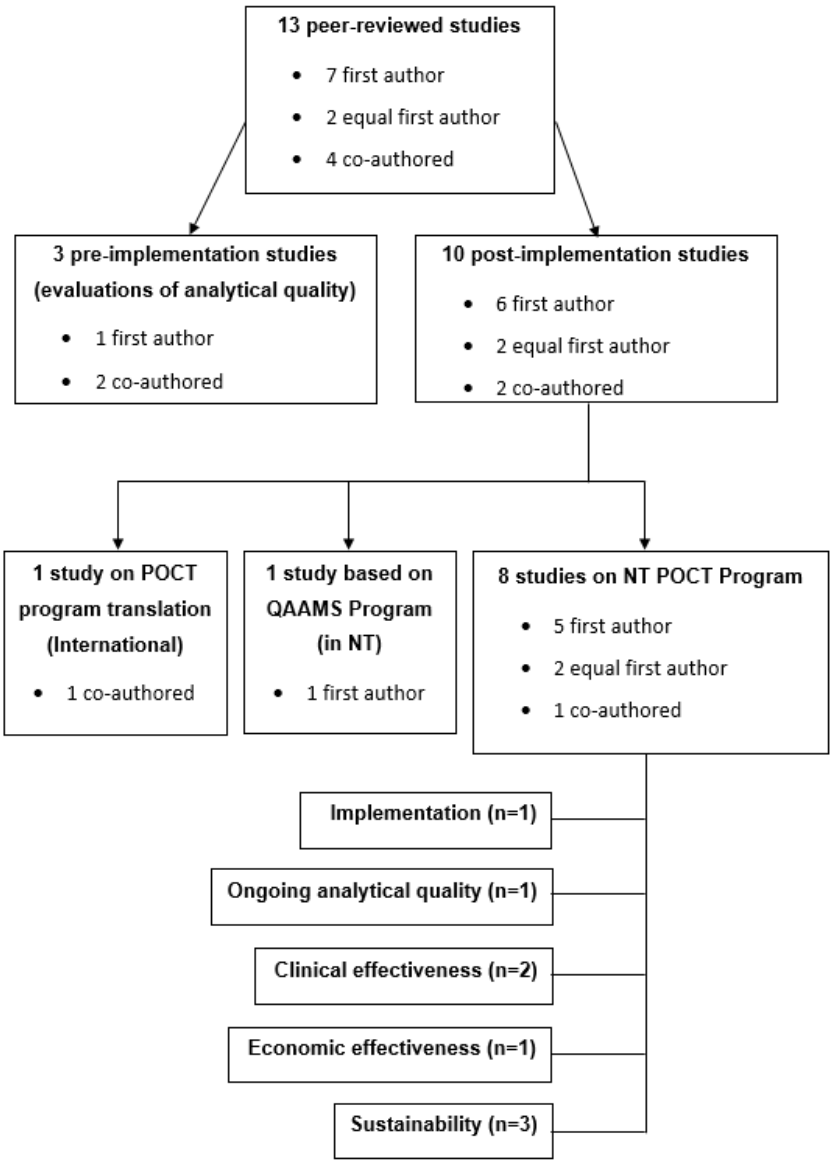

Figure 1 - Summary of this author's studies and the phase of POCT implementation.

Seven of the thirteen peer-reviewed studies presented in this thesis are based on research conducted on the Northern Territory Point-of-Care Testing (NT POCT) Program, which provides POCT to remote communities of the NT. The author of this thesis commenced her research career in 2009 as an honours student researching the effectiveness of the NT POCT Program in its first year of operation. In 2010, the author was employed by the Flinders University International Centre for Point-of-Care Testing (ICPOCT) as a research assistant/scientist supporting the NT POCT Program and, in 2011, became the POC Coordinator, with senior responsibility for managing the Program on a day-to-day basis and assessing the research outcomes (including the clinical, operational, analytical and economic effectiveness). The purpose of assessing these outcomes was to confirm the NT POCT Program was delivering the benefits for which it was introduced, and to ensure it was

sustainable in the long-term. Collectively, the studies presented in this thesis provide the framework for implementation, ongoing management and evidence base for the effectiveness of POCT in this remote setting. Through this work, the author has gained significant experience in all of the aspects of establishing a POCT network in one of the most remote and challenging locations for POCT, the remote NT of Australia. The experience gained over this time has provided this author with a knowledge base on remote health care provision and an empathy for the people that live and work in these isolated locations. Such insights have enabled the identification of the key challenges experienced in these remote areas and the development of techniques to address many of these obstacles. This experience has ultimately led to the advancement of knowledge on how to develop a sustainable framework for the management of POCT in remote and isolated settings.

A further three studies presented in this thesis evaluate the analytical quality of POCT devices within settings not previously examined, thus providing further original contributions to the field of POCT. These studies describe the methods and results for evaluating the analytical quality of POCT devices prior to their implementation for routine use. This initial phase is a key stage of POCT evaluation and provides the foundations for determining POCT device suitability in the setting of intended use. As the author was not involved with the initial evaluation or implementation of the NT POCT Program, these additional studies demonstrate this author's experience and knowledge in determining the suitability of POCT devices prior to routine implementation.

Two studies provide the novel methods for addressing the challenges and ensuring the sustainability of POCT in rural and remote locations. These additional contributions to the literature were based on the knowledge and experienced gained by this author as part of her role in coordinating the implementation and routine management of POCT in rural and remote settings.

The remaining study presented in this thesis provides evidence for the transferability of the knowledge and methods developed by this author for the application of POCT in rural and remote locations outside Australia. This study provides the results for a POCT model implemented to screen for anaemia in rural Pakistan, a location which has very limited access to pathology testing and poor quality laboratory services.

Together, these studies provide an evidence base for the efficacy of POCT in a clinical setting that has received little attention in the national or international peer-reviewed literature, namely,

remote primary health care in Australia. Several aspects of POCT utilisation in this unique setting are examined in the studies included in this thesis:

- Initial assessment of POCT device safety and quality;
- Implementation of a POCT model;
- Evaluation of the effectiveness of a POCT program(s) from clinical, operational, cultural, analytical and cost perspectives; and
- Translation of a POCT model to an alternative setting.

Through this systematic approach, the studies presented in this thesis build upon one another to construct a significant knowledge base on the sustainable implementation, management and evaluation of remotely located POCT networks.

The first section of this introduction provides descriptions of the key terms used in this thesis. Included is a definition of POCT technology and how this technology differs from pathology testing in the laboratory. To provide context for the studies presented in this thesis, a definition and description of remote health care in Australia is also provided. Additionally, a descriptive summary of the NT POCT Program is included, as it is within this POCT network that a majority of the studies included in this thesis have been undertaken. Finally, a brief summary of the current gaps in POCT literature will be outlined as a prologue to the next chapter, the literature review.

A review of current literature regarding the use of POCT in rural and remote locations will form the second chapter of this thesis. The literature review will provide a summary of the previous limited research investigating the use of POCT in rural and remote locations by grouping the studies into common themes, namely, POCT device evaluations; POCT for chronic, infectious and acute disease states; POCT for pregnancy; and POCT more generally in rural and remote locations. Within each of the themes, the gaps in knowledge are highlighted to create the foundation for the next chapter, the contextual statement.

The contextual statement will demonstrate where each of the studies by this author situate within the present POCT literature and highlight how each contributes to new knowledge in the field of POCT. A narrative description of the phases required to establish a POCT model then demonstrates how each of the studies systematically builds on one another to provide a significant evidence base supporting the use of POCT in remote primary health care settings. A summary of the initiatives

developed by this author to ensure the sustainability of POCT in remote locations is also provided to highlight the novel methods developed by the author of this thesis. How each study builds upon the next is reinforced in the next chapter.

The fourth chapter of this thesis, the linking statement, provides the studies in a logical order according to the phases of POCT evaluation, implementation and assessment. A linking statement is provided between each publication with a succinct summary of the study and a statement to demonstrate how each study builds upon the next. A declaration of this author's contribution to each study is also provided.

The final chapter of this thesis, the discussion, summarises the original contributions to knowledge presented in this thesis and provides discussion on the overall significance and limitations of the studies included. Directions for future research are also presented.

Lastly, the appendices includes the additional contributions to knowledge provided by this author in the field of POCT that were not peer-reviewed. This includes an editorial by this author invited after an oral presentation of a peer-reviewed study at the National Rural Health Conference in Australia. Also included are three invited book chapters co-written by the author of this thesis, one on POCT connectivity systems, another on POCT for drugs of abuse, and the last on stakeholder perspectives on POCT. While the book chapters do not specifically relate to the use of the POCT in rural and remote locations, they demonstrate this author's broader expertise and additional contributions to the literature outside those discussed in the body of the thesis.

1.1 Descriptions of Key Terms

1.1.1 Definition of Point-of-Care Pathology Testing

For the purpose of this thesis, Point-of-Care Testing (POCT) is defined as pathology testing performed at, or near to, the site of patient care with results available within the initial consultation. The rapid turnaround time of pathology test results at the point of care facilitates the making of timely clinical decisions regarding patient management and treatment. Key to this process is that the POC result(s) are acted upon by a clinician in a timely manner to enable more rapid changes to patient management and, thus, an improvement in the patient's outcome.

POCT devices are generally small, portable and require only a few drops of blood, urine or other specimen for analysis, with most able to generate a result within 20 minutes. The term POCT also has several synonyms that have been widely used in published literature over the past 20 years. These include:

- Near patient testing
- Bedside testing
- Extra laboratory testing
- Physician's office testing
- Rapid diagnostic testing
- Auxiliary testing
- Decentralised testing (Price 2001b).

The practice of diagnostic testing at the point of care is not new. In fact, many early diagnostic tests were first conducted by physicians at the patient's bedside. For example, in the 17th century, it was common practice for physicians to taste patients' urine to provide differential diagnoses for various ailments such as diabetes and kidney disease (Berger 1999).

Despite POCT not being a new field, it does not have one universal definition. Several definitions of POCT in the literature are summarised in Table 1. Much of the emphasis is placed on the immediate or rapid availability of diagnostic test results provided by POCT. However, just generating rapid results is not as critical as the need for that result to be acted upon clinically in a timely manner. Without this, POCT cannot delivery improved patient outcomes as the time for clinical action is the

limitation in the value of performing POCT (Bissonnette & Bergeron 2010; Pai, N, Vadnais, et al. 2012; Price 2001a, 2001b).

Table 1 - Definitions of Point-of-Care Testing from prominent authors in the literature.

Citation	Definition
Handorf (1994)	*Alternative site testing is diagnostic testing undertaken within a hospital's jurisdiction but outside of the traditional hospital laboratory setting.*
Delaney et al. (1999)	*Near patient testing is any investigation carried out in a clinical setting or the patient's home for which the result is available without reference to a laboratory and perhaps rapidly enough to affect immediate patient management.*
Price (2001a)	*Any type of testing undertaken close to the patient to enable a decision to be made on the care of that patient.*
Kost (2002)	*Point-of-care testing is testing at or near the site of patient care.*
Shephard, M (2010)	*Point-of-care testing can be defined as pathology testing performed on-site during the patient consultation. It allows a rapid test result to be generated and used to make an immediate, informed clinical decision.*
Asha et al. (2013)	*Point-of-care (POC) testing, defined as laboratory testing near a patient location with rapid availability of results, has the potential to reduce ED length-of-stay (LOS) through short turn-around times allowing clinical decisions to be made earlier.*
National Pathology Accreditation Advisory Council (2015)	*PoCT means pathology testing performed near or at the site of the individual by a PoCT Operator at the time of the consultation or encounter.*
Pai, M, Ghiasi and Pai (2015)	*POC testing is diagnostic testing that will result in a clear and actionable management decision such as when to start treatment or to require a confirmatory test, within the same clinical encounter.*

POC= Point-of-Care, ED=emergency department, LOS=length of stay, PoCT=Point of Care Testing

It is the experience of this author that the capacity to use POCT becomes most significant when a community or population does not have access to timely laboratory diagnostic tests for disease states that commonly affect that particular community. In remote or isolated locations, where the

access to diagnostic tests is further limited, POCT may offer the only effective means of obtaining timely diagnostic test results. In such settings, POCT can enable more rapid diagnoses and changes to treatment, which in turn may provide improvements in the clinical management of patients and population health status in general.

The vast majority of current literature focusses on the use of POCT for either chronic disease in the primary care setting, tropical infectious diseases in low-resource settings or acute care within the tertiary hospital emergency department (ED). However, the scope of POCT has now reached a variety of clinical settings. Shephard, M (2016a) provides a summary of the health care settings where POCT is currently being used, as provided below in Table 2.

Table 2 – Summary of clinical settings and applications of POCT published in the literature.

Hospital-based	**Community-based**	**Other Settings**
Emergency department	General practice/physician office	Disaster management
Adult intensive care unit	Pharmacy	Extreme environments
Neonatal intensive care unit	Community health clinic	Military
Coronary care unit	Aboriginal medical service	Space research
Operating theatre	Retrieval unit	
Ward	Workplace	
Outpatient clinic	Veterinary clinic	
	Leisure facility	
	Sports medicine	
	Home care	

Note. From 'An introduction to point-of-care testing and its global scope and application' (Shephard, M 2016a).

A further field of POCT is for drugs of abuse testing, which is commonly used either on the roadside or in the workplace. As part of her work at the Flinders University ICPOCT, this author has experience and knowledge in POCT for drugs of abuse and has made a contribution to the

literature in the form of a co-authored book chapter titled 'Point-of-care testing for drugs of abuse', provided in Appendix B.

In all clinical settings, the evaluation or assessment of POCT is most often compared to pathology testing conducted by the laboratory as this is the 'standard' or 'usual' method for obtaining pathology test results.

1.1.2 Laboratory-based pathology testing

POCT is different to pathology testing conducted within large centralised laboratories. Laboratory-based pathology testing services are often disconnected from the site of patient care and require patient samples to be transported from the site of patient care. Once the specimen has arrived at the laboratory, it is loaded onto large, generally automated, medical device with results reported back to the treating doctor either electronically or by phone. The centralisation of pathology services originated to achieve greater economies of scale and, thus, a reduction in costs associated with pathology testing (Plebani 2015). Therefore, this traditional form of pathology testing either requires the patient sample to be transported to the centralised laboratory, or the patient themselves to travel to the laboratory's pathology collection service. Further, when using laboratory-based pathology testing, the patient is required to return for a follow-up consultation, or wait in the ED until, until the pathology results are reported from the laboratory to the treating doctor. This process, therefore, delays diagnoses from being made as well as modifications to treatment and changes to a patient's clinical management. Delays in receipt of pathology test results are known to create issues with loss-to-follow-up of patients who do not return to their health facility (Cameron & Dupal 2009; Casalino et al. 2009; Poon et al. 2004). Additionally, slow turnaround of pathology results has also been shown to cause decreased medication compliance and delays in initiating treatment (Gialamas, Yelland, et al. 2009; Hawkins 2007). Problems with the preparation and transport of pathology samples, such as inappropriate storage or labeling, may result in pathology samples not being accepted by the laboratory (Astion et al. 2003; Cameron & Dupal 2009; Hammerling 2015; Hawkins 2007). In the case of lost or damaged specimens, or those affected by lengthy time delays, the patient is required to re-present to the collection centre to provide a new sample, causing inconvenience to the patient as well as further delays in clinical management. Significant issues have also been documented in relation to the review and follow up of pathology results once reported by the laboratory, with previous studies finding that as many as 26% of pathology results are not reported back to the patient by the treating doctor (Casalino et al.

2009). Failing to follow up abnormal pathology results with patients has also been known to cause significant medico-legal issues as this may jeopardise patient safety (Poon et al. 2004). In terms of its effects on the economy, delays in reporting pathology results are known to cause significant cost burdens to the Australian health system. For example, within hospital EDs, approximately half of all delays in treatment and increases in length of stay are attributable to prolonged times in receiving pathology results (Steindel & Howanitz 2001).

Although pathology test results are said to influence around 70% of all health care decisions and, as outlined, the issues caused by delays in pathology results are many, very little quantitative literature exists on the turnaround time of pathology results (Hawkins 2007; Royal College of Pathologists of Australasia 2008; Steindel & Howanitz 2001). Also, as laboratories generally report the turnaround times for results as the time from receipt of the specimen to the time the results are reported to the treating doctor, the time associated with transporting pathology specimens is not taken into account (Hawkins 2007).

1.1.3 Laboratory-based pathology testing in Australia

Pathology laboratories in Australia are most often located in large metropolitan or urban centres within either tertiary hospitals or private pathology businesses. Those living in metropolitan and urban areas can expect a relatively fast turnaround time for pathology results; either the same day or within a maximum of 24 hours for most tests. However, for those living in living in rural or remote locations, the access to pathology services is significantly reduced, causing further challenges and delays in receiving pathology test results (Cameron & Dupal 2009). Despite over one-third of pathology collection centres in Australia being located in regional, rural or remote locations, pathology samples must nevertheless be transported to centralised laboratory services for processing (Pathology Australia 2015).

The vast expanse of Australia's landscape creates a tyranny of distance between its metropolitan centres and its rural and remote communities. Extreme environmental conditions, such as Australia's hot and humid climates, also create significant problems with transporting pathology specimens from rural and remote locations to central laboratory services (Shephard, M, Tirimacco & Tideman 2010). Similar issues with transporting pathology specimens are experienced internationally, with other isolated locations, such as the mountainous areas of Italy and Thailand,

reporting difficulties in obtaining timely pathology results (De La Torre & Campoy 2009; Kost, Suwanyangyuen & Kulrattanamaneeporn 2006).

In Australia, the 2.6 million people living in rural and remote locations, who represent 11% of the total population (Australian Bureau of Statistics 2016b), experience significant delays in receiving pathology test results due to the distance from centralised laboratory services (Shephard, M 2013). These delays force the patient to return to the community health service to obtain pathology results, which in some cases may be more than a week after their initial presentation (Shephard, M et al. 2006). For patients requiring regular pathology testing, such as those on peritoneal dialysis for end-stage renal disease or anticoagulation therapy for cardiac disease, the long turnaround time of pathology results may necessitate the patient relocating closer to centralised pathology laboratories where more rapid pathology test results are made possible (Cameron & Dupal 2009). This requirement for more timely pathology tests can cause patients to be dislocated from family and friends causing significant stress. Approximately one third of the Australian population living in rural or remote locations are Indigenous (Australian Bureau of Statistics 2011b). For Indigenous people, the physiological stress caused by dislocation from family, community or traditional homelands is known to lead to mental health issues and deterioration of health in general (Elliot-Schmidt & Strong 1997; Zubrick et al. 2010). In some instances, the requirement to relocate to metropolitan centres for health reasons has resulted in the refusal of care leading to rapid declines in health status and unnecessary death (Devitt & McMasters 1998; Marley et al. 2010; Walsh & Kangaharan 2017).

In patient presentations where a possible acute cause cannot be ruled out without diagnostic test results, the long turnaround time associated with laboratory pathology testing is impractical. In these situations, the patient must be transported to the nearest tertiary hospital ED where the required diagnostic tests and other investigations can be performed rapidly to provide a differential diagnosis. To provide an example, up to one quarter of all hospital admissions are for patients presenting with chest pain (Goodacre et al. 2005), however, approximately 80% of these patients do not receive a diagnosis of acute coronary syndrome (ACS). Of these, almost half (40%) could be ruled out with the use of pathology testing alone, either by the laboratory or by POCT for cardiac markers such a troponin (Centre for International Economics 2016). As such, rapid pathology testing may significantly reduce the burden of unnecessary hospital admissions and hence the unnecessary use of valuable hospital resources. In rural or remote locations, the costs associated with unnecessary hospitalisation is significantly increased as patients often must be transported by air over vast distances to reach a tertiary hospital ED (Florkowski et al. 2017). These emergency medical

retrieval services are expensive, costing anywhere from $8,000 to $16,000 per one-hour return patient retrieval (Spaeth et al. 2018), with costs increasing significantly in line with the degree of distance from a major centre.

While traditional laboratories provide an integral service to the medical profession, as has been discussed, in some instances the turnaround time for results is not practical for patient care (Hawkins 2007). In this way, POCT does not necessarily replace the laboratory, but rather extends the pathology service to more isolated locations (Florkowski et al. 2017). Therefore, where a more rapid turnaround time for pathology results is required, POCT offers a practical solution as it is conducted at the site of patient care.

1.1.4 Benefits of POCT over laboratory-based pathology testing

As POCT enables the generation of pathology test results within the initial consultation, the need for a follow-up visit to obtain results and changes in clinical management is negated. Although not always the case, the availability of pathology results within the same consultation has been demonstrated to provide significant advances over standard pathology testing. These include:

- Increased satisfaction of both doctors and patients (Chaudhry et al. 2004; Laurence, Gialamas, et al. 2010; Motta et al. 2015; Natoli, L, Guy, RJ, Shephard, MDS, Causer, L, et al. 2015);
- Improvements in doctor-patient relationship (Jones et al. 2013; Shephard, M 2006c);
- Better medication compliance (Bogner et al. 2012; Gialamas, Yelland, et al. 2009);
- Increased motivation for patients to improve their own health (Laurence, Gialamas, et al. 2010; Shephard, M et al. 2006);
- Improved chronic disease management such as improved glycaemic control in patients with diabetes (Schnell, Crocker & Weng 2017; Shephard, M et al. 2006);
- Greater time within therapeutic range for anticoagulation therapy (Dennis et al. 2017; Fitzmaurice 2006; Spaeth & Shephard 2016);
- Reduced rates of transmission for sexually transmitted diseases (Sanders et al. 2010);
- More informed administration of medication such as antimalarial drugs (Mbonye et al. 2015; Zurovac et al. 2008);

- Reduced rates of unnecessary antibiotic prescription for respiratory tract infections (Cals et al. 2009; Cals et al. 2010; Cooke et al. 2015; Jakobsen et al. 2010; Little et al. 2013); and
- Rapid exclusion of pulmonary embolism and deep vein thrombosis (Geersing et al. 2009; Geersing et al. 2012).

For patients requiring regular pathology testing to monitor their condition, such as patients with diabetes, POCT provides increased convenience as patients can have the testing performed at their local health service with results available within the same presentation (Shephard, M et al. 2006; Shephard, M et al. 2005). In these instances, POCT eliminates the burden of multiple visits to obtain pathology results and to receive changes in treatment (Lee-Lewandrowski & Lewandrowski 2009). Within the hospital ED, POCT has been shown to enable earlier decision making (Kendall, Reeves & Clancy 1998) as well as reduced length of stay in the ED (Florkowski et al. 2017). POCT has also been demonstrated to reduce the anxiety associated with waiting for pathology test results as the results are provided, and can be discussed, with the patient within the same consultation (Bolvin & Lancastle 2010).

Several studies have also shown POCT to be more cost-effective compared to the standard laboratory, however, these results have been variable. The majority of studies demonstrating lower cost associated with POCT have attributed the cost savings to a reduction in length of stay in the hospital ED (Florkowski et al. 2017; Takakuwa et al. 2009; Tsai et al. 1994) or increases in quality-adjusted life years (Hendriksen et al. 2015). Regarding the cost-effectiveness of POCT in primary care settings, few studies have demonstrated reduced costs associated with POCT with the majority of studies determining that the POCT method is equivalent, or more costly, than the standard practice (Laurence, Moss, et al. 2010; Wells et al. 2017). However, many of these studies conclude the cost associated with improvements to clinical outcomes when using POCT was not factored into the cost-effectiveness analysis (Florkowski et al. 2017; St John & Price 2013). Furthermore, many cost-effectiveness analyses only take into account the cost per test for analysing pathology samples in the laboratory and do not take into account the costs associated with transporting and processing the pathology specimens in a central laboratory (Lee-Lewandrowski & Lewandrowski 2009). These extra-laboratory costs are likely to significantly increase the cost associated with standard laboratory testing and it is expected that the cost would increase the greater the distance travelled. For example, the pathology samples from most remote communities in Australia are couriered by air transport services, thus significantly increasing the cost of transporting these samples.

As has been discussed, POCT enables laboratories to extend their pathology testing services to even the most inaccessible locations. In rural and remote locations, the benefits that POCT offers are even more evident as the turnaround time to receive pathology results are significantly shortened from several days or weeks to just a few minutes (Shephard, M et al. 2006). However, these isolated locations, which ordinarily have either limited or no access to pathology services, pose additional challenges for pathology testing. The remote communities of Australia are one such example of these isolated and challenging environments.

1.1.5 Current limitations of POCT compared to laboratory-based pathology testing

While, intuitively, the immediacy of POCT results should produce significant improvements in the efficiency of health care delivery and therefore significant clinical benefits, there is a lack of literature establishing the link between more rapid turnaround time of pathology results and improvements to patient outcomes (Florkowski et al. 2017; Hawkins 2007). The primary reason for the potential of POCT not being realised is the current configuration of the health care system, which has at least in part been structured to meet the requirements of traditional laboratory pathology testing. This is evidenced by many published studies stating that health service delivery must be restructured to incorporate POCT into routine care (Engel, Ganesh, et al. 2015; Florkowski et al. 2017; Pai, M, Ghiasi & Pai 2015; Pai, N, Vadnais, et al. 2012; Wells et al. 2017). Another reason may also be due to health care providers/professionals recognising laboratories as the accepted norm for conducting pathology testing (Jones et al. 2013). It is these barriers and mindsets that pose challenges for POCT being effectively incorporated into routine practice. That being said, there is now a significant volume of published literature in support of the use of POCT in almost all fields of pathology and across many diverse clinical settings. The vast majority of literature has focussed the use of POCT for either chronic or infectious disease in the primary care setting or on acute illness in the hospital ED. However, as will be outlined in the literature review, very little research on the use of POCT in rural or remote locations has been conducted, with the majority of this research focussed on POCT use for chronic disease management or the identification of infectious disease or sexually transmitted infections (STI).

Although it is generally understood that primary health care in Australia does not include the management of acute presentations, due to the absence of an on-site doctor in many cases, in remote and also sometimes in rural settings, primary health services may be the only provider of health care in the area and, thus, must deal opportunistically with all forms of health care provision,

including acute presentations (Wakerman 2004; Wakerman et al. 2017). In remote primary care settings, the geographic isolation, limited infrastructure and lack of specialist services create the perfect niche for POCT; it is this niche that has led to the development of the studies included in this thesis.

1.1.6 Definition of Remote Health (in Australia)

The terms 'rural' and 'remote' generally refer to locations that exist outside of major metropolitan, urban and regional areas, with remote environments being more distant than rural locations in terms of geographical isolation, and more resource-poor in terms of level of access to goods and services (such as food, infrastructure, housing, schooling and health services).

First, to provide context of the extent of remoteness in Australia, the Australian Bureau of Statistics provides a map of Australia classifying remoteness areas as shown in Figure 2. Approximately 5.7 million square kilometres (74%) of Australia's landmass is defined as remote or very remote, with just over half a million people living in these locations (Australian Bureau of Statistics 2011a).

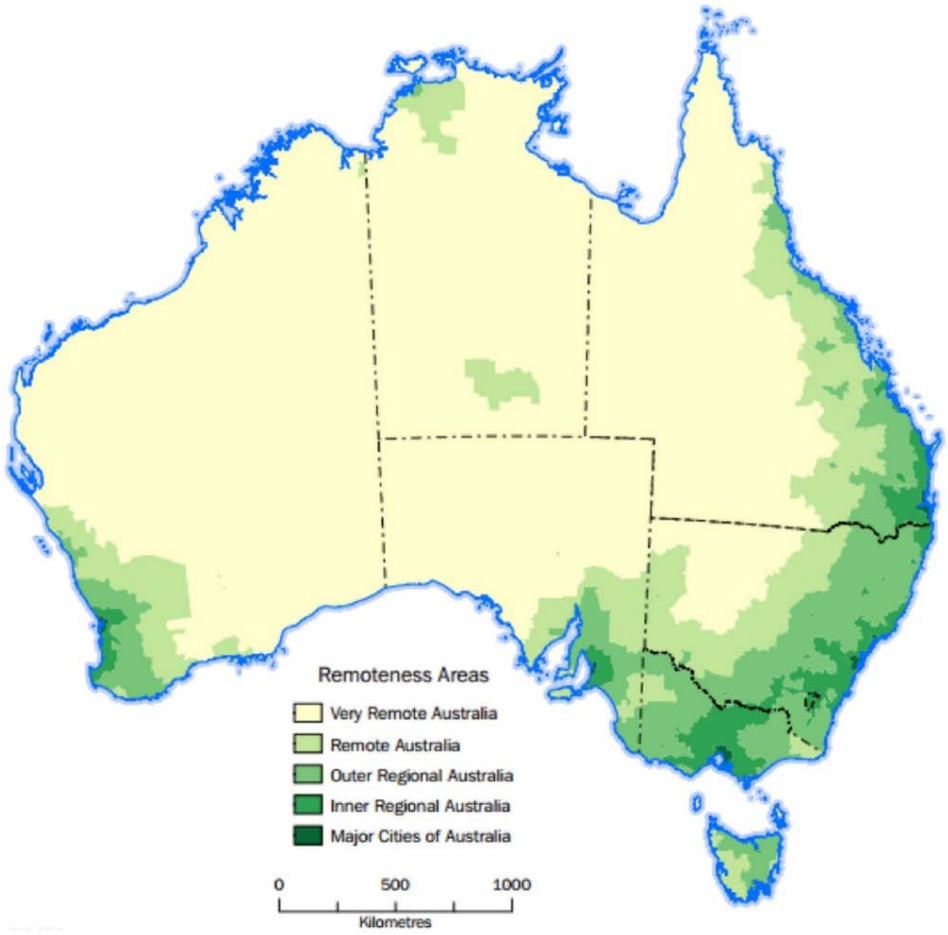

Figure 2 – Australian Bureau of Statistics Remoteness Structure Map of Australia

Source: Australian Bureau of Statistics (2011a)

The focus of this thesis is on the use of POCT in remote locations in Australia. Despite the use of the term 'rural and remote' in several of this author's studies, eight of the thirteen studies were conducted solely in remote locations. That being said, the outcomes and implications of these studies are likely to be generalisable to both rural and remote settings in Australia due to the similarities in inaccessibility of pathology services in both settings. The geographic isolation of rural and remote areas of Australia provides a unique set of challenges not experienced by metropolitan and urban health care settings. Lyle and colleagues stated that "*Nowhere is the challenge of improving access to health care more acute than in rural and remote communities*" (Lyle et al. 2017).

Wakerman (2004) defined the discipline of remote health through examining the existing international literature in the field. This search found the literature was lacking in a definition that adequately explained remote health in the Australian context. Therefore, Wakerman (2004) provided the following definition of remote health based on information from a literature search and through his expert knowledge and experience working in the remote health sector:

> *Remote Health is an emerging discipline with distinct sociological, historical and practice characteristics. Its practice in Australia is characterised by geographical, professional and, often, social isolation of practitioners; a strong multidisciplinary approach; overlapping and changing roles of team members; a relatively high degree of GP substitution; and practitioners requiring public health, emergency and extended clinical skills. These skills and remote health systems, need to be suited to working in a cross-cultural context; serving small, dispersed and often highly mobile populations; serving populations with relatively high health needs; and a physical environment of climatic extremes.*

According to the Australian Institute of Health and Welfare, people living in remote and very remote locations have poorer access to health services, higher rates of avoidable hospitalisations and lower access to most hospital procedures compared to those in rural or metropolitan areas (Australian Institute of Health and Welfare 2016). This is further evidenced by a later qualitative survey by Wakerman et al. (2017) involving rural and remote health experts in Australia to determine if there

was a distinct difference between rural and remote health. The majority of participants in this study indicated rural health was different to remote health in the following ways: remote populations are smaller, more isolated and more widely dispersed; socioeconomic disadvantage, morbidity, and mortality are all generally higher in remote locations; the turnover of health professionals is greater and the retention of staff more difficult in remote locations; and there is poorer access to health services in remote locations. Also, this study identified that the differences between rural and remote health were more pronounced in remote Indigenous health care compared to non-Indigenous health care settings.

In Australia, around one-quarter of Indigenous people live in remote or very remote locations and constitute around 45% of the population living in very remote areas (Australian Institute of Health and Welfare 2015). The health of Indigenous Australians is characterised by higher burdens of chronic and infectious disease for almost all disease states compared to non-Indigenous Australians (Al-Yaman 2017). These high burdens of disease significantly affect the life-expectancy of Indigenous people, which is approximately ten years less than non-Indigenous Australians at birth (Australian Institute of Health and Welfare 2015). Also, the age-standardised rates of death are two to four times higher for Indigenous compared to non-Indigenous Australians (Australian Health Ministers' Advisory Council 2015). Reasons for such high discrepancies in health status between Indigenous and non-Indigenous Australians are multifactorial with the social determinants of health being the most commonly cited cause of the inequalities experienced (Australian Institute of Health and Welfare 2016; Phillips 2009; Zubrick et al. 2010). These social determinants include lower levels of education and employment, and higher rates of overcrowding and homelessness (Australian Institute of Health and Welfare 2015; Quilty et al. 2016). These disparities in social determinants and health status increase with increasing remoteness (Australian Institute of Health and Welfare 2014), and nowhere are the disparities in Indigenous health status more pronounced than in the remote NT of Australia (Zhao et al. 2004). One reason for this may be the higher proportion of Indigenous people in the NT; approximately one-third of the NT population compared to 5% or less in other jurisdictions (Australian Institute of Health and Welfare 2015). Moreover, the NT has the highest proportion (49%) of Indigenous people living in its rural and remote communities (Australian Bureau of Statistics 2016a). In the Top End of the NT, the remote communities have been described as the most disadvantaged of all remote communities in Australia (Roberts et al. 2015). The disadvantages experienced in remote areas of the NT have been suggested to be due to the harsh environmental conditions and extreme remoteness (Quilty et al. 2016). These factors also pose

significant challenges for laboratory pathology testing which relies on the timely transport of the specimens to the central laboratory. This is particularly the case for pathology tests that require the specimen to be analysed within a stipulated short timeframe after the specimen has been collected. As such, the health care clinics serving remote communities rely on the availability of transport to courier pathology specimens to central laboratories. In the Top End of the NT, the wet season (November to April) often means roads are cut-off for months at a time, and aeroplanes are unable to land due to adverse weather. Also, there are many island communities in the Top End where air or water transport are necessary. In Central Australia, the desert conditions and extreme remoteness of the small communities mean that road transport, in particular, is slow, infrequent and prone to breakdowns. These challenges, combined with high burdens of chronic, infectious and acute disease, create an ideal niche for the use and uptake of POCT.

1.1.7 Northern Territory Point-of-Care Testing Program

Over the past eight years, this author has been the POC Coordinator responsible for the routine management of the Northern Territory Point-of-Care Testing (NT POCT) Program. Therefore, the majority of studies (eight of thirteen) presented in this thesis are based on research conducted within this Program. A description of the NT POCT Program is provided here to give the necessary background information to these studies.

The NT POCT Program commenced in 2008 after a review of pathology services in the NT in 2007 revealed that many remote health services had very poor access to pathology services (Shephard, M et al. 2012a). The poor access was attributed to the extreme remoteness of many of the communities, but was also due to a recent collapse in air services in the NT which significantly reduced the options available to transport pathology specimens to centralised laboratories in the territories major centres of Alice Springs and Darwin. To address the shortfall in pathology services, the former NT Government Department of Health and Families (DoHF) purchased 20 Abbott i-STAT (Abbott, USA) POCT devices. As pictured in Figure 3, the Abbott i-STAT device is a hand-held, cartridge-based POCT device, capable of providing a wide range of chemistry and haematology test results in under ten minutes.

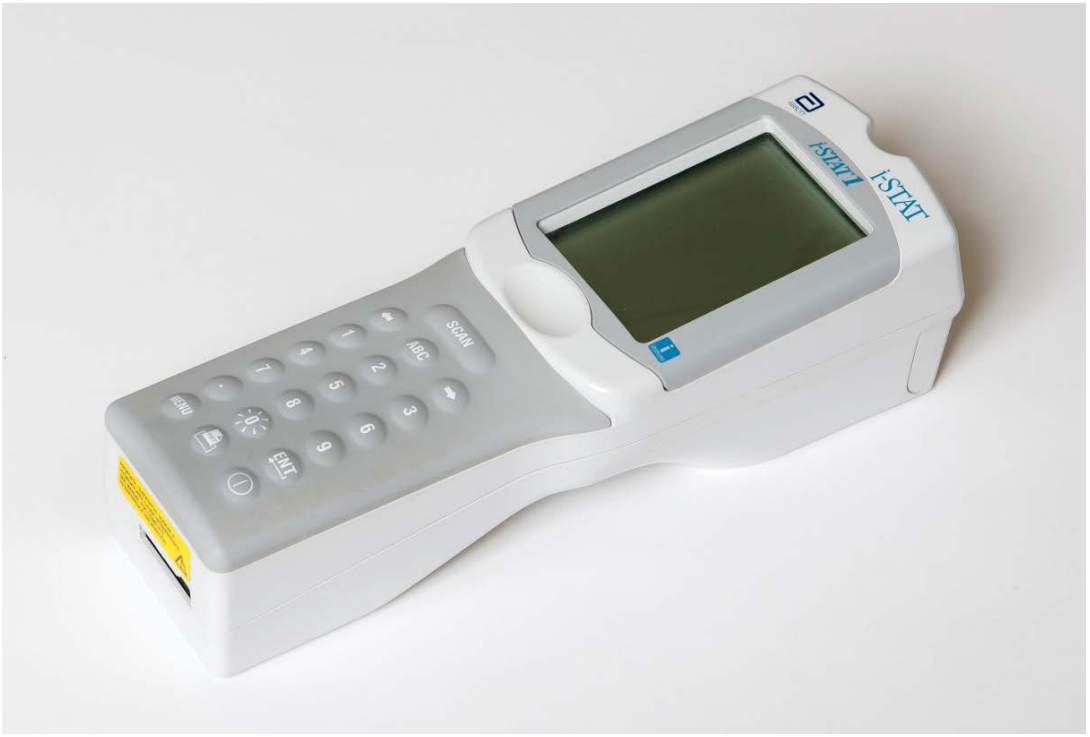

Figure 3 – Image of Abbott i-STAT device

The i-STAT device was chosen due to the wide range of pathology tests it could provide on a single platform. The i-STAT is battery-powered and light weight (520g), making it highly portable and, thus, suited to the remote health environment which is highly variable. A summary of the i-STAT cartridge types used in the NT POCT Program with corresponding analytes, test time and required blood volumes is provided in Table 3.

Table 3 – Summary of Abbott i-STAT cartridge types used in the NT POCT Program.

i-STAT Cartridge	Analyte(s)	Test Time	Blood sample required	Blood volume required
PT/INR	Prothrombin Time (PT)/International Normalised Ratio (INR)	Up to 5 minutes	Capillary or venous whole blood	20-45µL
cTnI	Cardiac Troponin I	10 minutes	Venous whole blood	17µL
Chem8+	Sodium, potassium, chloride, ionised calcium, total carbon dioxide (TCO_2), urea, creatinine, glucose, haematocrit, haemoglobin, anion gap	2 minutes	Venous whole blood	95µL
CG4+	pH, partial pressure of carbon dioxide (CO_2), partial pressure of oxygen (O_2), TCO_2, bicarbonate, base excess, oxygen saturation (sO_2), lactate	2 minutes	Venous whole blood	95µL

A further reason for the i-STAT being the POCT device of choice for the remote NT health services was that the pathology tests offered by the i-STAT device could assist with the management of several 'high burden' diseases in the NT. A summary of common chronic and acute disease states in the NT (and corresponding i-STAT analytes that can be measured by this POCT device) is provided in Table 4.

Table 4 – Summary of disease states and clinical applications of i-STAT analytes.

Disease type	Clinical Application	i-STAT Analyte(s)
Chronic disease	Anaemia	Haemoglobin
	Chronic Kidney Disease	Creatinine and Urea
	Monitoring glycaemic status	Glucose
	Monitoring patients on anticoagulation therapy	INR
Acute disease	Early risk stratification of acute coronary syndrome (ACS)	Cardiac Troponin I
	Assessment of hydration status	Electrolytes (sodium, potassium, chloride)
	Assessment of fluid and electrolyte balance	Electrolytes (sodium, potassium, chloride)
	Assessment of sepsis or septic shock	Lactate

Twenty i-STAT devices were supplied to the remote health services determined to have the greatest need based on their frequency of pathology transport services and highest burdens of disease.

While it was anticipated that the implementation of the i-STAT device would have immediate impact on access to timely pathology testing and, thus, predicted operational and clinical improvements to health service delivery, it was soon realised that the i-STAT devices were not being utilised to their full potential. Many devices were found packaged up and placed in a cupboard within the health service. After an investigation into the reasons for lack of use of the i-STAT devices, the primary cause was found to be a lack of staff training and troubleshooting support for the i-STAT device, together with concerns about the analytical quality of testing on the device and the perceived view that POCT results could not be as accurate or reliable as those from the laboratory. This led the NT DoHF to seek the expertise of the Flinders University ICPOCT (formerly known as the Community Point-of-Care Services [CPS] unit). At the time, the CPS unit was the only provider of POCT models in primary health care in Australia with significant experience in the delivery of evidence-based

POCT programs (Shephard, M et al. 2006; Shephard, M, Mazzachi, et al. 2009; Shephard, M, Shephard, et al. 2009). Due to the extreme remoteness of the NT and its high burdens of disease, the CPS unit recognised the critical need for POCT in this setting and agreed to assist with the implementation and ongoing coordination of the i-STAT device in the remote NT.

The high rates of diabetes and chronic kidney disease (CKD) in the remote NT also led the CPS unit to suggest the simultaneous implementation of the DCA 2000 (Siemens, Australia) POCT device which tests for Haemoglobin A1c (HbA1c) to monitor glycaemic control in patients with established diabetes and urine albumin-creatinine ratio (ACR) to screen for microalbuminuria in at-risk individuals. The DCA 2000 was the POCT device chosen for use within the Quality Assurance for Aboriginal and Torres Strait Islander Medical Services (QAAMS) Program due to its proven analytical quality, ease of use and high acceptability within the Indigenous health care setting (Shephard, M 2004c, 2006c; Shephard, M & Gill 2006). The clinical effectiveness of the QAAMS Program had also been established in terms of improving glycaemic control in Indigenous people with diabetes (Shephard, M 2006c; Shephard, M et al. 2006). For these reasons, the NT DoHF also agreed to enrol 20 remote health services with the highest burdens of diabetes into the QAAMS Program. At the time, this author was also the Quality Manager for the QAAMS Program, primarily responsible for the monitoring and assessment of quality control and quality assurance testing on the DCA 2000 device.

In August 2008, the CPS unit was formally contracted by the NT DoHF to implement and routinely manage the i-STAT device at 20 remote health services and, at the same time, 20 DCA 2000 devices were loaned to remote NT health services by the CPS unit for QAAMS. A set of agreed research outcomes were also formally incorporated into the contract which included:

- To determine the clinical effectiveness of POCT
- To determine the cultural effectiveness of POCT
- To assess the analytical quality of POCT
- To assess the safety and robustness of POCT

The implementation of the two POCT devices was modelled on the CPS unit's existing POCT programs with formal training, quality testing and support services in place (Shephard, M 2004b; Shephard, M & Gill 2005). A management committee, comprising key members of the CPS unit (including this author) and the NT Department of Health and Families to oversee the NT POCT Program. Training and quality management for POCT was structured to adhere to International

Organisation for Standardization (ISO) Standards for POCT (International Organization for Standardization 2006). Training incorporated both theoretical and practical training and a competency assessment process. For quality testing, initially only Quality Control (QC) testing was introduced to the remote health centres, with QC samples provided by the respective manufacturers (Abbott for the i-STAT and Siemens for the DCA system). Quality Assurance (QA) testing was not initially included for the i-STAT device due to the high associated costs and the limitations of the budget available for this program at the time. To assist with the monitoring of QC testing for the i-STAT devices, a unique and proven method for recording and acting upon QC results (used in the QAAMS Program) was introduced into this program (Shephard, M, Shephard, et al. 2009). Support services included ongoing training support using flexible training options; a range of hardcopy and electronic training resources for quality control and troubleshooting; a telephone hotline/helpdesk manned by CPS scientists (including this author); and quarterly newsletters with advice and updates on the POCT devices. The health professionals trained to use the POCT devices were most commonly remote area nurses (RANs) and Aboriginal Health Workers (AHWs), but also included some Rural Medical Practitioners (RMP), Chronic Disease Coordinators and Continuous Quality Improvement Officers.

Following the initial implementation of the POCT devices, this author was responsible for providing ongoing day-to-day management of the POCT Programs within the remote NT health services. This involved ongoing training of health professional staff, maintaining a competency register, coordinating quality control testing, monitoring and analysis of quality control results, troubleshooting device issues, updating of resources and producing the quarterly newsletter. This author was also responsible for collecting data on the agreed research outcomes. Initially, all tasks and research conducted were overseen by the author's supervisor, Professor Mark Shephard. Two Professional Practice Nurses (PPNs) with the NT DoHF Remote Health division were also assigned to assist with the ongoing management of the NT POCT Program, with one PPN based in Alice Springs and the other in Darwin, to assist with the coordination of Central Australian Health Services (CAHS) and Top End Health Services (TEHS) respectively. The author also routinely travelled to Alice Springs, Darwin and selected remote health services to provide training as required.

As will be outlined in the contextual statement chapter in this thesis, the results of the agreed research outcomes were disseminated as two key publications of which this author was an equal primary author. The full citation for each manuscript is listed below:

Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Loudon, J, Rigby, J & Daniel, V 2012, 'Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program', *Australian Journal of Rural Health*, vol. 20, no. 1, pp. 16-21.

Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Lingwood, A, Loudon, J, Rigby, J & Daniel, V 2014, 'Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program', *Point of Care*, vol. 13, no. 1, pp. 6-11.

Through these research studies, the NT POCT Program was found to be operationally effective, analytically sound and well accepted by health professional staff. Based on these preliminary results, 16 additional remote health services were enrolled in the NT POCT Program so that by January 2015 a total 36 remote health services in the NT had an i-STAT device. The approximate location of the remote communities with an i-STAT at this time is provided Figure 4.

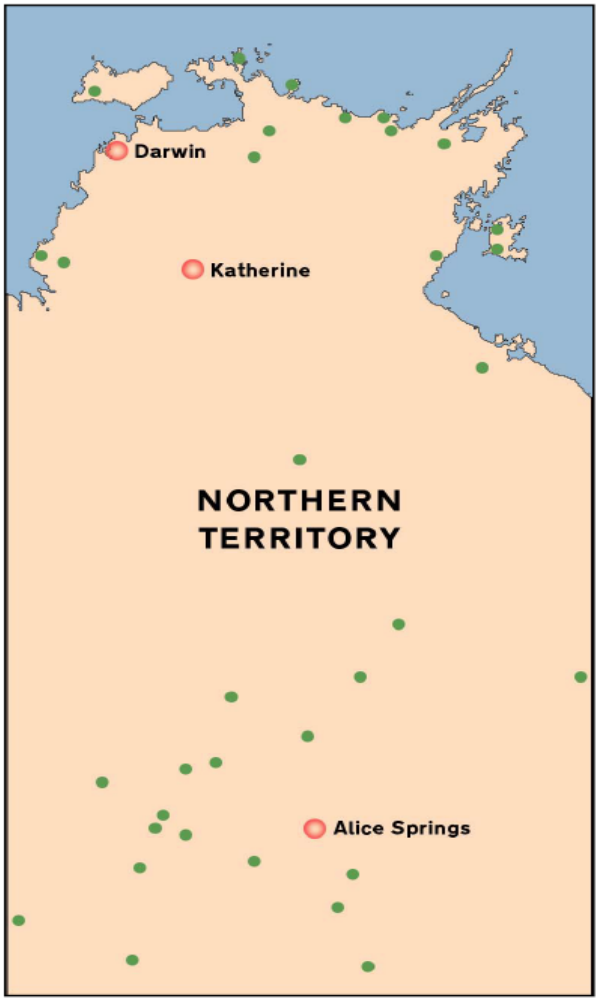

Figure 4 – Location of remote health services with an i-STAT device in 2015.

At the same time, an additional 25 remote health services in the NT had enrolled in the QAAMS Program, bringing the total to 45 services with a DCA 2000 device. During this period, further research studies had been conducted on the clinical utility and operational effectiveness of each POCT device. The full citation for each manuscript is provided below:

> **Spaeth, B**, Shephard, M & Schatz, S 2014, 'Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care', *Rural and Remote Health*, vol. 14, no. 4, p. 2849.
>
> **Spaeth, B** & Shephard, M 2016, 'Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's Northern Territory', *Point of Care*, vol. 15, no. 1, pp. 30-4.

In June 2015, the now NT Department of Health (DoH) (formerly the NT Department of Health and Families) secured additional funding and re-contracted the Flinders University ICPOCT to coordinate the Territory-wide rollout of the i-STAT device to all remotely located primary health care services. This decision was based on the research outcomes found and the long-term sustainability of the NT POCT Program. Another significant driver for the rollout was a formal recommendation by the coroner in 2014 stating that all remote health services in the Territory should have access to the i-STAT device. The coroner's recommendation came as a result of the death of a young Indigenous man which could have possibly been avoided if his ACS has been detected earlier using the i-STAT troponin I test, which provides early risk stratification of ACS (Northern Territory Magistrates Court 2014).

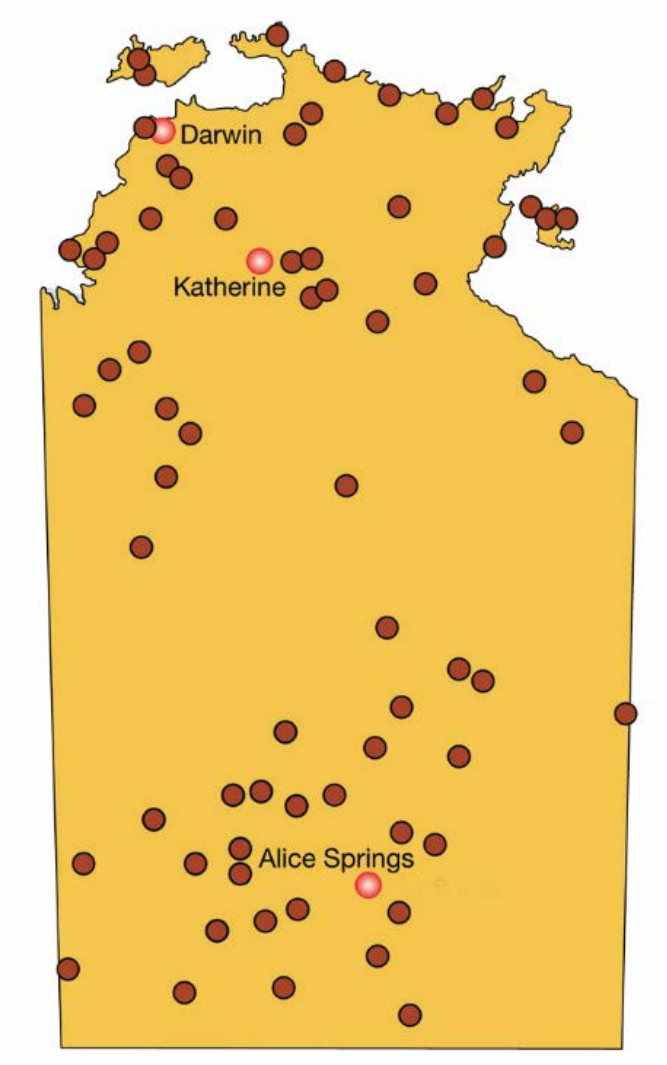

Figure 5 - Location of remote health services with an i-STAT device in 2016.

The rollout of i-STAT devices saw the Program double in size over a period of three months from 36 remote health services in October 2015 to 72 remote health services in December 2015. The approximate location of health services with an i-STAT device in December 2015 is provided in Figure 5. This rollout tested the robustness of the methods developed by this author in being able to withstand the doubling of the number POCT sites while remaining effective and sustainable. The methods and results of the i-STAT rollout were disseminated as a peer-reviewed publication in the 14th National Rural Health Conference Proceedings. The full citation for this publication is listed below:

> **Spaeth, B**, Shephard, M, Auld, M & Omond, R 2017, 'Immediate pathology results now available for all remote Northern Territorians', in L Coleman (ed.), *14th National Rural Health Conference*, Cairns; Queensland.

Up to 2015, the research conducted had firmly established the NT POCT Program was operationally and analytically effective, however, evidence for the clinical utility of POCT had primarily focussed on tests for chronic disease management (Spaeth & Shephard 2016; Spaeth, Shephard & Schatz 2014), with evidence for acute care mainly being anecdotal or provided as individual case studies. Also, evidence for the cost-effectiveness of POCT use in the remote primary health care sector (including the NT of Australia) was absent, as highlighted by the literature review chapter which follows this Introduction. To address these gaps in the current knowledge base, this author was a Chief Investigator for a research grant through the Emergency Medicine Foundation to conduct a study to examine the clinical and cost-effectiveness of POCT for acute care in the remote NT primary health care setting. The Emergency Medicine Foundation is a non-profit organisation providing funding to innovative research that improves the way people are cared for in medical emergencies with the aim of delivering better and more effective health services. A collaborative research team was formed which included a Health Economist and several members of the NT POCT Program Management Committee. A research proposal to examine the clinical and cost-effectiveness of POCT in terms of its utility in aiding decision making around aerial medical retrievals was submitted to the National Rural and Remote Grant Round 1 in 2015. The proposed study was the only grant awarded by the Emergency Medicine Foundation in its inaugural grant round from a total of 160 applications (B von Bibra 2015, pers. comm. 17 April). Two key peer-reviewed publications resulted from the research study. The full citations for each are listed below:

> **Spaeth, B**, Shephard, M & Omond, R 2017, 'Clinical Application of Point-of-Care Testing in the Remote Primary Health Care Setting', *Quality in Primary Care*, vol. 25, no. 3, pp. 164-75.
>
> **Spaeth, B**, Kaambwa, B, Omond, R & Shephard, M 2018, 'Economic Evaluation of Point-of-Care Testing in the Remote Primary Health Care Setting of Australia's Northern Territory', *ClinicoEconomics and Outcomes Research*, vol. (accepted 12 March 2018).

As will be highlighted by the literature review and further discussed within the contextual statement, these studies were the first to examine the clinical and cost-effectiveness of POCT for acute care in a remote primary health care setting.

In the next chapter, the literature review, the limited literature on the use of POCT, specifically in rural and remote locations, will be discussed and the key gaps in literature highlighted.

CHAPTER 2 LITERATURE REVIEW

2.1 Introduction

The aim of this thesis is to demonstrate an original contribution to knowledge in the field of POCT with respect to evaluation, implementation and assessment of outcomes in remote locations, as well as POCT specifically for acute care in remote primary health care settings. As such, this literature review will not provide a comprehensive review of all literature related to the field of POCT.

Therefore, the aims of this literature review are to:

1) Establish the existing literature on POCT use in rural or remote locations or contexts.
2) Demonstrate that little literature exists on the evaluation, implementation or outcomes of POCT use in rural or remote locations.
3) Expose the gap in knowledge in relation to POCT for acute care in remote primary health care settings.

These aims will be addressed through identifying previous studies in the literature that specifically discuss the use or potential use of POCT in rural or remote locations. Each of the studies will then be critically examined to determine their applicability for inclusion in the literature review process. Next, a narrative synthesis of the literature will allow the studies to be grouped into broad categories to demonstrate the themes that arise from the literature in relation to POCT in rural or remote locations. Within each of these sub-groups, the studies conducted in primary care settings will be distinguished from those conducted in secondary or tertiary care settings and the gaps in knowledge will be identified. Finally, the studies that specifically examine the use of POCT for acute care in rural or remote settings will be critically appraised as these studies are the most relevant to the studies presented in this thesis.

2.2 Literature Search Methodology

The literature review was performed by searching the Scopus (Elsevier B.V.) electronic database. Scopus is an abstract and citation database of peer-reviewed literature including scientific journals, books and conference proceedings, with focus on the fields of science, technology, medicine, social sciences and humanities. The methods and key terms used for this literature review are outlined in Table 5.

Table 5 - Summary of literature review search methods

Number	Connector	Search Fields	Search Terms
1		Article title	"point-of-care test*" OR "point of care test*" OR "near patient test*" OR "bedside test*"
2	And	Article title, abstract and key words	remote OR rural OR isolated OR inaccessible
3	Limit to	Language	English language
4	Limit to	Full-text	Studies with full-text available

The common synonyms for POCT were included in the primary search terms, and were sought within study titles to only extract those studies specifically related to POCT. The term 'rapid diagnostic test' was intentionally removed from the search terms to eliminate the large number of studies on the subject of rapid diagnostic tests (RDT) for malaria and other tropical infectious diseases (n=773). These RDTs use immunochromatographic test strips to provide qualitative test results, whereas this thesis focusses on quantitative POC tests for chronic and acute disease. A search of only the first set of terms described in Table 2 identified a total of 2,070 studies in relation to POCT, highlighting the significant volume of literature published in this field.

A second set of search terms were used to identify studies specifically on the use of POCT in rural or remote locations. Internationally, many definitions of rural and remote health care exist and, for these reasons, the literature review was expanded to include the additional terms 'isolated' and 'inaccessible' to capture other potential studies. These secondary search terms yielded a total of 113 studies, demonstrating the limited research that has been conducted on POCT in rural or remote contexts.

The search was further limited to studies published in the English language and those where full-text was available. A final study was removed from the literature review as it was identified as an

erratum to another study included in the literature review (Martin, D et al. 2005a). This search produced a total of 109 studies to be included in the literature review.

2.3 Literature Search Summary

A total of 109 studies were identified by the literature search method. Each study was reviewed for its relevance for inclusion or exclusion in the literature review process (see Figure 6).

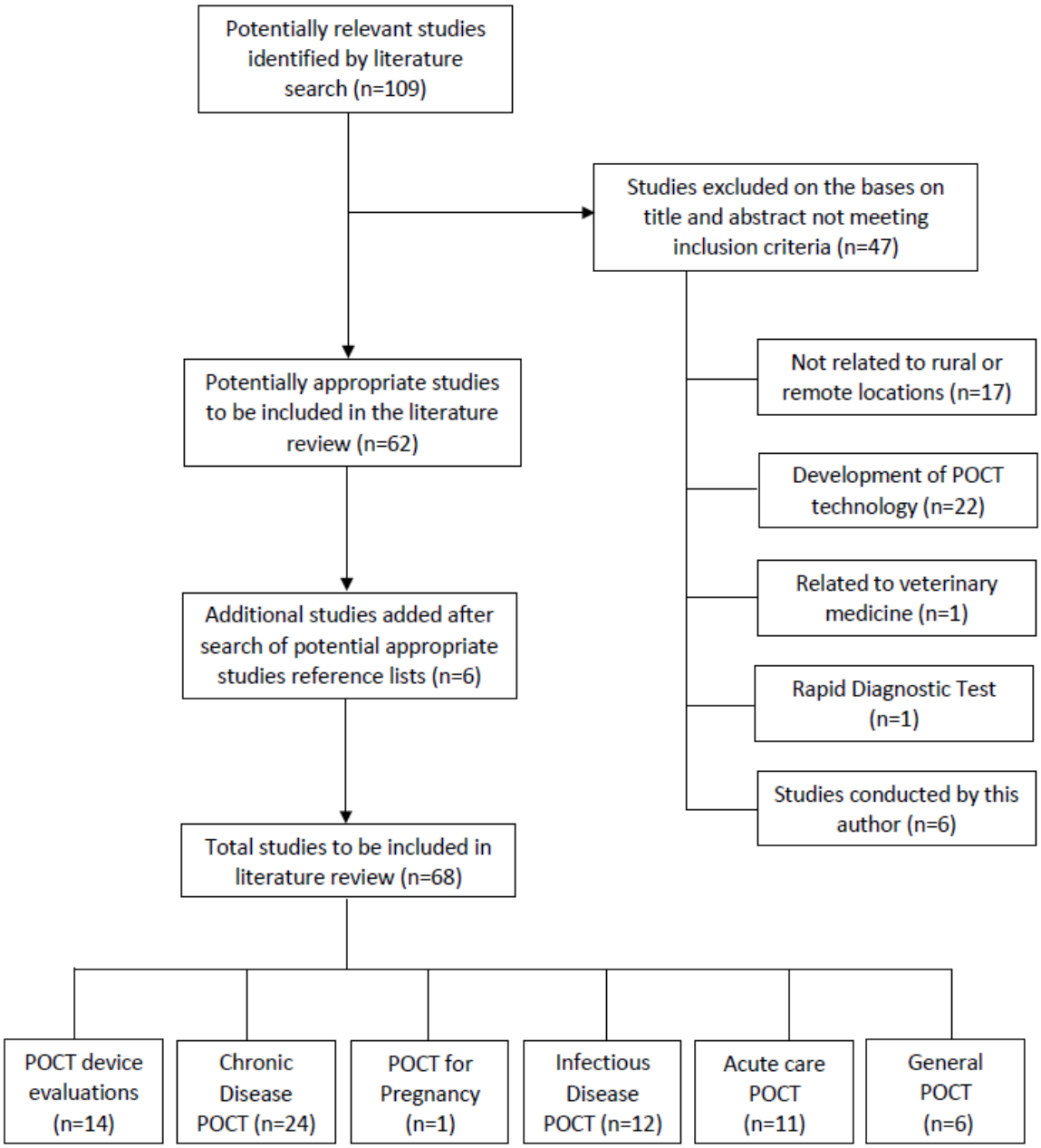

Figure 6 - Flow diagram of studies included excluded in the literature review.

After an examination of the study abstracts, 17 studies were excluded from the review process as they did not occur, or specifically discuss, the use of POCT in a rural or remote location (Badman et al. 2016; Bissell 2001; Cubitt et al. 2013; Davis et al. 2017; Gramz, Koerte & Stein 2013; Haldrup et al. 2017; Johnston & Conly 2002; Rack-Hoch, Laniado & Hübner 2017; Rao, Moiles & Snyder 2011; Smith et al. 2011; Wildberger et al. 1998; Bailey et al. 1997; Pai, N, Kurji, et al. 2012; Schlosser et al. 2007; Willmott & Arrowsmith 2008; Wiwanitkit 2011). These studies generally mentioned the search term 'remote' in relation to remote connectivity. Remote POCT connectivity systems allow remote communication between a POCT device and a central database, and are an important component of POCT as they enable the remote (electronic) monitoring and surveillance of POC test results. While remote connectivity in an integral component of POCT use, and particularly important in rural and remote locations, in these studies the connectivity system was not used in a rural or remote setting. For this reason, these studies were not included in the literature review process.

An additional 22 studies based on POCT technology development were removed from the literature review (Banpavichit et al. 2010; Beissner et al. 2015; Bercich et al. 2011; Chakera, Lucas & Lucas 2011; Dyer et al. 2001; Felder et al. 1995; Ge et al. 2012; Ingeholm et al. 2006; Jani et al. 2016; Knapp et al. 2011; Lewandrowski, Gregory & MacMillan 2011; Lin et al. 2017; Long, Yu & Cunningham 2015; Lu et al. 2012; Ma et al. 2015; Michael et al. 2016; Pastoor et al. 2008; Ramalingam et al. 2009; Stahl et al. 2015; Van Dorst et al. 2016; Wang et al. 2013; Yang et al. 2013). Each of the studies identified in this group met the search criteria as they predicted that the technology developed may be applicable to rural or remote settings. While the development of POCT technologies is important for application to rural and remote settings, these studies will not form part of this literature review as they did not evaluate or examine the use of the POCT technology physically within, or specifically in relation to, rural or remote settings.

One study evaluating the analytical quality of a malaria RDT passed the inclusion criteria because it mentioned the search term 'point-of-care testing' rather than RDT in the study's title. This study was removed from the literature review.

One study provided the guidelines for POCT in veterinary medicine (Flatland et al. 2013). While this study did state that POCT may be useful in remote areas, it did not examine the use of POCT for this application in a rural or remote location. In addition, the application of POCT in veterinary medicine will not be discussed in this thesis.

As expected, a number of studies identified in the literature search were authored or co-authored by the author of this thesis (McCormack et al. 2017; Shephard, M, Spaeth, Mazzachi, et al. 2014; Shephard, M et al. 2012b; Spaeth & Shephard 2016; Spaeth, Shephard & Omond 2017; Spaeth, Shephard & Schatz 2014). These six studies were removed from the literature review process as they will be placed within the contextual statement to demonstrate how these studies build upon previous literature in the field of POCT.

The removal of the excluded studies left a remaining 62 studies to be reviewed. Through an examination of the studies' reference lists, six additional studies were included in the literature review process due to their relevance to the studies presented in this thesis (Gialamas et al. 2010; Martin, C 2010; Shephard, M 2009; Shephard, M et al. 2005; Shephard, M, Shephard, et al. 2009; Tideman, Simpson & Tirimacco 2010).

A total of 68 studies will be examined in this literature review and are divided into categories as outlined in Figure 6. Separating the studies into these categories will highlight the areas where a majority of POCT research in rural and remote settings has taken place. Within each of these categories, the key outcomes related to POCT use in rural and remote settings will be identified and discussed. The key outcomes for the assessment of POCT effectiveness include: clinical effectiveness, operational effectiveness, analytical quality and cost benefit analysis. Within each subgroup, the lacking or missing research related to each of these key outcome measures will be highlighted to demonstrate where deficiencies in the literature exists. The literature focussing on POCT for acute care in rural or remote locations will be critically appraised as these are the studies most relevant to this thesis.

For ease of analysis, all studies were conducted in Australia unless otherwise stated.

2.3.1 Analytical Point-of-Care Testing Device Evaluations

Fourteen studies were identified as POCT device evaluations, comparing the analytical quality of a POCT device to a reference or standard laboratory method. As will be discussed in the contextual statement, when using a POCT device away from the setting of its intended use, it is important to ensure that the analytical quality of the device remains acceptable in the new setting. All fourteen studies were conducted, at least in part, in a rural or remote location. Eleven studies focussed on POC devices for chronic disease, and three on POC devices for a sexually transmitted infection.

A summary of the key characteristics and results for 13 of the 14 studies is summarised in Table 6. One further study comparing several POC device evaluations conducted by different operator groups will be discussed separately.

Table 6 – Summary of identified POC device evaluations conducted in a rural or remote location.

Study	Location / Setting	POC test (Model)	Comparator (Model)	No. Comparisons	Statistical tests	Regression Results	Other results	Conclusion
Jackson et al. (2004)	15 rural GPs across TAS, SA, and QLD	INR (CoaguChek S)	Standard laboratory methods (not stated)	169 patients, 401 paired results	Bland-Altman regression analysis and clinically relevant agreement	r = 0.89, P < 0.0001	Clinical agreement against published criteria = 90%	POC device compared well to the standard laboratory method
Yelland et al. (2010)	26 GPs in Australia (urban, rural and remote)	INR (CoaguChek S)	Standard laboratory methods (not stated)	417 patients, 1664 paired results	Bland-Altman regression analysis and clinically relevant agreement	Linear relationship between POC and lab method (P < 0.0001) r not reported	Clinical agreement = 89% (narrow), 91% (expanded)	POC test as reliable as pathology laboratory testing
Daly et al. (2003)	9 rural primary care practices in Ireland	INR (CoaguChek MD)	Standard laboratory method (Organon Technika MDA 180)	122 patients, 185 paired samples	Bland-Altman regression analysis and paired t-test	Regression coefficient = 0.00 (95% CI -0.38 to 0.38)	Paired t-test = 0.93, p=0.53 (no significant difference)	Confirmed acceptability of POC device for anticoagulant management in primary care

Seamark et al. (1997)	Rural GP in UK	INR (CoaguChek)	Standard laboratory method (Futura analyser)	306 paired samples	Bland-Altman regression analysis and time delay effect	Pearson r=0.945, (P<0.0001)	Tested < 5h = no significant difference. Tested > 5 h = significant difference.	POC INR robust and reproducible
Marley et al. (2007)	Seven remote primary health care services in Australia	Glucose (Accu-Chek Advantage and MediSense Optium)	Three different standard laboratories (not stated).	164 paired samples	Bland-Altman regression analysis and two-tailed Fisher's exact test	r =0.93 (P<0.001)	Mean difference in glucose results = 0.48mmol/L.	POC glucose analysers are appropriate for use in remote rural communities
(Martin, D et al. 2005a)	Remote Aboriginal Australian community	Glucose (HemoCue Glucose) and HbA1c (DCA 2000)	Standard laboratory method (Vitros 250 Analyser, OrthoClinical Diagnostics)	152 paired samples	Bland-Altman regression analysis and paired t-test	Glucose r= 0.98 (P < 0.001). HbA1c r = 0.99 (P < 0.001)	Glucose paired t-test P=0.007 (differed significantly). HbA1c paired t-test P = 0.95; no significant difference	HbA1c clinically and analytically identical to lab. Glucose concentration dependent difference compared to lab

Tirimacco et al. (2016)	10 rural and remote primary health services	HbA1c (Cobas b 101)	Standard laboratory method(s): Roche Integra; Roche Cobas 502; Bio-Rad Variant II	141 patient comparisons	Bland-Altman and regression analysis; Passing-Bablok correlation	r ≥ 0.97	%bias = 6.5%, average difference = 3.3mmol/mol	POC suitable alternative to lab method(s) in primary health care services
Shephard, M, Shephard, et al. (2009)	17 urban, 16 rural and 20 remote general practices	HbA1c, urine ACR, INR, Lipids (total cholesterol; HDL-C; triglycerides)	Analytical goals set for the POCTGP Trial (set by expert Government Working Party)	HbA1c=1026; urine ACR=3072; INR=553; lipids=3063	Calculation of within-practice imprecision expressed as a coefficient of variation (CV%)	HbA1c, urine ACR, INR, total cholesterol and triglycerides all met analytical goals. HDL-C met goal for 3 of the 4 QC lots/levels		POC tests suitable for use in GP, with exception of HDL-C
Shephard, M (2009)	17 urban, 16 rural and 20 remote general practices	HbA1c, urine ACR, INR, Lipids (total cholesterol; HDL-C; triglycerides)	Standard laboratory methods (not stated)	Quality Control (QC) testing (HbA1c = 1026; ACR = 3072; lipids = 3063; INR = 553)	Kruskall Wallis test to determine if statistical significant difference	No statistical difference in the median imprecision for QC tests across urban, rural and remote practices	All POC tests met the imprecision goal set for the POCTGP Trial (except HDL cholesterol)	Analytical quality of POCT was equivalent across urban, rural and remote general practices

Gialamas et al. (2010)	30 general practices across urban, rural and remote locations	Lipids (total cholesterol; HDL-C; triglycerides)	Standard laboratory methods (not stated)	2356 patient comparisons	Bland-Altman and regression analysis; percentage concordance between POCT and laboratory	Mean difference (limits of agreement) in mmol/L: total cholesterol = -0.2 (-1.04 to 0.48); HDL-C = -0.09 (-0.55 to 0.36); triglycerides = 0.09 (-0.40 to 3.04)	Percentage agreement between POCT and laboratory tests: total cholesterol = 85%; HDL-C = 86%; triglycerides = 89%	Analytical quality of lipid POCT device variable and requires further investigation
Causer et al. (2015)	Two remote Aboriginal health services	CT and NG (GeneXpert); Diaquick CT; Gonorrhoea Card	Gold standard laboratory comparison = NAAT (model not provided)	198 samples (RDTs CT=104 and NG =29)	McNemar's test for agreement was used to calculate P-values	POC sensitivity, specificity, p-value: CT = 100%, 99.5%, 0.32; NG = 100%, 100, 1.00 (1 discordant result)	RDTs sensitivity and specificity: CT =27%, 98.5%, NG = 67%, 77%	Accuracy of GeneXpert CT/NG make it very suitable in this setting. RDT not suitable for use

Robertson, Gilmore and Norton (2014)	One remote Sexual Health Service	Rapid POCT for syphilis (SD Bioline Syphilis 3.0)	Gold standard laboratory methods: EIA (Abbott USA); TPPA (Fujirebio Japan); RPR (BD USA)	238 patient specimens	Not provided	Sensitivity = 81.5% [95% CI = 76.6% – 86.4%], and specificity = 100%		POCT not recommended for syphilis screening in a population with low prevalence of infection
Ayove et al. (2014)	Two remote communities in Papua New Guinea	DPP Syphilis Screen and Confirm assay (Chembio Diagnostic Systems) for treponemal (T1) and non-treponemal (T2) antigens	Rapid plasma reagin (RPR) tests and *T pallidum* haemagglutination assay (TPHA) (model not provided)	703 children	McNemar's test and Fisher's exact test to compare the sensitivity of the DPP T2 assay to different RPR concentrations	DPP T1 sensitivity = 88·4% (95% CI 84·8–91·4) and specifi city = 95·2% (95% CI 92·2–97·3). DPP T2 sensitivity of 87·9% (83·7–91·3) and specificity of 92·5% (89·4–94·9)	DPP T2 sensitivity = 94·1% (95% CI 89·9–96·9) at RPR concentration ≥1:8	POCT is accurate for identification of antibodies to T1 and T2 antigens in patients with yaws and therefore avoids the need for laboratory support

Standard laboratory method = laboratory method routinely used by participating health service; TAS = Tasmania; SA = South Australia; QLD = Queensland; r = correlation coefficient; INR= international normalised ratio; HbA1c= Haemoglobin A1c; GP= General Practice; p-value= probability value; POC= point-of-care; NAAT = nucleic acid amplification testing; CT= Chlamydia trachomatis; NG= Neisseria gonorrhoeae; EIA= enzyme immunoassay; TPPA= *Treponema pallidum* particle agglutination; RPR= rapid plasma regain; CI= confidence interval; HDL-C= high density lipoprotein cholesterol; ACR= albumin creatinine ratio; DDP= Dual Path Platform.

Four studies evaluated the analytical quality of POCT devices measuring INR through comparing the results to a standard laboratory method. Three studies were conducted in rural primary care settings (Daly et al. 2003; Jackson et al. 2004; Seamark et al. 1997) and one across urban, rural and remote locations (Yelland et al. 2010). The latter study was conducted as part of a randomised control trial (RCT) conducted with Australian GPs from 2005 to 2007. This trial, called the Point-of-Care Testing in General Practice Trial (hereafter abbreviated as POCT in GP Trial), is the largest trial of its type undertaken anywhere in the world, and included 53 GPs across urban, rural and remote settings (Laurence et al. 2008; Shephard, M 2006d). The POC tests investigated by the trial included HbA1c, INR, urine ACR and lipids. The POCT in GP Trial compared the largest known dataset of POC INR results in the GP setting with 1,664 paired samples analysed (Yelland et al. 2010). The study concluded that the INR POCT device had comparable analytical quality to the laboratory method (see Table 6). However, the differences in POC test performance between each geographical location was not compared and, therefore, it is not possible to determine if the INR POCT device in this study performed better or worse than in the rural or remote locations. In addition, the POC test results were compared to various laboratory methods, limiting the results of this study (Yelland et al. 2010). The remaining three INR POCT device studies were conducted in only rural locations and determined that device performance was acceptable as the results correlated well with the standard laboratory method as per Table 6 (Daly et al. 2003; Jackson et al. 2004; Seamark et al. 1997). Therefore, only one study was identified which evaluated an INR POCT device specifically in remote primary health care settings; this was the study conducted as part of the POCT in GP Trial. However, as noted, the results of this study were not split between urban, rural and remote settings. As will be discussed in the contextual statement, a study conducted by this author provides results on the analytical quality of INR POCT conducted solely in a remote setting (Spaeth & Shephard 2016).

Two studies evaluated the analytical quality of POCT devices measuring HbA1c, one in combination with a glucose POCT device (Martin, D et al. 2005a; Tirimacco et al. 2016). Both studies were conducted in rural or remote primary care settings and compared the POCT results to the standard laboratory method routinely used by each of the participating health services. Each study determined the POC tests correlated very well to the standard method and were therefore suitable for use in remote as well as rural primary care settings (see Table 6). While the first study examined a large number of patient comparisons (n=152) representing over 80% of the community population, it did not calculate imprecision due to the small number of quality control results

obtained (Martin, D et al. 2005b). The second study analysed 141 patient comparisons to determine accuracy of an INR POCT device (Tirimacco et al. 2016), however, the results from the POCT device were compared to various laboratory methods, limiting the results of the study as each laboratory method has different performance characteristics. This study also performed an imprecision analysis, although again using only a small number of repeat tests (n=10) across the remote services. An additional intra-assay imprecision study was conducted, though this was performed by laboratory trained personnel and not remotely located health professional staff, therefore limiting the generalisability of the findings of this study (Tirimacco et al. 2016).

A further study evaluated the analytical quality of a glucose POCT device alone (Marley et al. 2007). The study was conducted across seven remote primary health care services in Australia and highlighted the difficulties in providing timely diagnoses and, thus, changes to patient management in these remote locations. Information was also provided on the issues in using central laboratories to provide pathology results. This included infrequent transport for pathology specimens and vast distances to the laboratory which meant the time taken for specimens to reach the laboratory varied from 30 minutes to seven days. This study also reported that on many occasions the blood samples did not arrive at the laboratory in a suitable state and, therefore, could not be measured, leading to further delays and/or missed diagnoses. This study concluded that there was high concordance of capillary glucose measured on the POCT devices and the venous laboratory results and that POCT significantly improved the management of patients with diabetes in these remote locations. While this study did not list any limitations, one limitation was that comparison samples were sent to three different laboratories and the laboratory methods were not provided.

Three additional studies in the POCT in GP Trial were identified after searching the reference lists of studies found by the literature search. The first study described the design, implementation and results of the quality control program for the Trial (Shephard, M, Shephard, et al. 2009). This study determined that all POC tests (HbA1c, urine ACR, lipids and INR) met the goals for analytical quality set for the trial, with the exception of High-density Lipoprotein Cholesterol (HDL-C) (see Table 6). Based on these results the authors determined the POCT devices were appropriate for use in GP settings, with the exception of the lipid POCT device which required further improvement. Also mentioned in this article was a heat wave that affected one of the POCT devices at several rural and remote GPs that participated in the Trial, highlighting the extreme climatic conditions experienced by rural and remote locations in Australia. The second study examined the imprecision of POCT for HbA1c, INR, urine ACR and lipids using quality control material across urban, rural and remote

settings (Shephard, M 2009). This study found there to be no statistical difference in quality control test results across geographic regions (see Table 6). The third study examined the level of agreement between POCT device measuring lipids and the standard laboratory method (Gialamas et al. 2010). This study found the concordance between POCT and laboratory results to be variable as per Table 6 and commented that the POCT device requires further evaluation. A limitation of this study is that no results were provided on the geographical split between urban, rural and remote locations.

A further three studies calculated the sensitivity and specificity of STI POCT devices in remote primary health care settings. The first study examined a rapid POC test for syphilis against the standard laboratory method (Robertson, Gilmore & Norton 2014). The second study evaluated a new molecular POC test for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) against the gold standard laboratory method (Causer et al. 2015). The first study determined the analytical quality of the rapid POCT device to be less than desirable compared to the laboratory (see Table 6), however, this result may be due to the low prevalence of syphilis in the setting in which the device was evaluated (Robertson, Gilmore & Norton 2014). The molecular POCT device compared very well against the gold standard laboratory method for CT and NG (see Table 6) and was therefore determined to be suitable for use in remote Indigenous communities (Causer et al. 2015). The study of Ayove et al. (2014) was conducted in remote villages of Papua New Guinea and examined the sensitivity and specificity of a rapid POC test for the diagnosis of yaws, a tropical disease affecting the skin that is endemic is several developing countries. The POCT device evaluated was a Dual Path Platform (DPP) syphilis assay which detects antibodies to treponemal and non-treponemal antigens for the detection of *Treponema pallidum pertenue*, which is closely related to syphilis. The study determined the POCT device to be of appropriate quality compared to the laboratory method as per Table 6. However, the authors commented that the requirement for electricity and the cost of the automatic test reader which increased the accuracy of ready POC test results could be prohibitive in this low-resource setting.

Finally, the study of Higgins (2007) provided results for two analytical performance evaluations conducted by different technical and non-technical operator groups. One evaluation involved a POCT device measuring glucose and was conducted across 29 metropolitan locations by more than 100 non-technical trained staff. The other evaluation involved a POCT device measuring HbA1c conducted in a remote hospital in Canada by three different operator groups. The latter study included both experienced and inexperienced technologists as well as nurse educators. The glucose POCT device evaluation found that the results (n=1286) correlated well (r=0.84) to the reference

laboratory method, thus supporting the use of the device by non-technical trained staff in metropolitan locations. The remote hospital evaluation found POC HbA1c testing conducted by nurse educators, inexperienced technical staff and experienced technical staff correlated well with the laboratory method with correlation coefficients of r=0.96, r=0.99 and r=0.93 respectively. The authors of this study commented that analytical performance evaluations performed in a laboratory setting by experienced technologists may not be a good reflection of the analytical performance in the setting where the POCT device is used by non-laboratory personnel. As such, this study highlights the importance of evaluating the analytical quality of a POCT device using staff who will be the operators of the device in a real-life setting (Higgins 2007).

In summary, these studies highlight the importance of evaluating the analytical performance of POCT devices in the setting of intended use by staff with the same level of experience and training to those who will normally use the POCT device. Overall, the studies discussed here demonstrate that POCT devices generally perform well in rural and remote settings. However, the majority of studies focussed on POC tests for either diabetes, coagulation or STIs. As such, there are significant gaps in the literature on POCT analytical evaluations for other disease states such as cardiovascular disease, kidney disease, anaemia, other infectious diseases and acute illness (some of which are addressed by the author's body of work presented in the contextual statement of this thesis).

2.3.2 Application of Point-of-Care Testing in rural or remote - Chronic Disease

Twenty-four studies were identified that discuss the use of POCT for chronic disease, all of which were conducted in, or focussed on, POCT use in rural or remote locations.

Ten of the 24 studies related to the Australian POCT in GP Trial, which examined the safety, clinical effectiveness, cost effectiveness and acceptability of POCT in the GP setting across urban, rural and remote locations. The POCT in GP Trial was the largest study conducted globally in the GP sector. The Trial was designed to address the lack of evidence on the use of POCT in the GP setting in Australia highlighted by an earlier review by Guibert et al. (2001). This was also highlighted in a systematic review of POCT use in the GP settings conducted as a prologue to the implementation of the trial (Gialamas, St John, et al. 2009). The systematic review aimed to determine the following outcomes in relation to POCT in GP:

i) did POCT improve patient health outcomes;

ii) did POCT have comparable analytical quality to pathology laboratory testing;

iii) was POCT cost-effective compared to usual care; and

iv) did POCT improve the satisfaction of patients and health professionals with respect to pathology testing?

The systematic review found there were very few high-quality evaluations of POCT in GP settings and concluded that no studies existed in the literature which provided strong evidence supporting the use of POCT in GP (Gialamas, St John, et al. 2009). A further three publications provided descriptions of the POCT in GP Trial design, rationale and methods. Shephard, M (2006d) outlined of the governance structure for the POCT in GP Trial and a description of the urban, rural and remote GPs. Laurence et al. (2008) provided the Trial design, rationale of methods used, and methods for implementation of POCT (Laurence et al. 2008). Tirimacco et al. (2011) described the development of an accreditation program for the POCT in GP Trial. As discussed in the previous section on the analytical evaluation of POCT, an additional three studies provided results on the analytical quality of the POCT devices used in the POCT in GP Trial (Gialamas et al. 2010; Shephard, M 2009; Yelland et al. 2010). As previously mentioned, the Trial involved a total or 53 GPs based in urban, rural or remote locations. A total of 1,958 patients from 23 control GPs and 3,010 patients from 30 intervention practices participated in the RCT. Five published studies examined the main findings from the POCT in GP Trial. A summary of outcome measures and key findings for each study is provided in Table 7.

Table 7 – Summary of outcome measures and key findings of POCT in GP Trial studies.

Author (year)	Outcome measured	Methods	Key finding(s)
Shephard, M, Mazzachi, et al. (2009)	POCT operator satisfaction with POCT training resources and workshop	Quantitative and qualitative survey of POCT device operators	Satisfaction with POCT training resources = 100%. Satisfaction with POCT training workshop =78%. Lowest satisfaction recorded by rurally located operators regarding confidence in the accuracy of POCT results = 7.3 out of 10.
Laurence, Gialamas, et al. (2010)	Patient satisfaction with POCT versus pathology laboratory testing in GP	Questionnaire to patient in intervention (POCT) and control group (Laboratory) to determine level of agreement with a variety of statements	Patients in POCT group had a higher level of satisfaction with sample collection process and confidence in the process (P<0.001). Patients in POCT group viewed POCT as strengthening their relationship with their GP (P<0.010) and motivational in terms of better managing their condition (P<0.001).
Gialamas, Yelland, et al. (2009)	Effect of POCT on patient medication compliance	Medication adherence assessed twice by a self-administered questionnaire	POCT (39.3%) was non-inferior to pathology laboratory testing (37.0%) in relation to patient medication adherence (P<0.001).
Bubner et al. (2009)	Effect of POCT on therapeutic control of chronic disease	Proportion of patients and tests with results in a target range for POCT compared to control group	Proportion of patients with results in target range the same or better for POCT, except for HDL and INR. Proportion of test results in target range same or better for POCT, except for HDL.
Laurence, Moss, et al. (2010)	Cost-effectiveness of POCT in GP compared to pathology laboratory testing	Incremental costs and health outcomes associated with POCT compared to pathology laboratory testing	No statistical difference in per patient costs to the health care sector. POCT led to significant cost savings for patients and their families.

Both device operators and patients indicated a high level of satisfaction with POCT. Compared to the control group where normal laboratory practices were used, patients reported higher satisfaction with the sample collection process for POCT (e.g. capillary versus venous), a better relationship with the GP due to POCT and increased motivation to want to improve their health (Laurence, Gialamas, et al. 2010). The operators of the POCT devices had a higher preference for POCT over laboratory services as well as high levels of satisfaction with POCT training and the ease of use of the POCT devices (Shephard, M, Mazzachi, et al. 2009).

Regarding clinical effectiveness, these studies determined that having access to POCT provided the same or better therapeutic control for all tests except INR and HDL-C, which were determined to be inferior to standard care (Bubner et al. 2009). Improved medication adherence for all POC tests was identified compared to the control group where standard pathology laboratory practices were used (Gialamas, Yelland, et al. 2009).

In terms of cost-effectiveness of the POCT in GP Trial, while the costs to patients and their families were found to significantly reduced, health system cost per patient was higher for all POC tests except ACR, however, the difference in costs were not statistically significant (Laurence, Moss, et al. 2010). The cost-effectiveness analysis did not provide a breakdown of costs across the urban, rural and remote services, therefore, it is unknown if POCT was more or less cost-effective with increasing distance from a pathology laboratory as might be expected.

Despite each study highlighting that GPs in rural and remote locations could be the main beneficiaries of POCT, only two of the ten studies reported on the differences in research outcomes between urban, rural and remote settings. The study evaluating the training program used in the POCT in GP Trial highlighted that the turnover of health professional staff was much greater in the rural and remote practices and, thus, may require more flexible training options if routinely implemented (Shephard, MD et al. 2009). However, there were some conflicting results between rural and remote health professional in relation to their satisfaction with POCT. Staff from remote services reported the highest satisfaction with the training program, the ease of use of the POCT devices and confidence in the accuracy of POC test results, while staff from rural locations reported the lowest satisfaction with the quality of training, competency assessment and confidence using the POCT devices. Notably, remote staff reported a higher preference for POCT over laboratory testing (Shephard, M, Mazzachi, et al. 2009). These differing results highlight that while the characteristics of rural and remote health care settings are generally thought to be similar, the

experiences of the health professionals working in these locations may be quite different. As discussed in the background section of this thesis, this difference is likely due to the extreme isolation experienced in remote locations which poses a greater need for access to resources including diagnostic tests.

The second study to comment on the difference in outcomes between geographic locations described the development of, and results from, the accreditation program for the POCT in GP Trial (Tirimacco et al. 2011). This study reported that fewer rural and remote health services fully complied with the first accreditation visit compared to metropolitan participants. However, the potential causes for this difference in adherence were not discussed, limiting the findings of this study.

From the references within the POCT in GP Trial published studies, a major national POCT model for diabetes management in Indigenous Medical Services in Australia was identified, known as the Quality Assurance for Aboriginal and Torres Strait Islander Medical Services (QAAMS) Program. Due to this author's knowledge of the POCT field in Australia, it was known that a significant proportion (80%) of the Indigenous medical services within the QAAMS Program was located in rural and remote locations. As such, an iterative literature review was performed to source further papers on this POCT model. A review of the papers found they were missed by the initial literature search as the terms 'rural', 'remote' or 'isolated' were not included in any of the titles or abstracts. Nonetheless, QAAMS has a national focus and is the largest POCT network in Australia and, in the opinion of the author, it would be a major omission to not include a brief discussion of this model. The POCT device used by the Program was the Siemens DCA 2000, which has now been superseded by the Siemens DCA Vantage. This device measures HbA1c for the management of established diabetes and urine ACR tests to detect the kidney disease as a principle complication of diabetes. A summary of five key studies on the QAAMS Program is provided in Table 8. QAAMS commenced in 1999 with just 45 Aboriginal medical services enrolled, and now includes 200 services nationally. Recently, HbA1c testing on the DCA Vantage has been extended to include the diagnosis of diabetes due its proven analytical quality. The longevity of the QAAMS Program is sustained by several key services including continuous training and competency assessment for POCT device operators, regular surveillance of POCT analytical quality and ongoing support services.

Table 8 – Summary of five key studies on the QAAMS Program.

Title	Outcome measured	Key finding(s)	Citation
Results of an Innovative Education, Training and Quality Assurance Program for Point-of-Care HbA1c Testing using the Bayer DCA 2000 in Australian Aboriginal Community Controlled Health Services	Describes the development, implementation and management of the QAAMS Program and provides key results on POCT efficacy	45 Aboriginal medical services enrolled from 1999. Implementation included culturally appropriate POCT training and education resources for AHWs; a quality assurance program to enable the analytical quality of POCT to be monitored and telephone support hotline. AHWs were able achieve acceptable analytical quality for POCT in the first 3.5 years of the program (median CV%=3.8%) with the precision progressively improving (from 4.3% in first cycle to 3.4 in the most recent cycle) and comparing well the median laboratory CV%=3.5%. Medicare rebate introduced for HbA1c tests performed with in the Program to ensure its long-term sustainability.	(Shephard, M & Gill 2003)
Cultural and clinical effectiveness of the 'QAAMS' point-of-care testing model for diabetes management in Australian Aboriginal medical services	Provides results of a detailed survey to assess key stakeholder (doctors, POCT operators and patients with diabetes) satisfaction with the QAAMS Program and	65 Aboriginal medical services enrolled. Greater than 90% of doctors (n=41) felt POCT was more convenient than the laboratory, were confident in the accuracy of POCT and stated that POCT impacted positively on patient care. Greater than 90% POCT operators (n=65) felt QAAMS resources were culturally appropriate, were confident in using the POCT device and understood the need to perform quality testing procedures. Greater than 90% of patients with diabetes (n=161) stated they were very satisfied with the convenience of POCT, the finger-prick collection process was less stressful and reported that POCT improved self-motivations to control their diabetes.	(Shephard, M 2006b)

	results on clinical outcomes	A statistically significant reduction in HbA1c (-0.7%) was observed in a group of 74 patients monitored for 12 months after the introduction of POCT (p=0.003). The percentage of patients able to achieve optimal glycaemic control (HbA1c<7%) increased by 12% (from 15% to 27%).	
The national QAAMS Program–a practical example of PoCT working in the community Review of the cultural safety of a national Indigenous point-of-care testing program for diabetes management	Descriptive study of results on analytical and clinical effectiveness and key milestones for the Program	115 Aboriginal medical services enrolled. Average median CV% = 2.5% (range 2.4 to 2.5%) for POC HbA1c testing now equivalent to laboratory testing CV% = 2.8% (range 2.5 to 2.9%) during the same time period. Statistically significant reduction in % of patients (n=272) with an HbA1c now less than <8% from baseline to their most recent POC test (p=0.01). An independent review by the National Aboriginal Community Controlled Health Organisation (peak body in Indigenous health care in Australia) found the QAAMS Program enhanced the management of diabetes through a more patient centred focus. QAAMS Program translation demonstrated by development of three new POCT models, POCT in GP Trial (Australian GPs), Diabetes Management Along the Mallee Track Program (Rural Australian GPs) and the Ngati Porau Hauora Warfarin Management Program (remote Indigenous health services in New Zealand).	(Shephard, M & Gill 2010)
Review of the cultural safety of a national Indigenous point-of-care testing program	Review of QAAMS Program cultural safety through focus groups with QAAMS Indigenous leaders team and	180 Aboriginal and Torres Strait Islander medical services enrolled. QAAMS Indigenous leaders (n=4) provided verbal feedback indicating QAAMS was culturally sensitive, ensures that POCT operators are competent and the quality assurance aspect of QAAMS provides confidence in the accuracy of POCT.	(Shephard, M et al. 2016)

for diabetes management	an electronic questionnaire to POCT operators	104 of 470 POCT operators (response rate 22%) completed the questionnaire. Greater than 90% stated that POCT in the QAAMS Program raises awareness of diabetes in the community and is effective in improving clinical outcomes for diabetes clients. Greater than 80% felt that becoming a POCT operator was culturally empowering and improved their relationship with patients.	
Results from 15 years of quality surveillance for a National Indigenous Point-of-Care Testing Program for diabetes	Reports on the past 15 years of quality testing in QAAMS and examines the performance of HbA1c POC testing	200 Aboriginal and Torres Strait Islander medical services enrolled. 29,093 EQA tests conducted between 2002 and 2016. Average median CV% = 2.81% (SD 0.50; range 2.2 to 3.9%). No significant difference was observed between the median imprecision achieved in QAAMS and by Australasian laboratories from 2002 to 2016 (p = 0.05; two-tailed paired t-test). Percentage acceptable QC results averaged 90% for EQA testing from 2002 to 2016 and 96% for QC testing from 2009 to 2016. At a target HbA1c value (6.8%) close to that used for diabetes diagnosis (6.5%) the imprecision averaged 2.75% (range 2.5% to 2.9%) over a period of 5 years (within desirable analytical goal for HbA1c of <3%).	(Shephard, M et al. 2017a)

EQA= External Quality Assurance, QC= Quality Control, CV%= coefficient of variation.

As per Table 8, continual research and evaluation of QAAMS has proven the POCT program to be analytically sound, clinically and culturally effective and well received by Indigenous and non-Indigenous health professional staff.

Only one additional RCT was identified by the literature search on the use POCT for chronic disease (Wells et al. 2017). This New Zealand based study investigated the effect of using POCT for HbA1c and lipids on the completion of cardiovascular disease (CVD) risk assessments in GP settings across a total of 20 months. The study involved ten POCT GPs and ten control GPs which varied in location between urban and rural practices. A CVD risk assessment entry was recorded for 7,421 patients at POCT practices and 6,217 patients at control practices. The study found there was no difference in the number of CVD assessments performed between GPs using POCT compared to the control group (adjusted odds ratio 1.02 [95%CI 0.61–1.69]). One of the challenges identified by this study was the difficulty in implementing POCT into routine clinical practice. This was evidenced by the health professional staff indicating that POCT was more an additional tool rather than an integral component of the CVD risk assessment. This study concluded that the use of POCT provided equivalent outcomes to standard methods, while changes to external policy impacted most significantly on completion of CVD risk assessments (Wells et al. 2017).

Of the remaining 13 studies, six were conducted in rural and remote primary health care services. The study characteristics and key findings are summarised in Table 9. A further four studies discussed the potential use of POCT in rural or remote locations and three studies only mentioned POCT in the context of rural or remote health care, each of which will be discussed separately.

Table 9 – Summary of study characteristics and key findings for studies focussing on POCT for chronic disease.

Author (year)	Study design	Clinical Setting	Numbers studied	POC tests measured	Duration of study	Outcome measured	Key findings
Motta et al. (2015)	Qualitative and quantitative survey of patient satisfaction	Rural community health service in Australia	60 patients with type 2 diabetes	HbA1c, glucose, and lipids	4 months	Level of patient satisfaction before and after the introduction of the new POCT devices	Statistically significant improvement in patient satisfaction with pathology testing after introduction of POCT (Fisher exact probability, $P<0.05$).
Kulrattanamaneeporn, Wongboonsin and Kost (2009)	Cohort study	Primary care units in rural Thailand	29 patients in POCT + telemedicine group, 68 patients in hospital group	HbA1c and glucose	24 months	Difference in waiting time, travel expense between HbA1c, glucose POC results + telemedicine and hospital management	POCT waiting time = 5 minutes versus 150 minutes for hospital. Travel expense was US$0.3 for POCT versus $2.90 for hospital. Statistically significant lower difference in HbA1c results for patients in POCT group (6.9%) compared to hospital group (8.4%), ($p<0.001$).

Shephard, M et al. (2006)	Pre- and post-study and qualitative survey of stakeholder satisfaction	4 rural and remote Aboriginal medical services in Australia	45 patients in HbA1c comparison 58 patients in satisfaction	HbA1c and lipids	24 months	Change in HbA1c result and satisfaction with diabetes service before and after POCT introduced	Statistically significant (p=0.02) reduction in HbA1c of 0.7% (9.5% to 8.8%) was observed after POCT introduced. Percentage of patients satisfied with diabetes service increased significantly after POCT introduced from 64% to 88% (p=0.02).
Mayega et al. (2014)	Population-based survey	Rural villages in Uganda	795 people	Fasting plasma glucose (FPG) and HbA1c	Not provided	Agreement of (FPG) and HbA1c POCT in classifying abnormal glucose regulation	11.3% of patients classified as diabetic with HbA1c compared to 4.8% with FPG. Nurses can conduct POCT in this setting if training provided.
Shephard, M et al. (2005)	Observational study and a patient survey	Rural GPs in seven towns	54 patients comparisons 36 patients for survey	HbA1c, urine ACR, lipids and glucse	18 months	Proportion of patients achieving optimal glycaemic control (HbA1c <7%) and controlled	The mean HbA1c fell from 7.6% to 7.1% (p=0.03, paired *t*-test) since comencement of POCT. Patients achieving optimal diabetes control increased by 30% (33% to 63%). Patients achieving

						glycaemica (HbA1c <8%).	controlled glycaemia increased by 32% (59% to 91%). Number of patients satisfied/very satisfied with their diabetes service increased from 18 (64%) before POCT to 29 (91%) after POCT was introduced (p=0.01).
Leke, Portwood and Maboh (2013)	Observational study	Rural health centres in Cameroon	329 patients	Glucose	10 weeks	Proportion of patients at risk and diagnosed with diabetes.	117 (35.78%) were at risk, 37 (11.31%) were at high risk, 16 (4.89%) were diagnosed with diabetes.

All six studies focussed on POCT for diabetes screening, diagnosis or management in rural or remote locations. One study assessed the use of POCT for glucose measurement alone, and five studies examined the use of POCT for HbA1c in combination with either glucose or other chronic disease POC tests such as urine ACR for kidney disease and lipids for CVD.

One study examined the cost and waiting time of POCT for glucose and HbA1c compared to the laboratory in rural primary care units in Thailand (Kulrattanamaneeporn, Wongboonsin & Kost 2009). This study found POCT was more cost effective and had statistically significant reduced waiting times for patients (5 minutes versus 150 minutes), as per Table 9. However, these improvements were not solely caused by POCT, as POCT device use was combined with telemedicine to also reduce the costs and time associated with the transport of patient to the community hospital. A further limitation of this study was that only a small number of patients were in the intervention (n=29) and comparison groups (n=68). Despite these limitations, this is the only study to demonstrate that POCT can produce cost savings in addition to significant improvements diabetes control in rural settings (Kulrattanamaneeporn, Wongboonsin & Kost 2009).

Another study compared the user-friendliness and accuracy of a glucose POCT device to an HbA1c POCT device in classifying diabetes and abnormal glucose control in rural Uganda (Mayega et al. 2014). Accuracy of the POCT devices was not compared to a laboratory or reference method prior to use in this setting. The POC tests compared poorly in classifying diabetes and abnormal glucose regulation status, as per Table 9. Nurses reported they were able to conduct both POC tests with appropriate training, however, the authors determined that the POCT device for HbA1c was less user-friendly compared to the glucose POCT device. This study highlights the need to analytically evaluate a POCT device before it is implemented. The authors concluded that further development of appropriate diagnostic tests was needed for the early detection of diabetes in low income countries (Mayega et al. 2014).

A further study provided results on a POCT program for HbA1c, urine ACR and lipids operating in three rural and one remote Aboriginal Medical Service (AMS) in Australia (Shephard, M et al. 2006). Despite the small patient group (n=45), this study reported statistically significant reductions in HbA1c, total cholesterol and LDL cholesterol as measured by POCT (see Table 9). Four patient case studies were provided to further demonstrate the clinical utility of POCT in the rural and remote AMSs. Also reported was that patients who were unable to take advantage of the POCT service exhibited poorer health, however, no quantitative results were supplied to support this statement.

This study also examined stakeholder satisfaction with POCT through providing a survey to doctors (n=12), Aboriginal Health Workers (AHW) (n=13) and patients (n=58). The study stated there was unanimous agreement by the doctors and AHW that POCT had improved the service at their AMS, however, no quantitative data was provided. The study did however provide quantitative data on the satisfaction of patients with the diabetes service, in which a statistically significant increase in patient satisfaction was reported after the introduction of POCT. The authors listed the cost of POCT as being prohibitive in this setting and stated that this would be an important element for sustainability of POCT programs in rural and remote Australia (Shephard, M et al. 2006).

Another study also included results of survey of patient satisfaction with POCT for diabetes management in a rural GP setting (Motta et al. 2015). A high response rate was observed (98%) with 60 out of 61 patients completing the questionnaire. Respondents reported improved convenience of POCT compared to the laboratory and confidence in the accuracy of the POCT devices for HbA1c and lipids (see Table 9). Also credited to POCT was an increased patient motivation to manage their diabetes and an improvement in doctor-patient relationship (Motta et al. 2015). This study also confirmed the analytical performance of POCT devices in this rural GP. A limitation of the study was that quantitative improvements in diabetes control were not calculated in terms of a decrease in HbA1c levels. The authors attributed this limitation to the short timeframe of the study (Motta et al. 2015). After examination of this study's reference list, an additional study was included in the literature review (Shephard, M et al. 2005). This study established the clinical effectiveness of this rural POCT program through demonstrating statistically significant improvements in diabetes control and a reduction in cholesterol and blood pressure for rurally located patients (Shephard, M et al. 2005), as per Table 9. This study also conducted a survey of patient satisfaction which determined there was a statistically significant increase patients who were satisfied or very satisfied with their diabetes service (see Table 9).

The final study to investigate the use of POCT in a rural or remote setting took the form of a short communication which described a small community screening project undertaken by nursing students trained to use POCT in a rural community in central Africa (Leke, Portwood & Maboh 2013). The study found that a significant proportion of the rural community were at risk of developing diabetes and that POCT provided a new diagnosis of diabetes for approximately 5% of the population (see Table 9). Observational findings included initial resistance to POCT from laboratory technicians and patients; patients reporting improvements in their general health; and nursing students stating they enjoyed using the POCT devices.

A further three publications were not conducted in a rural or remote location, but did relate to the use of POCT for diabetes management in these locations. One report provided a position statement on the use of POCT glucose meters in Australia (Australian Diabetes Educators Association 2010). The below quote was provided in in regards to the use of POCT in remote locations, further confirming the general consensus that POCT is likely to provide the most benefits in remote settings.

> *"Testing at the point of care may be appropriate in defined circumstances, such as in remote indigenous communities where laboratory testing is unavailable and postponement of treatment would be potentially harmful for the individual."* (*Australian Diabetes Educators Association 2010)*

A further study discussed the setting of analytical goals for diabetes management outside of the laboratory setting in Australia (Shephard, M 2006a). However, this study did not discuss the specific requirements for POCT in rural or remote locations but rather commented that POCT in rural and remote environments is vastly different to laboratory settings in the following ways:

- Issues with the long-term retention of staff in rural and remote health services created difficulties in sustaining POCT;
- Issues with the efficient and timely delivery of reagents and quality products for POCT due to the isolation of health services in rural and remote locations;
- Limited refrigerator space at remote health services causes issues in storing POCT consumables;
- Extreme environmental conditions in rural and remote locations causes regular power fluctuations, heat and humidity which may affect POCT; and
- Limited infrastructure at rural and remote health services can cause issues such as poor lighting and dust within the working environment.

The author concluded these factors can impede POCT in rural and remote locations and, thus, aspects related to establishing and monitoring the quality of POCT in rural and remote settings should be considered separately to those in large metropolitan centres (Shephard, M 2006a).

The remaining study identified by the literature search, while not specifically related to POCT, reported a strength of their rural diabetes management program was that POCT was used to monitor diabetes control (Cooper et al. 2007). POCT was not discussed further by this study beyond making this statement.

Finally, four separate studies examined the potential, rather than actual, use of POCT for chronic disease in rural and remote locations. Two studies determined the extent of POCT use in primary care settings within a specific country (Thailand and India). One study examined the current use of POCT in rural Thailand through a series of surveys and interviews and stated that 'integrated' POCT would improve the efficiency of referrals (Kulrattanamaneeporn, Tuntideelert & Kost 2006). The second study found that while POCT was being used quite widely across rural and urban health services in India, its benefits had not been realised due to the challenges of integrating POCT, which included limited infrastructure and staff resources to support POCT. The authors therefore determined that POCT could be more effective if better incorporated into the Indian health system (Engel, Ganesh, et al. 2015). Two further studies examined POCT within a particular clinical setting. One reviewed the potential benefits of POCT for chronic disease testing in rural aged care facilities in Australia (Khalil et al. 2013), while the other study examined the factors that influence the dissemination of POCT for celiac disease in the Mediterranean (Costa et al. 2014). Both of these studies reasoned that rural areas would benefit the most from POCT due to the vast distances to laboratory pathology services which are concentrated in major centres (Costa et al. 2014; Khalil et al. 2013).

In summary, much of the current literature provides support for the use of POCT for chronic disease in rural and remote locations. However, the majority of the research focussed solely on POCT for diabetes diagnosis, screening or management, either alone or in combination with POCT for related chronic diseases. As mentioned in the introduction, two of this author's studies relate specifically to POCT for chronic disease in remote locations, one on HbA1c POCT (Spaeth, Shephard & Schatz 2014) and the other on INR POCT (Spaeth & Shephard 2016). As previously mentioned, the study on HbA1c provides new results on the timeliness of HbA1c in remote Australia. In terms of POCT for INR, the POCT in GP Trial studies were the only ones to investigate the use of INR POCT in a rural or remote location. In these studies, INR POCT was found to improve therapeutic control but did not improve medical compliance. However, as mentioned, many of the POCT in GP Trial studies did not differentiate the results between urban, rural and remote locations, nor did the studies provide examples of how therapeutic control was improved through the use of POCT (gaps that will be addressed by this authors studies as discussed in the contextual statement).

A common theme in many of the studies included in the literature review was that POCT increased convenience and improved satisfaction for patients and health professionals in rural and remote locations. In terms of the clinical benefits of POCT, the POCT in GP Trial found POCT improved

therapeutic control for all POC tests investigated but only improved medication compliance for some POC tests. Conflicting results were obtained by a RCT conducted in New Zealand where POCT was found not to provide any benefit over laboratory testing in terms of completing CVD risk assessments. Also, the New Zealand RCT reported no differences in outcomes between urban and rural locations. As mentioned, many of the POCT in GP Trial studies also did not differentiate results between urban, rural and remote locations, therefore, it is not possible to determine if the impact of POCT was different in these settings. However, several smaller studies did provide evidence for the clinical effectiveness of POCT in rural and remote locations through demonstrating significant improvements in therapeutic control for diabetes. In addition, several studies commented on the challenges faced by POCT in rural or remote settings and, therefore, highlight the need for practical solutions to be developed to overcome these issues. As will be discussed in the contextual statement, several of this author's studies provide novel methods to address the challenges confronted by POCT in rural and remote locations.

2.3.3 Application of Point-of-Care Testing in rural or remote – Pregnancy

The literature review identified only one study to discuss the use of POCT during pregnancy. The study was conducted in rural Peru and surveyed pregnant women and their partners about the potential use of POCT during pregnancy (Bayer et al. 2014). A total of 67 mothers and fathers participated in ten focus groups. The study found there to be a high demand for POCT in this setting, particularly as the participants believed that POCT was more patient-centred and provided shorter waiting times. While this study only examined the potential use of POCT in this rural setting, it did determine that there was a high level of demand for POCT for this particular application in rural communities of Peru. As such, this study identified a gap in POCT literature and a possible future direction for research in the field of POCT for pregnancy.

2.3.4 Application of Point-of-Care Testing in rural or remote - Infectious Disease

The literature review identified twelve studies examining the use of POCT for infectious disease, all of which focussed on rural or remote primary health care settings. These studies comprised three qualitative studies, two quantitative studies and seven descriptive studies. Studies examining the use of POCT for STIs were the most common (n=8) with the remaining studies either discussing POCT for respiratory tract infections (n=2), infectious disease in general (n=1) or the use of POCT for a skin infection only found in tropical third world countries (n=1). As this author's work primarily focusses on POCT for chronic disease and acute care, the studies related to POCT for infectious disease and STIs will only be discussed in brief. A summary of the study characteristics and key findings for each of the two quantitative and three qualitative studies is provided in Table 10.

Table 10 - Summary of study characteristics and key findings for studies focussing on POCT for infectious disease or STIs.

Author (year)	Study design	Clinical Setting	Numbers studied	POC tests measured	Duration of study	Outcome measured	Key findings
Orda et al. (2016)	Retro-spective study of accuracy of clinical decision making	A remote Australian Emergency Department	248 paediatric patients	Group A streptococci (GAS)	8 months	Accuracy of clinical decision for detecting GAS infection compared to POCT diagnosis	Positive predictive value for clinician decision-making for a positive GAS swab (bacterial infection) was 29% (95% CI 17–43), negative predictive value 78% (95% CI 63–88).
Yebyo et al. (2016)	POCT feasibility study	Primary Health Care Units in rural Northern Ethiopia	414 adult patients with acute URTIs	C-reactive protein (CRP)	Not provided	Distribution of CRP levels and frequency of antibiotic prescribing	For CRP ranges <20 mg/l, 20–99 mg/l and >100 mg/l the patient distribution was 66.6%, 27.9% and 5.5% respectively. 87.8% of patients prescribed antibiotics.
Natoli, L, Guy, RJ, Shephard, MDS, Whiley, D, et al. (2015)	Qualitative interviews	Sexual health and remote primary health in Australia	18 key stakeholders in sexual health in Australia	*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG)	6 months	Determine the public health implications of POCT integration into remote primary care in Australia	POCT may decrease community prevalence of STIs and associated morbidity by reducing time to treatment and expediting partner notification. STI surveillance systems must be introducted with POCT to avoid under-reporting.

Natoli, L, Guy, RJ, Shephard, MDS, Donovan, B, et al. (2015)	In-depth qualitative interviews	Sexual health in Australia	18 key stakeholders in sexual health in Australia	*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG)	6 months	To determine the settings in Australia where POCT for CT and NG may be the most beneficial.	POCT would have greatest benefit in remote Aboriginal communities where prevalence of STIs is high and treatment delays common.
Natoli, L, Guy, RJ, Shephard, MDS, Causer, L, et al. (2015)	In-depth qualitative interviews within a RCT	Primary care services in remote Australia	16 staff (nurses and Aboriginal Health Workers/ Practitioners)	*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG)	Not provided	To determine the acceptability of the GeneXpert POC device to primary care staff in remote Australia	POCT device easy to use and useful in this clinical context. POCT improved management of STIs and enabled more timely treatment. Manual POC test recording processes are time consuming and could be improved by POC connectivity/automatic transfer of POC test results into patient files.

The first quantitative study was conducted in a remote emergency department in Australia and compared the accuracy of clinical decision making to diagnosis by POCT for Group A Streptococcus (GAS) (Orda et al. 2016). Results were provided on the sensitivity and specificity of clinical decision making to guide appropriate antibiotic prescription for the treatment of pharyngitis as per Table 10. In this study, the use of clinical decision making alone resulted in 11 (42%) of the 26 patients testing positive for GAS via POCT not being prescribed antibiotics. This study suggests clinical decision making combined with POCT for GAS may provide better diagnostic accuracy and, thus, improve the appropriate administration of antibiotic treatment. However, a significant limitation of this study is that the accuracy of the POCT device was not compared to a reference laboratory method and, therefore, its reliability for the detection of GAS cannot be confirmed.

The second quantitative study examined the potential impact of POCT on antibiotic prescription rates in rural primary care services in Ethiopia (Yebyo et al. 2016). This study investigated the use of a POCT device (NycoCard) measuring C-reactive protein (CRP) to determine the distribution of CRP levels in patients presenting with upper respiratory tract infections (URTI). Also investigated was the antibiotic prescription rate for URTI in this setting. The results indicated that around two-thirds of patients with URTI had low CRP levels (<20 mg/l), and that only a small proportion (5.5%) of patients had CRP levels (>100 mg/l) indicating the prescription of antibiotics (see Table 10). However, more than three-quarters of all patients were prescribed antibiotics, suggesting significant overuse of antibiotics in this location. While the authors suggested POCT may facilitate the more judicious prescription of antibiotics in this setting, also stated was the need for further research to determine the impact of POCT in this setting (Yebyo et al. 2016).

All three qualitative studies were published by the same group of authors and aimed to determine the suitability of POCT for STIs in Australia through conducting interviews or surveys with key stakeholders (Natoli, L, Guy, RJ, Shephard, MDS, Causer, L, et al. 2015; Natoli, L, Guy, RJ, Shephard, MDS, Donovan, B, et al. 2015; Natoli, L, Guy, RJ, Shephard, MDS, Whiley, D, et al. 2015). In the first study, those interviewed (n=18) included sexual health physicians, nurses, academics, policy makers and laboratory-based microbiologists to assist in determining the most appropriate setting for STI POCT for CT and NG (Natoli, L, Guy, RJ, Shephard, MDS, Donovan, B, et al. 2015). A common theme throughout the interview responses was POCT would have the greatest benefit in remote Aboriginal communities where the prevalence of STIs is high and treatment delays are common. The second study discussed the public health implications of introducing POCT into the remote primary care setting and interviewed the same set of participants as in the first study (Natoli, L, Guy, RJ, Shephard,

MDS, Whiley, D, et al. 2015). Responses indicated there was a high level of support from clinicians and practitioners for wider access to POCT for CT and NG. The third qualitative study examined the acceptability of POCT in remote settings with a high burden of STIs (Natoli, L, Guy, RJ, Shephard, MDS, Causer, L, et al. 2015). This study was conducted as part of a RCT conducted in twelve Aboriginal community controlled health services in remote communities in Australia investigating the use of POCT for CT and NT. This RCT is known as the TTANGO (Test, Treat and Go) Trial. Primary health care staff (n=16) with experience using the POCT device in the TTANGO Trial were interviewed. These participants included nurses, AHWs and Aboriginal Health Practitioners. Respondents indicated that POCT for CT and NG had resulted in more timely treatment as results were available on the same day and reduced workload through fewer patient follow-up appointments. However, several respondents indicated that patients left the clinic before the POCT result was available, meaning the patient had to be followed up the next day. The main challenge for POCT in this setting was determined to be the manual recording of POCT results. Participants suggested that a POCT connectivity system would negate the need for manual recording and improve workflow. While all three studies surveyed a relatively small number of representatives, as per Table 10, a wide range of participants were included in terms of both qualifications and experience, thus ensuring a relatively balanced assessment. The authors concluded that while there is a high level of support for the use of POCT for STIs in rural and remote Indigenous communities, more research was needed to assess POC test performance, cost, acceptability and outcomes (Natoli, L. et al. 2015; Natoli, L, Guy, RJ, Shephard, MDS, Donovan, B, et al. 2015; Natoli, L, Guy, RJ, Shephard, MDS, Causer, L, et al. 2015). Therefore, these studies indicate a gap in knowledge regarding the clinical and cost-effectiveness of POCT for STIs in rural and remote settings.

Of the seven descriptive studies identified, five focussed on POCT for STIs, one on detecting a rare side effect of antiretroviral therapy (ART) for human immunodeficiency virus (HIV), and one on infectious disease more generally. A summary of the study characteristics and key outcomes is provided in Table 11.

Table 11 - Summary of study characteristics and key findings for descriptive studies focussing on POCT for infectious disease or STIs.

Author (year)	Study design	Clinical Setting	POC tests discussed	Key findings
Ward et al. (2012)	General commentary (as editorial)	Aboriginal and Torres Strait Islander remote communities	POCT for HIV and STIs (chlamydia, gonorrhoea and trichomoniasis)	Before POCT for HIV and STIs can be considered, further research is required on: impact on clinician workload, quality assurance requirements, costs of POC tests, analytical performance of POC tests, impact of POCT on re-infection and disease prevalence and acceptability of POCT by health professional staff.
Hui et al. (2013)	Mathematical modelling	Remote Indigenous communities in Australia	*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG)	POCT devices with 95% sensitivity could reduce the prevalence of NG and CT from 7.1% and 11.9% to 5.7% and 8.9%, respectively at screening coverage of 44% per year. Screening coverage of 80% per year may result in the near elimination of CT and NG if POCT is introduced. Cost-effectiveness of POCT needs to be determined before implementation can be considered.
Guy et al. (2013)	Description of study protocol for cross-over cluster RCT	12 regional or remote Indigenous health services in Australia (6 control, 6 intervention)	*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG)	Will be first RCT of CT and NG POCT internationally. Outcome measures to include clinical effectiveness, cost-effectiveness and cultural and operational acceptability of molecular POCT for CT and NG. Primary outcome is repeat positivity at three months after treatment of an initial CT or NG infection.
Hui et al. (2014)	Mathematical modelling	Remote Indigenous communities in Australia	Rapid POC test for *Trichomonas vaginalis* (TV)	POCT devices with 95% sensitivity could reduce the prevalence of TV from 13.1% to 8.7% at screening coverage of 44% per year. If screening coverage increased to 60%, POCT devices could reduce prevalence of TV from 5.3% to 1.8%.

				Emphasis on testing for TV in older women due to high prevalence observed in this group (15% and 11% for females aged 24–29 years and 30–34 years, respectively).
Smit et al. (2013)	Descriptive study of POCT External Quality Assurance program (EQA)	10 rural health centres in Tanzania	HIV and syphilis	Low-cost EQA program implemented where by POCT results compared to laboratory method by spotting a patient sample obtained at health facility on to dried blood spots (DBS) cards and sending to a reference laboratory. 92.5% of 2201 DBS cards were correctly spotted. Average time between DBS at health facility and and arrival at laboratory = 95 days (62 days to 142 days). Health care workers found the EQA method easy and quick (2–6 minutes).
Clerc and Greub (2010)	Review of commonly available POC tests for infecious disease	Patient bedside and remote care centres	GAS, Group B streptococci, Pneumococcal, *Legionell*a, MRSA, *Clostridium difficile*, CT, malaria, *Giardia lamblia*, RSV, Influenza, Rotavirus, Adenovirus, HIV, enterovirus.	Some POC tests exhibit insufficient sensitivity and confirmatory tests are needed. POC test performance characteristics in a specific clinical setting must be considered. POCT clinical-effectiveness combined with cost-effectiveness should be demonstrated in the current setting.
Ivers and Mukherjee (2006)	Descriptive study	Rural Haiti (resource-poor setting)	Lactic acid POC test to detect lactic acidosis induced by antiretroviral therapy (ART) for HIV.	Lactic acidosis is a rare but potentially life-threatening complication of ART (no quantitative data provided). Low-cost POCT for lactic acidosis useful in assisting with clinical decision making in this setting.

Guy was an author on four of the six studies related to STIs, all of which evaluated POCT in rural or remote Aboriginal or Torres Strait Islander populations in Australia. Each of the four studies built upon the next, starting with a discussion on the potential benefits of POCT for HIV and STI in the rural and remote Indigenous setting (Ward et al. 2012); then examining the potential impact of POCT on the prevalence of CT and NG in remote Indigenous communities (Hui et al. 2013); describing the aims and methods of a the TTANGO RCT for CT and NT (Guy et al. 2013); and, finally, a study examining the additional impact of POCT on the prevalence of *Trichomonas vaginalis* (TV) in remote Indigenous communities (Hui, B et al. 2014). Each study determined a potential and significant role for POCT in remote Indigenous primary care settings (see Table 11). However, each study indicated further research was needed in four key areas: 1) clinical effectiveness; 2) cost effectiveness; 3) impact of POCT on clinician workload; and 4) quality assurance requirements for POCT in rural and remote Indigenous settings. As such, these studies identify several further gaps in knowledge related to POCT use for STIs in the rural and remote primary care setting.

Of the three remaining descriptive studies, one study reviewed the sensitivity and specificity of the most commonly used POC devices for infectious disease and summarised the potential clinical applications of the POC tests (see Table 11) (Clerc & Greub 2010). This study only stated that POCT enabled the generation of tests results at remote care centres but did not provide any results or outcomes on the use of POCT in a remote setting. However, the authors highlight the performance characteristics of POCT devices must be evaluated in the specific setting for which they are intended to be used.

The second descriptive study discussed the potential use of a POCT device previously used in intensive care settings to detect lactic acidosis for potential application to detect a rare side effect of HIV antiretroviral therapy in rural Haiti (Ivers & Mukherjee 2006). The authors stated this POCT device maybe useful in detecting this rare side-effect (see Table 11), however, no quantitative data was provided in this study to support this statement. The authors concluded this novel use of POCT should be investigated further.

The final study provided methods and results for a novel and low-cost external quality assurance (EQA) program for HIV and syphilis POCT in rural primary health care clinics in Tanzania (Smit et al. 2013). Also highlighted by this study was the significant time delay (average 95 days) between obtaining patient samples and the samples arriving at the laboratory, as per Table 11. The authors

concluded this method of EQA testing could be translated to other developing countries wanting to implement quality assured POCT.

In summary, many of the studies discussed the potential use (n=7) rather than actual use (n=5) of POCT for infectious disease in rural or remote settings. The majority of studies focussed on POCT for STIs, all of which were conducted in Australia with the exception of one study based in Tanzania. A majority of the STI studies were based in high prevalence Indigenous settings, which was determined to be the most applicable setting for STI POCT use in Australia (Natoli, L, Guy, RJ, Shephard, MDS, Donovan, B, et al. 2015; Natoli, L, Guy, RJ, Shephard, MDS, Whiley, D, et al. 2015). Also, qualitative surveys found POCT was well received by health professionals in rural and remote locations. A small number of studies examined the use of POCT for infectious disease in low-resource countries where environmental conditions, limited infrastructure and the cost of POCT were recorded as common challenges for POCT.

2.3.5 Application of Point-of-Care Testing in rural or remote – Acute Disease

Eleven studies were identified on the use of POCT for acute disease in rural and/or remote locations. These studies will be critically appraised as these are the most relevant to this author's studies presented in this thesis.

Of the eleven studies, eight studies were based in rural hospital emergency departments or critical care units, with one study also including two remotely located hospitals. A summary of the study characteristics and key findings for these eight studies is provided in Table 12.

Table 12 - Summary of study characteristics and key findings for studies focussing on POCT for acute care in hospital settings.

Author (year)	Study design	Clinical Setting	Numbers studied	POC tests measured	Duration of study	Outcome measured	Key findings
Kost, Suwanyangyuen and Kulrattanamaneeporn (2006)	Descriptive study (survey of community hospital facilities)	Primary care units and community hospitals in 7 hill tribe villages	Not applicable	Not applicable	Not provided	Explored potential for POCT in health care delivery	Currently limited application of POCT in PCUs and community hospitals. Community hospitals lacked blood gas and electrolyte testing. Hypothesised that POCT combined with telemedicine will improve health care for mountain hill tribes.
Kost et al. (2010)	Qualitative and quantitative field surveys	Rural emergency rooms located in low-resource community hospitals in Thailand	3 referral hospitals (RH), 5 province regional hospitals and 10 community hospitals (CH)	Cardiac biomarkers: Cardiac troponin I (cTnI), cardiac troponin T (cTnT)	Not provided	Determine cardiac biomarker tests currently used. Determine travel time and distance from CH to RH	POC cardiac biomarker testing currently offered in only 1 RH and 2 CH. Survey identified that average travel times from CH to RH via ambulance were close to, or greater than, 1 hour (range 15 to 150 minutes). POCT for cardiac biomarkers will facilitate triage decisions in CH regarding patient transport to distant RH where cardiologists are available to administer definitive treatment.

Blattner, Nixon, Jaye, et al. (2010)	Qualitative interviews (no quantitative data provided)	Rural hospital in New Zealand	13 health professionals (doctors, nurses and health workers)	Electrolytes, blood gases, urea, creatinine, Hb, cTnI and INR	Not provided	To identify the perceived impact of POC testing on clinicians and the community	POCT increased clinicians' confidence in clinical decision making and improved diagnostic certainty and this impacted on patients and their families. Several respondents indicated that POCT enabled earlier decision making and more timely treatment which was life-saving on occasion. The challenges associated with POCT testing included increased workload, pressure to up-skill and over-testing.
St John et al. (2015)	Descriptive study	Rural and remote hospitals and general practices in South Australia	Nurses and doctors	Glucose, HbA1c, lipids, urine ACR, INR, NT-proBNP, D-dimer and troponin	POCT program for 12 years	Describe online training program for POCT	Since launch of POCT training website (date not provided), nearly 2000 trainees recorded and 1300 competency tests completed with each trainee taking an average of 3 attempts before passing. QC performance by those trained via the website compared well with those receiving face-to face training (no data provided). On-line POC training less expensive alternative to face-to-face support (no data provided).

Dahm et al. (2017)	Qualitative interviews and focus groups (no quantitative data provided)	4 rural and 4 remote emegency departments in New South Wales, Australia	14 clinical professionals	Not stated in methods, survey responses indicated: cTnI, potassium and blood gases used	1 month	Gain an understanding of the operational impact POCT across rural and remote ED settings	POCT facilitated more efficient and effective patient care via faster test turnaround and time to treatment. POCT enabled more informed triage of patients requiring transfer to appropriate sites and thus also reduced costs. Staff identified both innovative and disruptive challenges to clinical work patterns associated with PoCT.
Blattner, Nixon, Dovey, et al. (2010)	Quantiative before and after study	Rural hospital in New Zealand	177 patients	Electrolytes, blood gases, urea, creatinine, Hb, BNP, cTnI and INR	6 months	Determine differential diagnosis and planned patient management before and after POCT introduced Provide cost versus tangible benefit of POCT	269 POC tests recorded. POCT significantly increased diagnostic certainty from 2.5 diagnoses pre-test to 1.3 diagnoses post-test ($p< 0.001$) and altered management for 43% of patients ($p< 0.001$). Patient transfers to base hospital reduced by 62% (52 pre-test and 20 post-test). Patient discharges increased by 480% (7 pre-test and 34 post-test). Substantial treatment change reported in 75% of cases, some change in 22%, and no change in 3%. POCT produced annual cost benefit of $452,360.

Tideman, Simpson and Tirimacco (2010)	Descriptive study (describes program and provides initial results)	Rural hospitals in South Australia	1 hospital with POCT and 2 control hospitals of similar size and resources	Troponin and NT-proBNP	Not provided	To measure patient outcomes following the implementation of POCT with cardiac care framework	POCT + cardiac care reduced 30-day readmission rates from 10.4% to 4.2% (p = 0.03). POCT + cardiac care reduced in-hospital death rates from 15.8% to 9.8% (p = 0.1). POCT combined with integrated cardiac care can improve patient outcomes for ACS.
Shihana, Dawson and Buckley (2016)	Quasi-experimental comparison	Three rural hospitals in Sri Lanka	401 patients	Methemoglo-bin oncentra-tion	7 years	Determine clinical outcomes and treatment of patients presenting with propanil poisining after POC test introduced	Fatality for propanil poisoning fell by two-thirds, from 10% (38/401) to 3% (8/262). Use of first line treatment (methylene blue) increased after the POC test was introduced from 10% (13/136) to 55% (59/107). No significance factors provided.

Five were qualitative surveys or interviews of key stakeholders utilising POCT for acute care; one provided quantitative results on the clinical and cost effectiveness of a POCT trial in a rural hospital based in New Zealand; one provided results of POCT use in specific emergency scenarios; and one study delivered a systematic review on the use of POCT for ACS. From the five qualitative studies, three were conducted solely in hospital settings, and a further two focussed on both tertiary and primary health care settings combined.

The first study examined the current and potential for use of POCT for acute care in hospitals and primary care facilities in mountainous regions in Thailand (Kost, Suwanyangyuen & Kulrattanamaneeporn 2006). The survey found there was limited use of POCT in both community hospitals and primary care units (see Table 12). The authors proposed that POCT combined with telemedicine could enhance decision making in this setting and may improve the triage of critically ill patients.

The second study was by the same authors and investigated the current cardiac biomarker use in central hospitals compared to the more rural hospitals in Thailand (Kost et al. 2010). Also surveyed were distances and travel times from the rural hospitals to the larger centralised hospitals where cardiac services were available. As per Table 12, the survey found there was limited cardiac biomarker use in the rural hospitals and the travel time to central cardiac services was in most cases greater than one hour. As such, the authors proposed POCT combined with telemedicine at the rural hospitals would enhance triage decisions for patients requiring transfer to larger centres (Kost et al. 2010).

The third qualitative study provided the results of a survey of key stakeholders involved with a trial of acute POCT in a rural hospital in New Zealand (Blattner, Nixon, Jaye, et al. 2010). The interview included a small number of participants (n=13), however, this group did include all doctors currently employed by the hospital as well as several key nursing and health worker staff. Qualitative survey responses indicated POCT provided increased confidence in clinical decision making and that fewer patients were transferred to a major facility, therefore reducing costs (see Table 12). However, no results on cost effectiveness were provided. Overuse of POCT was raised as a potential challenge as well as increased workload in managing patients who would have previously been transferred. The time required to complete POCT device training was also cited as a challenge by several respondents (see Table 12). The study concluded that POCT improved the acute medical care to a predominately indigenous and lower socioeconomic population (Blattner, Nixon, Jaye, et al. 2010). The authors

also identified a gap in knowledge in relation to the use of POCT in rural locations, as evidenced by the following quote:

> *"There is surprisingly little research into the role of POC testing in small rural hospitals. It is likely that the benefits in rural settings, where the turn-around time for conventional laboratory tests is extended, will be far greater than in hospital settings where results can be more immediately available" (Blattner, Nixon, Jaye, et al. 2010).*

The fourth qualitative study described the impact of an online training program for a POCT network based in both rural hospitals and primary care clinics in South Australia (St John et al. 2015). The POCT network included tests for both acute illness and chronic disease, but did not state which POC tests were used in each jurisdiction. The authors stated that training health professional staff over a wide geographic spread of was a key challenge of managing the POCT network. While a description of the online training program was not provided within this study, results on the number of trainees accessing the training program were provided as per Table 12. However, no information on the duration for which these statistics were collected was provided. The authors concluded this method of training reduced the cost of administering the POCT program, though no cost benefit data was reported. A further limitation of the study was that the appropriateness of the new training format was not examined in terms of user satisfaction and level of competency/understanding of POCT post-training (St John et al. 2015).

The most recent qualitative study provided survey results after the implementation of a state-wide POCT program for acute care in rural hospital EDs in eastern Australia (Dahm et al. 2017). A significant limitation of this study was that while the authors stated POCT was implemented in more than 150 regional, rural and remote EDs, and the model was described as "one of the largest POCT networks in the world", only a small number of clinical staff (n=14) from only four rural and four remote EDs were included in the surveys and focus groups (Dahm et al. 2017). Survey responses were similar to those in the New Zealand study in that access to POCT was found to provide nursing staff with increased confidence in making decisions for acutely ill patients and there was a perceived reduction in costs through a decrease in the number of unnecessary patient transfers as per Table 12. Again, no data on cost effectiveness was presented in this study. The survey identified several concerns with POCT. These included limited communication with rural and remote nursing staff regarding the implementation of POCT as well as quality control and EQA processes; alleged overuse

of POC tests led to delays in patient management when having to wait for the POCT equipment to become available; and an initial low confidence in the accuracy of the POC test results by POCT users. The authors made little attempt to provide potential solutions to the challenges raised and concluded further research was needed to overcome operational issues related to POCT use in rural settings (Dahm et al. 2017). Again, this study did not provide any evidence on the methods for POCT implementation or any outcome measures for using of POCT in these rural and remote settings.

An additional three studies provided quantitative results on POCT use for acute care in hospital settings as per Table 12. The first study was conducted by the same research group that performed the qualitative survey in a rural New Zealand hospital (Blattner, Nixon, Jaye, et al. 2010). This study provided the quantitative results for clinical and cost effectiveness of this POCT trial (Blattner, Nixon, Dovey, et al. 2010). Also provided was additional information regarding the characteristics of the clinical setting that was described as a 'remote rural hospital'. For later comparison within the contextual statement, these features included the following: a 2- to 4-hour travel time to the nearest tertiary hospital; limited diagnostic services; no on-site laboratory services; seven on-site doctors; ten acute beds; and 750 acute admissions annually. Results of the study revealed that POCT provided better diagnostic certainty for acute presentations and an increased number of diagnoses post POCT implementation as per Table 12. Cost effectiveness was measured through examining the number of patient transfers and discharges pre- and post-introduction of POCT. The number of patient transfers reduced by more than half, and patient discharge increased almost 5-fold leading to an estimated annual cost saving of approximately $450,000 as per Table 12. These findings support the qualitative survey responses in the previous study in which respondents suggested POCT reduced the number of patient transfers and would therefore lead to cost savings. A limitation of this study is that the reduction in transfers was not deemed to be statistically significant. The authors concluded POCT assisted in addressing the heath care inequities experienced by this rural and socioeconomically disadvantaged community (Blattner, Nixon, Dovey, et al. 2010).

A further quantitative study titled *Integrating PoCT into clinical care* described the initial results of an integrated cardiac care program using POCT to detect ACS and health failure in rural hospitals in South Australia (Tideman, Simpson & Tirimacco 2010). The 30-day readmission rates and in-hospital deaths were compared to two control hospitals of similar size and resources that did not have access to POCT. As per Table 12, a statistically significant decrease in the 30-day readmission rate was found post cardiac care program implementation (10.4% to 4.2%). Also, a reduction in in-hospital deaths was observed, however, this decrease was not significant when compared to the control groups

(see Table 12). The authors made no comment on the limitations of this study (Tideman, Simpson & Tirimacco 2010). POCT was just one component of this cardiac care program. The program also involved protocols on the triage, risk stratification and treatment of patients with suspected ACS or heart failure. As such, the results of this study cannot be solely attributed to POCT. The authors did, however, indicate the program would not have been feasible if not for POCT due to the significant time delays in receiving diagnostic pathology results in these rural locations (Tideman, Simpson & Tirimacco 2010). A further limitation was that while authors stated POCT should be implemented with quality testing and training structures in place, the methods or a description of these key structures was not provided. Despite these drawbacks, this study supports the use of POCT for acute care in rural hospital settings. The authors commented that integrating a similar clinical support system using POCT into primary care settings was also required to produce optimal outcomes (Tideman, Simpson & Tirimacco 2010). This last statement suggests that further research is required to determine the outcomes of POCT for acute care use in primary care settings, thus identifying a gap in the current literature.

The last quantitative study evaluated a simple bedside POC test to detect propanil poisoning in agricultural workers in three rural hospitals in Sri Lanka (Shihana, Dawson & Buckley 2016). The study found that POCT was associated with an increased use of the first line treatment for propanil poisoning (from 10% to 55%) and a decreased number of deaths (from 10% to 3%) post intervention as per Table 12. It was not stated if the decrease in deaths was statistically significant. The authors also noted the decrease in deaths could not be solely attributed to the introduction of POCT alone as additional education on detection and treatment had also been provided (Shihana, Dawson & Buckley 2016). A further limitation of the study was that only 13 paired samples were tested to determine the accuracy of the POCT device compared to the laboratory method prior to implementation (with most guidelines stating a minimum of 40 pairs is required). Despite the limitations of this study, a marked reduction in deaths for this particular acute indication was demonstrated through the use of POCT in this rural setting.

Until now, studies examining the use of POCT for acute care have been predominantly based in rural or remote hospital settings, with the exception one study which discussed the use of an online POCT training program in both rural hospitals and primary care health facilities (St John et al. 2015). A further three studies examining POCT for acute care outside of the hospital setting were identified; two in mobile emergency service settings and one in a primary health care setting.

Of the two articles examining the use of POCT in mobile emergency service settings, one was a study published in the *Point of Care* journal and the other a report published in a magazine on emergency care. The first was a qualitative study which examined the potential impact of POCT on patient safety in mobile critical care units in rural areas of Spain (De La Torre & Campoy 2009). This study surveyed each rural health care facility within a mountainous and geographically challenging area of Spain. The factors affecting patients' safety were found to be the wide geographic dispersion and long patient transfer times to nearest hospital. This study also found that in one year there were 5,593 medical emergencies outside a health facility and 1,757 (31%) required transfer to hospital, of which many could be triaged more appropriately using diagnostic test information. The authors concluded POCT could produce substantial benefits to patient safety in this geographically isolated location and described the initial implementation of a POCT device measuring a variety of analytes for acute care. However, no data was provided after the implementation of POCT. The authors emphasised that training and quality control programs would be essential to the success of introducing POCT in this setting (De La Torre & Campoy 2009).

The second article provided case studies on the use of POCT in mobile emergency medical services on how POCT had improved patient outcomes (Fuller 2008). The article did not state if patient cases occurred in a rural or remote location but did provided the following statement:

> *"Clearly, it* [POCT] *has uses for remote and rural settings. It* [POCT] *can aid in more quickly identifying patients who need expedient care for such diverse medical conditions as ACS, internal bleeding, undifferentiated respiratory distress and electrolyte emergencies." (Fuller 2008).*

This study was published in the Emergency Care Magazine and it is not known if the article was peer reviewed. However, this article was the only one to provide real patient case examples on the use of POCT in acute presentations.

The literature search identified only one study to examine the use of POCT for acute care in a rural or remote primary health care setting, with the exception of the studies conducted by this author. This qualitative study provided a survey of clinicians' opinions on the potential use of POCT to detect acetylcholinesterase (AChE) in case of organophosphorus (OP) poisoning in rural Sri Lanka (Rajapakse, Neeman & Buckley 2014). The survey included clinicians (n=23) with differing levels of experience with patients with OP poisoning found. The responses indicated there was a low level of

support for POCT in this setting for this particular application. The authors reasoned the lack of support was likely due to the complex management of OP poisoning and difficulty in interpreting AChE results and concluded further education should be provided on this potential use of POCT (Rajapakse, Neeman & Buckley 2014). This study does not support the use of POCT in this niche setting, however, it does highlight the need for training and education to be provided prior to implementation of POCT.

In summary, seven studies examined the actual use of POCT in a rural or remote location, six of which were based in rural hospital settings and one in a mobile emergency service setting. Several studies (n=3) were surveys or interviews of key stakeholders with experience using POCT technology. A common theme arising from the surveys included the perception that POCT increased confidence in clinical decision making for acutely ill patients and resulted in a reduction in unnecessary patient transfers. One quantitative study found the improvement in clinical decision making by POCT produced a substantial, but not a significant, cost benefit. The limitations identified for POCT in these settings were the difficulties in communication with isolated health facilities, challenges in managing training for rural or remotely located staff with high turnover rates and the perceived overuse of POCT which was suggested to increase the costs related to POCT. Finally, this literature review found no previous studies to investigate the use of POCT in acute primary health care settings, therefore identifying a significant gap in the literature.

2.3.6 Application of Point-of-Care Testing in rural or remote - General

A further three book chapters and three studies discussed the use of POCT in rural or remote locations more generally.

The first of the book chapters highlighted the greatest need for POCT is in remote locations such as the military battlefield, exploratory expeditions, space voyages, disaster sites, and geographically isolated populations (Satava & Jones 2002). The book chapter then provided examples of POCT use in the military setting and described the desirable characteristics for POCT technology to operate specifically in this environment, such as being lightweight and small in size, only requiring low power and being easy to operate (Satava & Jones 2002).

The next book chapter summarised several POCT models working in rural areas of Australia and specifically discussed POCT programs operating in rural or remote Indigenous health care settings

(Shephard, M 2004a). This chapter also outlined the benefits of POCT to rural Indigenous communities, which included that:

- POCT eliminates the 'disadvantage of distance' in terms of pathology testing;
- POCT improves patient compliance with taking medication;
- POCT empowers Aboriginal Health Workers to take responsibility for the health of their community members; and
- POCT negates the need for a follow-up visit to obtain pathology results.

The challenges faced by POCT in the rural Indigenous setting were also summarised in this chapter. These included:

- environmental extremes;
- power fluctuations;
- inadequate resources for POCT use and storage;
- high rates of staff turnover in rural locations;
- translation of complex medical/scientific terms to Aboriginal health professionals; and
- ensuring POCT is culturally appropriate.

Shephard, M (2004a) also provided a thorough review of the POCT programs that exist in Australia which serve rural Indigenous populations and these POCT models have been discussed previously in this literature review.

Shephard later co-authored another book chapter on POCT specifically in remote environments (Shephard, M, Tirimacco & Tideman 2010). Highlighted by this chapter are the additional challenges faced in remote locations, these included:

- extreme isolation;
- lower socioeconomic status compared to less isolated locations;
- poorer access to services; and
- higher burdens of disease of chronic, infectious and acute disease.

The benefits of POCT in this setting were similar to those discussed in the previous book chapter. A summary of POCT programs that exist in Australia were again provided, with all except one covered elsewhere in this literature review (Bubner et al. 2009; Gialamas, Yelland, et al. 2009; Shephard, M 2006d; Shephard, M et al. 2006; Tideman, Simpson & Tirimacco 2010). The remaining study, not yet

discussed, provided a discussion around the use of POCT for acute and chronic disease in country hospitals and remote primary health care services in Queensland, Australia. No reference or further information was provided in relation to this POCT program.

The further study conducted by Shephard, M (2013) discussed the status and benefits to using POCT, specifically in Australia, through summarising the results from previous literature. The majority of this article focussed on stakeholder satisfaction with POCT for chronic disease and referenced studies discussed earlier in this literature review. Clinical uses for acute POCT included the early risk stratification of ACS, rapid stabilisation of septic shock and reduction in cardiovascular mortality. In terms of stakeholder approval, a study co-authored by the author of this thesis was referenced, which reported an increased satisfaction with POCT for electrolytes compared to standard pathology testing (Shephard, M et al. 2012b). The Queensland POCT program was again cited by this study, though again no in-depth discussion was provided. This time, however, a reference to this POCT program was provided titled *i-STAT – Combining Chemistry and Haematology in PoCT* published in the *Clinical Biochemist Reviews Journal* (Martin, C 2010). This article was not found in the initial literature review search as it did not contain the terms rural or remote or isolated in the title, abstract or keywords.

This study was examined further for its relevance to the studies conducted by this author. The Queensland POCT model was described as a large POCT network (n=140 sites) designed primarily for acute care across rural and remote Queensland. The study included some key statistics on the number of POCT devices, number of POC tests performed and number of POCT operators trained. The article, which was not peer-reviewed, also described the governance structure, quality testing and training structures put in place in this POCT program. While the author stated that POCT may increase patient safety, or be the difference between the patient remaining in the community or being evacuated to a major hospital, no results on outcomes were provided in this study (Martin, C 2010).

Frese et al. (2016) provided the results of a questionnaire examining the use of POC tests by GPs in Germany. It surveyed 63 GPs and compared the current POCT use in urban and rural based GPs. Interestingly, rural GPs were more familiar with a greater range of POC tests than urban GPs. Primarily, GPs reported using POCT for chronic and infectious disease, while the only POC test for acute care widely used was troponin for ACS. The authors rationalised the benefit of POCT for reducing diagnostic uncertainty around cases of chest pain was the reason GPs placed high

importance on the troponin POC test (Frese et al. 2016). This study examined knowledge on only 27 different POC tests, around half of which were determined to be useful, however, information on other POC tests may have been missed. The outcomes related to POCT use in these settings was also not assessed in this study.

Finally, a qualitative survey by Engel, Davids, et al. (2015) examined the extent of POCT use in South Africa. Key stakeholders from both rural and urban hospitals and clinics were included, with 101 interviews conducted across a variety of jurisdictions. These included clinicians, patients, technicians, policymakers, hospital managers and POCT industry representatives from both public and private health care sectors. The many environmental challenges that prevented the effective use of POCT in South Africa were highlighted; these included long distances to diagnostic facilities, poor road conditions, worker strikes and bad weather. After further reading, it was found the primary challenge was the transport of pathology samples to a centralised POCT site rather than the POCT device being used directly at the site of patient contact. The findings of this study are, therefore, not translatable as POCT was not performed at the site of patient care but rather used as a cheaper alternative to large-scale laboratory devices. This mode of use of POCT is not examined in this thesis.

Once again, these studies highlight that rural and remote settings are likely to benefit the most from the introduction of POCT. Some additional challenges were also raised in terms of POCT use, particularly in remote settings. While an additional study was identified, describing the key statistics of a state-wide POCT program for acute care management, again no outcomes were provided on the use for POCT testing in this setting. One study also highlighted the limited use of POCT for acute care in rural primary health care services in Germany, therefore suggesting there is limited use of POCT for this application also outside of Australia.

2.4 Summary of gaps in literature identified by literature review

To conclude, a summary of the gaps in literature related to the application of POCT in rural and remote settings is provided in Table 13. The gaps in knowledge that are addressed by the studies conducted by this author are also summarised in Table 13. These will be further discussed in the next chapter, contextual statement.

The aims and methods underpinning the studies conducted by this author will be discussed and outcomes providing new knowledge in the field of POCT will also be highlighted within the contextual statement.

Table 13 – Gaps in knowledge identified by literature review and addressed by studies conducted by this author.

Gap identified by literature review	How this author's body of work addresses these gaps	Reference(s)
All of the evaluations of the analytical of POCT devices in rural and remote locations focus just on POC tests for diabetes, coagulation and STIs	Conducted the first evaluation of a POCT device for measuring creatinine to screen for chronic kidney disease in a rural setting. Conducted the first evaluation of a POCT device for measuring WBC count for detection of infections in a remote setting.	(Spaeth, Shephard, Shephard, et al. 2015) (Spaeth, Shephard, McCormack, et al. 2015)
Limited information on timeliness of POCT compared to laboratory testing in rural and remote locations	Evidence provided for the first time on the timeliness of POCT for HbA1c and time to consultation compared to laboratory testing in a remotely located cohort of patients.	(Spaeth, Shephard & Schatz 2014)
Lack of evidence for improvement in anticoagulation control by POCT in rural and remote locations	First evidence provided for the clinical effectiveness of INR POCT for monitoring warfarin therapy in patients from remote locations.	(Spaeth & Shephard 2016)
No previous studies on use of Hb POC tests to screen for anaemia in rural or remote location	First study to demonstrate clinical and operational benefits of using POC Hb testing for patient in a rural location.	(McCormack et al. 2017)
Only one study was identified in relation to the	Nil.	

use of POCT for pregnancy in rural or remote settings		
Outcomes on the clinical and cost effectiveness of POCT for infectious disease have not yet been reported	Nil.	
No evidence exists on the use of acute POCT in rural or remote primary health care settings	First quantitative data on the clinical effectiveness of acute POCT in remote primary health care settings. First quantitative data on cost effectiveness of acute POCT in remote primary health care settings.	(Spaeth, Shephard & Omond 2017) (Spaeth et al. 2018)
Limited evidence for the ongoing analytical quality of acute POCT in rural or remote locations	Two studies provide detailed evidence for the sustainable analytical quality of acute POCT in remote settings, showing quality equivalent to laboratory benchmarks.	(Shephard, M, Spaeth, Mazzachi, et al. 2014) (Shephard, M, Spaeth, Motta, et al. 2014)
Limited evidence for the acceptance of acute POCT in rural and remote primary health care settings	Two studies provide the first qualitative and quantitative evidence for the acceptability of acute POCT in remote primary health care settings through surveys of key stakeholder satisfaction.	(Shephard, M et al. 2012b) (McCormack et al. 2017)
No studies describing the responsibility of a POC Coordinator in managing remotely located POCT networks	First description of the challenges for a POC coordinator and potential solutions in managing remotely located POCT networks.	(Shephard, M et al. 2013)

CHAPTER 3 CONTEXTUAL STATEMENT

This contextual statement demonstrates how the studies included in this thesis originated, and provides the narrative for how they build upon one another to form a significant evidence base for the use POCT in rural and remote locations. The narrative is based on the ten years of research conducted by the author. Eight of these ten years have been spent as the Coordinator of the NT POCT Program which operates in one of the most challenging clinical settings for POCT; the remote NT of Australia. As such, ten of the studies were based on research conducted as part of the NT POCT Program, with two studies conducted elsewhere in Australia and the one remaining study conducted in rural Pakistan.

As stated in the literature review, the studies conducted by this author have also addressed several gaps in knowledge related to the use of POCT in remote primary health care settings. The contextual statement will further highlight and discuss these original contributions to knowledge, as well as begin to establish the links between the studies conducted by this author. These links will then be defined with the linking statements between each study in the next chapter.

In accordance with the Flinders University policy on academic integrity the author's role in each study will be made clear for academic integrity purposes.

3.1 Principles of Establishing and Managing a POCT Service

There are several stages that must be considered when establishing, managing and evaluating a POCT service (Shephard, M 2016b). Figure 7 summarises these key processes in a flow chart developed by this author based on her knowledge and experience in evaluating POCT devices, implementing sustainable POCT models and assessing outcomes related to POCT use.

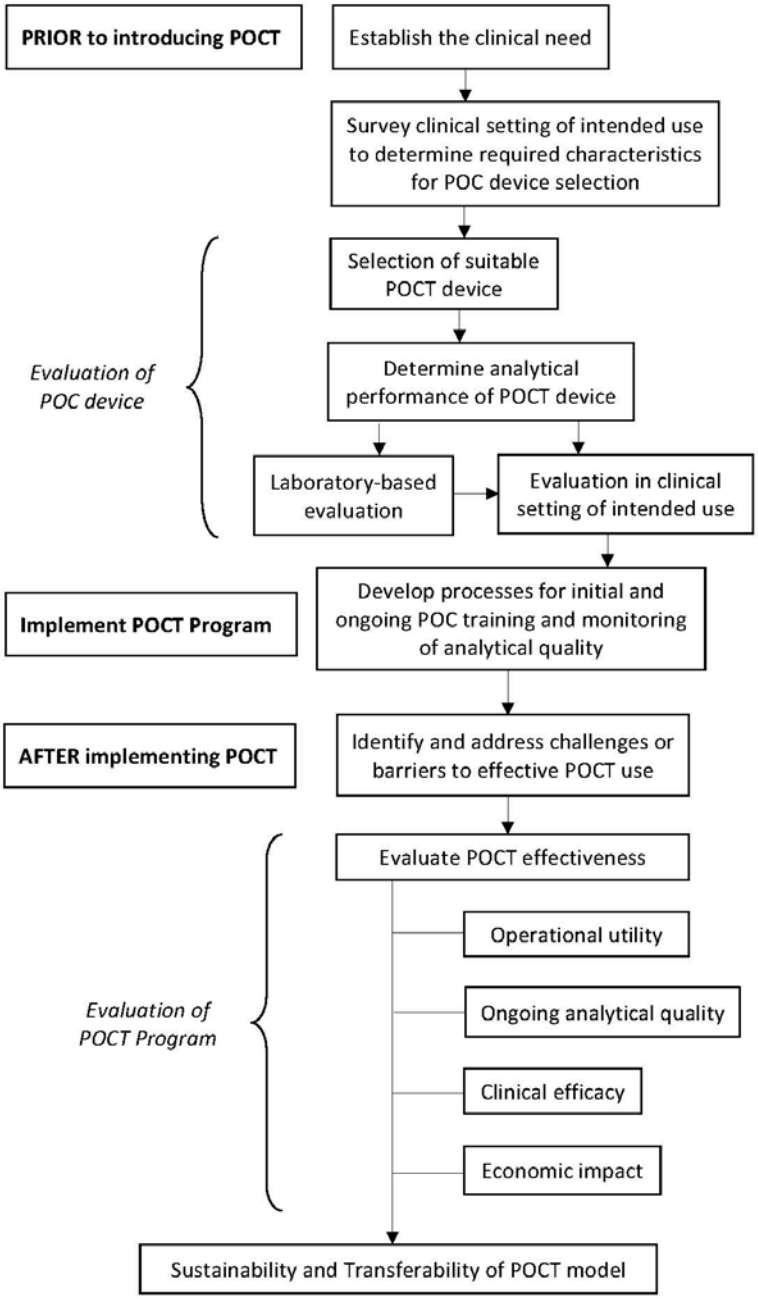

Figure 7 – Flow diagram of processes for establishing and managing a POCT service.

Prior to its introduction, the clinical need for a POCT service must first be established. There is little point in introducing a POC test if it does not address a specific or defined clinical need as per Figure 7. For example, in a community with a high prevalence of CKD, there is logical clinical need for a POCT program that detects renal disease early, with the aim of preventing or slowing progress of the disease. Next, the setting of intended use should be surveyed to determine the environmental conditions (such as the climate, lighting and physical space) and availability of resources (such as

access to power, water or internet connection), which may affect the operation of a POCT device. This survey will form a set of selection criteria to be used when selecting a suitable POCT device. For instance, a POCT device able to use battery power may be more suitable in a clinical setting where POCT is undertaken in a mobile context or in a location without access to power. In a hot and humid climate, a POCT device with a wide operating temperature range that is not affected by humid conditions may be required. The POCT device chosen for the service should then be evaluated to determine its analytical performance, either initially through a laboratory-based evaluation and then, ideally, in the clinical setting of intended use.

Once the POCT device is determined to be appropriate for the clinical setting and analytically sound, it can be implemented along with systems or processes developed for initial and ongoing operator training, and the continuous monitoring of analytical quality (see Figure 7). To ensure these processes are effective and appropriate, the intended POCT operator group should be surveyed to determine their level of knowledge and experience with POCT. This information can then be used to tailor POCT training and quality testing processes to suit the needs of POCT operators in the setting of intended use.

Once routine patient testing has commenced, the challenges and barriers for POCT should then be identified and strategies to address these issues should be introduced to ensure the POCT model is effective and can be sustainable in that setting. The POCT model should be continually evaluated in terms of its operational utility, ongoing analytical quality, clinical efficacy and economic impact (see Figure 7) to confirm model is delivering the defined benefits for which it was introduced. Ideally, if the POCT model developed is robust, then its principles and methods should be readily transferable to a new or different clinical setting. As such, translation of a POCT model to a new setting provides verification that the methods and processes developed are rigorous and sustainable.

Table 14 provides a summary of how each of the published studies included in this thesis addresses, and add new knowledge to, these different phases of POCT implementation, management and evaluation in rural and remote primary care settings.

Table 14 - Summary of how each published study addresses each stage of POCT implementation and evaluation

Stage of POCT implementation and evaluation	Title of Publication	How study addressed this stage of POCT implementation and evaluation
Establishing the clinical need for POCT	*1. Assessment of the Nova StatSensor whole blood point-of-care creatinine analyzer for the measurement of kidney function in screening for chronic kidney disease*	CKD is highly prevalent in Australia and internationally. There is a major clinical need for a POCT device that can be used to identify CKD risk in targeted populations. This study assessed the analytical quality of a new POCT device that had physical attributes to be useful for identifying CKD in at-risk populations.
	8. Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory.	Infections and sepsis are highly prevalent in remote Indigenous communities of Australia's NT. Due to significant delays in accessing laboratory services for a WBC count (a marker of infection), there is a major clinical need for a POCT device that can measure WBC and differential counts on-site with rapid turnaround of result. This study evaluated a new POCT device which addressed the clinical need for measuring WBC and differential count at the point of patient care.
Initial evaluation of analytical quality of POCT	*1. Assessment of the Nova StatSensor whole blood point-of-care creatinine analyzer for the measurement of kidney function in screening for chronic kidney disease*	This was the first evaluation in Australia of a newly released POCT device measuring creatinine using capillary sampling. The paper provides methods and results from an initial 'in-house' evaluation of this POCT device. Results were fed back to manufacturer to make improvements to the device.
	7. Assessment of a point-of-care device for measuring creatinine in a community screening program for chronic kidney disease	This study describes methods and results from a field evaluation of a POCT device at the site of its intended clinical use. The study re-evaluated the analytical quality of the POCT device measuring creatinine after the manufacturer had made modifications to the device.

	8. Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory	This study conducted the first evaluation in Australia of a new POCT device that could measure WBC and differential count at the point of patient care. The study was conducted in one of the most remote and challenging clinical settings in Australia, the remote NT.
Methods for implementation of POCT	*2. Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program.*	This was the first study to describe the implementation of a POCT program for acute and chronic care in a remote Australian primary health care setting. The study describes the design, implementation and preliminary results of a remote POCT network (NT POCT Program).
Evaluation of POCT ongoing analytical quality	*4. Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program*	Describes how the analytical quality of POCT has remained consistent across the first four years of the NT POCT Program.
	5. Point-of-care testing in Australia: Practical advantages and benefits of community resiliency for improving outcome	Provides results on ongoing analytical quality of POCT in the NT POCT Program for acute care tests across years 1 to 5 of the program.
	10. Immediate pathology results now available for all remote Northern Territorians	Demonstrates the stability of the analytical quality of POCT across a period when there was a doubling of the number of health services enrolled in NT POCT Program.
Evaluation of POCT operational effectiveness	*2. Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program.*	Provides initial results on the operational effectiveness of POCT in the NT POCT Program.
	4. Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program	Provides evidence for the acceptance of POCT in the remote health setting by assessing remote health professional satisfaction with POCT.
	10. Immediate pathology results now available for all remote Northern Territorians.	Describes how POCT has been successfully incorporated into all remote health services in the NT of Australia.

	6. Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care.	Provides results on the significant improvements in turnaround time for HbA1c POCT for diabetes management in remote NT compared to standard pathology laboratory practices.
	9. Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's Northern Territory.	Describes the acceptance of POC testing for INR into remote health services, as evidenced by increased number of INR tests and increased patient satisfaction with INR POCT.
Sustainability of POCT	*3. Management challenges for point-of-care coordinators in delivering training and competency programs*	Provides a summary of the challenges experienced by POCT coordinators and describes strategies (some developed by this author) to address challenges in delivering POCT training to remotely located POCT operators.
	4. Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program	Provides an assessment of the ongoing analytical quality, operational and clinical effectiveness of the NT POCT Program four years after its initial implementation; describes challenges for the program's sustainability.
	5. Point-of-care testing in Australia: Practical advantages and benefits of community resiliency for improving outcome	Provides examples of the strategies employed for POCT in rural and remote locations to increase community resilience and improve outcomes in the long-term.
	10. Immediate pathology results now available for all remote Northern Territorians	Demonstrates the stability of analytical quality, as well as operational and clinical effectiveness during a period of significant expansion of the NT POCT Program. Provides additional methods to ensure long-term sustainability of POCT in remote settings.
Evaluation of POCT clinical effectiveness	*4. Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program.*	Provides results on the clinical effectiveness of POCT through patient case studies where POCT produced a defined clinical benefit.
	6. Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care.	Provides results on the clinical effectiveness of POCT for HbA1c in remote communities of the NT, as evidenced by an improvement in glycaemic control post the introduction of POCT.

	9. Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's Northern Territory.	Demonstrates clinical effectiveness of INR POCT in the NT POCT Program through four patient case studies. Clinical benefits include greater time within therapeutic range, increased patient safety, and a more culturally appropriate method of monitoring anticoagulation therapy.
	10. Immediate pathology results now available for all remote Northern Territorians.	Demonstrates clinical effectiveness of POCT using a patient case study involving a child with dehydration where POCT for electrolytes produced a defined clinical benefit.
	11. Clinical Application of Point-of-Care Testing in the Remote Primary Health Care Setting.	Provides results on the ability of POCT to assist with the effective triaging of acutely ill patients. Also demonstrates increased patient safety through using POCT to diagnose and monitor patients in remote locations.
Evaluation of POCT cost effectiveness	*10. Immediate pathology results now available for all remote Northern Territorians.*	Provides results of a pilot evaluation of the cost benefit of POCT to rule out medical retrievals through on-site stabilisation of patients or through ruling out ACS using the troponin I POC test.
	13. Economic Evaluation of Point-of-Care Testing in the Remote Primary Health Care Setting of Australia's Northern Territory.	Using detailed economic modelling, this study is the first in Australia to provide evidence of the cost effectiveness of POCT in triaging emergency medical retrievals and stabilising patients on-site in the remote NT.
Translation of POCT	*12. Point-of-care testing facilitates screening and treatment for anaemia in women and children in rural Pakistan.*	Describes the translation of POCT methods and systems developed by this author to implement a community screening program using POCT for detection of anaemia in rural Pakistan.

3.2 Pre-Implementation of a POCT program

3.2.1 Establishing the clinical need for Point-of-Care Testing

The first stage of introducing a new intervention, such as a diagnostic test, is to complete a clinical needs assessment in the setting of intended use. Fitzmaurice et al. (1995) state that:

> *"the full potential of near patient testing can be exploited only by finding the clinical niches where its use would be most likely to influence practice beneficially".*

Current literature suggests the needs assessment should include the following questions (Freedman 1999; Shephard, M 2016b):

- Which patient group needs the test?
- Why is the POC test required?
- What is the problem with the current method of pathology service delivery by the local laboratory?
- What patient benefits will there be from having the immediate POC test result(s) available?

Two studies included in this thesis provided an evaluation of a POCT device anticipated to address clinical needs for disease states with high regional/global prevalence (namely CKD and infection). The respective references for each of these articles are provided below.

> Shephard, M, Peake, M, Corso, O, Shephard, A, Mazzachi, **B, Spaeth**, B, Barbara, J & Mathew, T 2010, 'Assessment of the Nova StatSensor whole blood point-of-care creatinine analyzer for the measurement of kidney function in screening for chronic kidney disease', *Clinical Chemistry and Laboratory Medicine*, vol. 48, no. 8, pp. 1113-119.
>
> **Spaeth, B**, Shephard, M, McCormack, B & Sinclair, G 2015, 'Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory', *Pathology*, vol. 47, no. 1, pp. 91-5.

The first study evaluated a POCT device which could be used to screen populations at high risk for CKD, a condition in which symptoms do not usually appear until kidney damage is well advanced

(Australian Institute of Health and Welfare 2016; Berns 2014). The study provided the first evaluation in Australia of a newly developed POCT device - the Nova StatSensor (Roche Diagnostics, Australia) - for measuring whole blood creatinine by capillary/finger-stick sampling. An additional feature of the POCT device was that it uses the creatinine result to provide an automatic calculation of estimated glomerular filtration rate (eGFR) using the modification of diet in renal disease (MDRD) equation (factor 186) (Peake & Whiting 2006). The calculation of eGFR is used to stage the level of CKD according to the internationally accepted scale (Levey et al. 2005). The ability to screen and identify those at risk enables earlier detection and treatment of the disease, which can potentially limit its progression to end-stage kidney disease (Berns 2014; Mathew & Corso 2009). Previous studies performed in collaboration with Kidney Health Australia had identified that no POCT device existed to screen for CKD using a capillary sample (Shephard, A et al. 2011). CKD is known to be a global health problem (El Nahas & Bello 2005; Levey et al. 2005; Mills et al. 2015). Within Australia, the rates of CKD are particularly high in rural farming areas and remote Indigenous communities (Australian Institute of Health and Welfare 2016). Therefore, if the analytical quality of this POCT device was determined to be suitable, it was anticipated to have national and international impact in providing a rapid and accurate means to screen for CKD.

The second study evaluated a POCT device providing a total and 5-part differential white blood cell (WBC) count using a capillary or venous sample to detect and manage sepsis and a range of acute infections. The HemoCue WBC DIFF (Radiometer Pacific, Australia) device uses novel imaging system technology to differentiate and count WBCs (Lindberg et al. 2014). This author, in consultation with a senior medical practitioners from the NT, identified an unmet clinical need relating to the diagnosis and management of infection in NT remote primary health centres. This clinical need was supported by several factors:

1) the most frequently requested pathology test is a full blood examination (FBE) which includes a 5-part differential WBC count (Britt et al. 2012);

2) a high proportion of FBE pathology reports were being returned from the local pathology laboratory in the NT with comments indicating the blood sample had taken too long to reach the laboratory causing the WBC results to be unreliable and therefore not reported;

3) the high rates of sepsis and high prevalence of infectious disease in the NT (Davis et al. 2011; O'Grady, Torzillo & Chang 2010; Quinn, Massey & Speare 2015); and

4) the high number of evacuations in the NT due to respiratory, gastrointestinal, skin and septic infections (Barker & Ross 2014; Parker 2015).

Based on this evidence, an evaluation of analytical quality of this POCT device was conducted in the setting of its intended use (a very remote health facility in the NT).

Once the clinical need for POCT has been established, several processes must be considered prior to implementation of a POCT program. The following sections describe these processes.

3.2.2 Review of clinical setting to determine factors affecting POCT device selection

Once a clinical need is established for POCT, additional operational aspects should be considered to determine the most appropriate POCT device for the chosen setting. The operational considerations should include: who will perform the POC test; how many staff are available; what is the level of education of the available staff members; and what is the preferred method of sample collection (Freedman 1999). The level of infrastructure available in the location to support the use of POCT must also be considered, such as power, water, bench space and availability of refrigeration (Pearson 2004). Environmental factors such as temperature, humidity and atmospheric pressure should also enter into consideration as these may also affect the choice of POCT device (Louie et al. 2002).

3.2.3 Selection of suitable POCT device

The next stage should involve the selection of a POCT device suited to the clinical setting. The selection process should first be based on which POCT device meets all essential criteria (such as POCT devices measuring creatinine using a capillary blood sample). If multiple POCT devices are identified, the device with the most desirable characteristics can be selected (Shephard, M 2016c). Desirable characteristics may include the ease of use of the POCT device, the shortest time to test result(s), or the POCT device with consumables not requiring refrigeration for example.

For example, the Nova StatSensor device was selected as it was only POCT device available at the time the study was conducted to measure creatinine on a capillary sample. The additional desirable characteristics for screening purposes included the ability of the POCT device to work off battery power for the ease of movability as well as the device's ease of use for non-technical trained staff. While several POCT devices providing a WBC count were available, the HemoCue WBC DIFF device was the only POCT device to work off battery power and able to use a capillary sample. In addition,

the HemoCue WBC DIFF was the smallest POCT device available, which was a major consideration due to the limited bench space available at the remote health services.

Once a POCT device has been chosen, the next stage of the selection process should involve an evaluation of analytical quality to determine if the POCT device has suitable accuracy for the intended clinical application (Linnet & Boyd 2012).

3.2.4 Determining the analytical performance of a POCT device

Burtis, Ashwood and Burns (2012) state that assessing the analytical robustness of a POC test against the current or usual method of obtaining pathology results is a fundamental step in the evaluation POCT technology. As such, evaluation of analytical performance is a key component of POCT pre-implementation, as it is imperative that POC test results are of an equivalent standard to laboratory test results. This is to ensure patient safety is upheld and the POC test results enable appropriate clinical decisions on patient treatment and management to be made.

The POCT device manufacturer will commonly provide data on POCT device performance characteristics, along with the device specifications. However, manufacturer-led device evaluations generally involve a small number of samples tested under tightly controlled conditions with tests conducted by highly trained laboratory or scientific personnel (Burtis, Ashwood & Burns 2012). Therefore, manufacturer performance data usually reflects optimal performance and is unlikely to be achievable in routine field use. Performance data from independent POCT device evaluations are therefore a better source of such data, with results from evaluation studies conducted in settings identical or similar to its intended use providing the most reliable estimation of true POCT device performance (Drain et al 2014; Yip et al 2018). If no suitable evaluations exist, an independent evaluation should be conducted (Shephard, M 2016b).

Drain et al. (2014) state the following in relation to the use of POCT in low-resource settings:

> *"an evaluation of POC test accuracy compared to the laboratory in a controlled environment is not sufficient and that assessments of POC tests should be comprehensive and include accuracy in the specific clinical scenario of intended use".*

Three of the author's studies included in this thesis are evaluations of POCT device analytical performance. The first study provided the initial 'in-house' evaluation of a newly released POCT

device. The second study examined the analytical quality of the same POCT device, after modification had been made to its design based on the results of the first study, with the device evaluated as part of a screening program conducted in a rural farming town (i.e. at the site of intended use). The third study provided an analytical evaluation of a POCT device in a remote NT health facility (again at the site of intended use). The full citations for these studies are provided below in the order in which they were conducted.

> Shephard, M, Peake, M, Corso, O, Shephard, A, Mazzachi, B, **Spaeth, B**, Barbara, J & Mathew, T 2010, 'Assessment of the Nova StatSensor whole blood point-of-care creatinine analyzer for the measurement of kidney function in screening for chronic kidney disease', *Clinical Chemistry and Laboratory Medicine*, vol. 48, no. 8, pp. 1113-119.
>
> **Spaeth, B**, Shephard, A, Shephard, M & Mathew, T 2015, 'Assessment of a point-of-care device for measuring creatinine in a community screening program for chronic kidney disease', *Medical Research Archives*, no. 3, pp. 1-6.
>
> **Spaeth, B**, Shephard, M, McCormack, B & Sinclair, G 2015, 'Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory', *Pathology*, vol. 47, no. 1, pp. 91-5.

In the first study, the evaluation results (as shown in the paper) indicated the POCT device (Nova StatSensor) had inadequate accuracy due to a strong negative bias, and the imprecision of the device did not meet profession-derived analytical goals (with all imprecision studies conducted by the author) (Shephard, M et al. 2010). It was therefore recommended the POCT device be recalibrated to the IDMS-aligned laboratory method to address the significant bias issue.

Subsequent to the manufacturer making adjustments to the Nova StatSensor device, a repeat evaluation of analytical quality formed the second analytical evaluation study presented in this thesis (Spaeth, Shephard, Shephard, et al. 2015). This time, the evaluation of the StatSensor device was conducted as part of a screening program conducted by Kidney Health Australia in a rural farming community and represented the first study to evaluate this POCT device in a rural primary care setting. Results indicated that the POCT device again correlated poorly to the laboratory method and the between-device imprecision (again conducted by the author) had not improved

since the initial evaluation. This study concluded that the search remained for a suitable POCT device for screening CKD using a capillary sample.

Subsequent to the first evaluation of the StatSensor, the National Institute for Health Research (NIHR) released a report in 2014 summarising all commercially available POCT devices testing for CKD, and concluded that the Nova StatSensor was the only device available to measure creatinine using a small capillary sample. The NIHR report referenced the initial study included in this thesis as the first evaluation of the Nova StatSensor device (National Institute for Health Research 2014).

The two studies of the Nova StatSensor device identified a significant gap in the POCT literature in regards to POC tests for screening for CKD using a capillary whole blood sample. Shephard, M and Mathew (2016) recently stated the following in relation to POC device availability for screening CKD:

> *"With the global prevalence of CDK increasing, analytically sounds POCT methods for identifying CKD risk are needed. POCT creatinine measurement also has a role for identifying patients at risk of CIN* [contrast induced nephropathy]*. A POCT device fit-for-purpose in these settings requires capillary sampling, fast result turnaround automatic eGFR calculation, and sound analytical performance to correctly categorise risk of CKD and CIN. Currently no device fulfils these requirements."*

The third study evaluating the HemoCue WBC DIFF device measuring total and 5-part differential WBCs was the first of its type in Australia (Spaeth, Shephard, McCormack, et al. 2015). Results of the study demonstrated that the device was able to achieve appropriate analytical quality in this remote and challenging environment. The study also determined qualitatively that the POCT device was easy to use by non-technical staff and it suited the intended clinical application by enabling the more rapid initiation of treatment for infections. An additional operational benefit regarding the timeliness of WBC test was also identified in the study, whereby 11% of comparative pathology laboratory results did not reach the laboratory in time for accurate measurement, with results being reported as 'unreliable' or 'not reported'. The study concluded that the novel POCT device was both analytically and operationally effective and would have significant clinical application in the remote primary health care setting.

At the time of this Australian study, only five previous studies in other countries had evaluated the analytical quality of the HemoCue WBC DIFF device (Carlsson 2011; Hockum, Johnsson & Reed 2014;

Kok et al. 2015; Lindberg et al. 2014; Russcher, Van Deursen & de Jonge 2013), with studies concluding the HemoCue WBC DIFF device had acceptable analytical quality. However, four of the five studies evaluated the device in a laboratory setting with trained laboratory technicians conducting testing. The remaining study evaluated the HemoCue WBC DIFF device at three sites, two of which were in a laboratory setting with trained laboratory personnel, and the third site a physicians' office with untrained nurses performing the tests (Lindberg et al. 2014). However, in the evaluation conducted in the physician's office, only 31 samples were collected for comparison with the laboratory method. A minimum of 40 patient samples is generally accepted as the minimum number required for a comparison study (Shephard, M 2016c). The study conducted by this author was therefore the first to evaluate the HemoCue WBC DIFF in a remotely located primary health care setting and in a challenging environment.

As demonstrated by the literature review, very few POCT device evaluations have occurred in rural or remote settings. Of these, most were for tests for either chronic diseases such as diabetes and coagulation disorders or for STIs. The literature review did not identify any studies conducted in rural or remote locations that examined the analytical quality of POCT devices for creatinine or WBC, thus, the evaluations conducted by the author on these two tests have made new and original contributions to knowledge in this area.

These three studies highlight the importance of conducting an evaluation study prior to implementation of a POCT device. As demonstrated, not all POCT devices will have sufficient analytical quality for their intended purpose. If the analytical performance of the POCT device is deemed acceptable, it may be implemented for routine use.

3.3 Implementation of a POCT program

Many guidelines exist that provide recommendations for key systems to be put in place when implementing a POCT device or program, such as for training and quality processes. Guidelines for the routine conduct of POCT now exist in most developed countries. Shephard, M (2016b) provides a recent summary of the guidelines for POCT available internationally as shown in Table 15.

Table 15 – Examples of international organisations that have published guidelines on establishing and maintaining a POCT service

Country	Organisation	Title	Year of Publication	Reference
Australia	National Pathology Accreditation Advisory Council	Guidelines for Point of Care Testing	2015	(National Pathology Accreditation Advisory Council 2015)
Canada	Ministry of Health and Long-Term Care	Policies, procedures and quality assurance for point-of-care HIV testing in Ontario.	2008	(Ministry of Health and Long-Term Care 2008)
Germany	German Society for Clinical Chemistry	Recommendations of the German working group on medical laboratory testing (AML) on the introduction and quality assurance procedures for point-of-care testing (POCT) in hospitals.	1999	(German Society for Clinical Chemistry 1999)
Ireland	Joint Committee for POCT in primary care and community care	Guidelines for safe and effective management and use of POCT in primary and community care.	2009	(Joint Committee for POCT in Primary Care And Community Care 2009)
Netherlands	Dutch College of Practitioners, Dutch College of Clinical Chemists, Dutch College of Microbiologists and Association of Laboratories	Point-of-care testing (POCT) in de huisartsenzorg.	2015	(Hopstaken et al 2015)
Spain	Spanish Society of Clinical Biochemistry and Molecular Pathology	Proposed guidelines for point-of-care testing services in Spain.	2009	(Spanish Society of Clinical Biochemistry and Molecular Pathology 2009)
United	Medicines and Healthcare	Management and use of IVD point of care test	2013	(Medicines and Healthcare

Kingdom	Products Regulatory Agency	devices.		Products Regulatory Agency 2013)
	British Society for Haematology	Guidelines for point-of-care testing: haematology.	2008	(British Society for Haematology 2008)
United States of America	The National Academy of Clinical Biochemistry	Evidence-based practice for point-of-care testing.	2007	(Nichols et al. 2007)
	Department of Health and Human Services Centers for Disease Control and Prevention	Good laboratory practices for waived testing sites.	2005	(Department of Health and Human Services Centres for Disease Control and Prevention 2005)

Note. Amended from 'Principles of establishing and managing a point-of-care testing service' (Shephard, M 2016b).

The World Health Organization (WHO) has also produced guidelines for POCT for many disease states of global health concern which are generally aimed at low resource settings such under-developed countries (World Health Organization 2011), notably for the detection and management of malaria using RDTs (Bell & Peeling 2006).

As previously discussed, the author of this thesis has been the Coordinator of the NT POCT Program for the past eight years. Part of this role has involved assessing the outcomes associated with the initial implementation of POCT in this setting, which were documented in the following published paper:

> Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Loudon, J, Rigby, J & Daniel, V 2012, 'Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program', *Australian Journal of Rural Health*, vol. 20, no. 1, pp. 16-21.

This study described the methods used, and assessed the preliminary results for, the implementation of POCT for both acute and chronic disease in the POCT network established for

remote primary health care facilities of the NT. Components of POCT implementation for these very remote primary health care services included:

- A governance structure and POCT Management Committee
- An operator training and competency assessment process
- A surveillance system to monitor analytical quality
- A connectivity system for POCT devices to send patient and quality testing results to a central data station
- A process for POCT consumable ordering and distribution.

The following section will discuss the ways in which these components were specifically tailored by this author to meet the needs of the health services in the NT.

A NT POCT Management Committee was established to provide overall governance and oversight to the Program. The Management Committee comprised representatives (with different skills sets and attributes) from ICPOCT, the NT DoH and a representative of the Aboriginal Community Controlled Health Services (ACCHS) group. A summary of the governance structure for the NT POCT Management Committee is provided in a later study conducted by this author titled *Immediate pathology results now available for all remote Northern Territorians* and is provided on page 339 of this thesis. The NT POCT Management Committee communicated regularly with the health centre managers and district managers at each remote health service. This allowed effective communication with remotely located health professional staff and enabled any issues to be identified and resolved quickly. On-call rural medical practitioners (RMPs) and the clinical advisor on the Management Committee also provided overarching clinical support to remote health professional staff in interpreting POC test results and subsequent patient management plans.

POCT training and competency assessment systems were designed with a range of flexible training options and resources both in hard-copy and available online. This was to improve access to training and accommodate for the high rates of staff turnover, the latter being one of the main challenges for POCT in this remote setting.

A connectivity system between the POCT devices and a central data station was established to enable regular monitoring and surveillance of POCT use and rapid identification of any issues (by the POC Coordinator, this author) with POCT at the remote health services. The connectivity system also enabled the POC Coordinator (this author) to generate monthly reports for the Management

Committee to ensure that key performance indicators for the Program (as outlined in the introduction to this thesis) were regularly monitored and assessed. This author has provided additional contributions to literature in regards to POCT connectivity for managing remote POCT networks in the form of an invited co-authored book chapter titled *Use of connectivity for managing point-of-care testing results* (McAteer et al. 2016). The section subtitled *Role of the POCT Coordinator in Connectivity* is written solely by this author and provides methods for surveillance of POCT data and templates to feedback information on POCT use to health services and at the management level (see Appendix A).

The ordering and transport of POCT consumables was organised through two main centres within the NT; Darwin in the Top End of the NT, and Alice Springs in Central Australia. This method allowed large batches of POCT consumables, with relatively short expiration dates to be ordered and delivered from the POCT distributers to a central location where they could then be divided in to smaller numbers for delivery to the small remote health services to prevent consumable wastage.

This study also provided initial results to highlight the effectiveness of the NT POCT Program. In the first year of the Program, the number of POC tests increased steadily with a low error rate. In addition, more than 150 remote health professionals completed POCT training across the 33 health services, a significant proportion considering many health services have less than five staff members on site. Operational effectiveness and acceptance was also assessed through a survey of health professionals to determine their satisfaction with the POCT device and the coordination of the NT POCT Program. The results of the satisfaction survey indicated a statistically significant ($P<0.001$) increase in satisfaction with the pathology service post implementation of POCT. The suitability of the training methods developed for the Program was confirmed by 90% of respondents indicating the level of training and support services were appropriate. The effectiveness of the governance structure was confirmed with 90% of respondents stating the level of support provided for POCT was appropriate. The survey also provided initial evidence for the analytical and clinical effectiveness of the Program, with 86% of respondents indicating they felt confident in the accuracy of the POC test results, and 84% indicating POCT had assisted in stabilising acutely ill patients. The modest response rate of 31% (39 of 127) to the survey was in part due to the high level of staff turnover in this setting, as evidenced by 33% of staff initially trained having left the health service during the first year of the Program.

As identified by the literature review in this thesis, very few studies have provided detailed methods for, or results on, the implementation of POCT within rural or remote settings. The only studies to discuss the implementation of POCT in detail were those from the POCT in GP Trial and the QAAMS Program (Shephard, M & Gill 2003; Shephard, M & Gill 2010; Shephard, M, Shephard, et al. 2009; Tirimacco et al. 2011). However, the POCT in GP Trial and QAAMS Program only included POC tests for chronic disease management and did not include acute POCT. One additional study provided detailed methods for implementation of an EQA program for POCT for HIV and syphilis in Tanzania (Smit et al. 2013). This study included information on the transport of specimens, training and methods to minimise workload for the busy health care workers. However, this study focussed on POCT for STIs in developing countries and included information on only the implementation of EQA, which is just one aspect to be considered when implementing POCT. Therefore, the 2012 study co-written and conducted by this author is the first to provide the detailed methods as well as results on the implementation of POCT in a remote setting, thus providing an original contribution to knowledge in this field.

After a POCT program or model has been successfully implemented, its effectiveness should be regularly and continually assessed to ensure it provides and continues to deliver the benefits for which it was initially introduced.

3.4 Evaluating the effectiveness of a POCT model

Measures of POCT program effectiveness should include the on-going assessment of the following:

- Operational utility
- Analytical quality
- Clinical efficacy
- Cost effectiveness/economic impact

These effectiveness measures should be assessed after initial implementation and also across the life of a POCT program to ensure its long-term effectiveness. The results and outcomes from the studies included in this thesis will be discussed separately according to how they address one or more of these POCT effectiveness measures.

3.4.1 Assessment of Operational Effectiveness

The assessment of operational effectiveness includes measures of how well POCT is incorporated into the clinical setting, and how POCT improves the efficiency of health service delivery. Several studies included in this thesis provide evidence for the operational effectiveness of the remote NT POCT Program. These include (in chronological order):

> Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Loudon, J, Rigby, J & Daniel, V 2012, 'Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program', *Australian Journal of Rural Health*, vol. 20, pp. 16-21.
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> Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Lingwood, A, Loudon, J, Rigby, J & Daniel, V 2014, 'Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program', *Point of Care*, vol. 13, no. 1, pp. 6-11.
>
> **Spaeth, B**, Shephard, M, Auld, M & Omond, R 2017, 'Immediate pathology results now available for all remote Northern Territorians', in L Coleman (ed.), *14th National Rural Health Conference*, Cairns, Queensland.

These studies build upon one another to provide results and key milestones across the first seven years of the NT POCT Program. For operational effectiveness, the positive integration of POCT into the remote primary health services of the NT is evidenced by an increased number of POC tests being conducted across the life of the Program. The initial study in 2012 reported a total of 2,290 POC tests (monthly average = 191) in the first year, with the number tests increasing from less than 100 in the first month to almost 300 tests in the 12th month. The 2014 study reported a total of 6,837 POC tests (monthly average = 570) in year four. Finally, the POCT study in 2017 reported a monthly average of 876 POC tests (estimated annual total =10,500) before and 1,146 POC tests (estimated annual total =13,750) after the rollout of i-STAT devices to all health services in the remote NT occurred across 2015.

Evidence for the positive acceptance of the NT POCT Program is also supported by the increasing number of health services enrolled in the Program, the increasing number of staff accessing POCT training and high levels of satisfaction with POCT reported by remote health professional staff. The number of health services participating in the NT POCT Program increased from 33 in year one to 36 by the fourth year; a small but noteworthy increase as the remote health services had to source outside funding to purchase the POCT device. In the first year of the NT POCT Program, 164 staff

completed POCT training across 33 health services. In each of the subsequent years, 131, 73 and 138 new trainees completed POCT training. In 2015, the i-STAT rollout saw the Program double in size from 36 sites to include all 72 remote health services in the NT. The number of new POCT trainees increased significantly to 337 new POCT operators within the first six months of the rollout; more than double the number of trainees in the first year of the Program. Now in 2018, the number of remote health professionals trained as POCT operators in the NT has reached a total of more than 1,500. This represents a significant contribution to the workforce capacity in this setting, which has, in turn, assisted in strengthening the resilience of the remote communities.

Health professional satisfaction with the NT POCT Program was demonstrated through three surveys conducted across the initial seven years of the Program, all of which were conducted and analysed by this author. The methods and results of the first survey were reported in the initial implementation study (Shephard, M et al. 2012a) with further results included in the second study on sustainability (Shephard, M, Spaeth, Mazzachi, et al. 2014). The initial survey conducted in 2009 aimed to assess the satisfaction with pathology testing before and after the NT POCT Program was implemented. As mentioned previously, this survey also assessed satisfaction with the level of support and the quality of the training resources provided for the Program. Responses indicated the greatest increase in satisfaction was for the timeliness of POCT compared to the laboratory method. Regarding satisfaction with POCT training, more than 95% of respondents indicated the training manual was appropriate and instructive, and greater than 90% understood the need to perform quality testing after attending a training session. Further demonstrating the positive uptake of POCT, more than 80% of respondents were confident and enjoyed conducting testing on the POCT device. In terms of patient acceptance, more than 70% of health professionals indicated patients were satisfied with the POCT service. A further 20% of respondents indicated they were unsure if patients were satisfied with the POCT service, highlighting a future direction for research to investigate patient satisfaction with the NT POCT Program.

Results of the second survey assessing health service manager satisfaction with the POCT Feedback Reports were included in the most recent study (Spaeth et al. 2017). This survey and the POCT Feedback reports will be discussed separately in the section related to the sustainability of a POCT program but, again, feedback was overwhelmingly positive for POCT.

The third survey assessed satisfaction with POCT training during the rollout of the NT POCT Program across 2015 and 2016, with results provided in the most recent study (Spaeth et al. 2017). This

survey was conducted as the POC Coordinator (this author) believed the significant increase in trainees and training sessions during the expansion of POCT may affect the quality of the training with the increasingly high workloads of POCT resource staff. Similar to the initial survey, a moderate response rate of approximately one third (54 out of 158) was achieved; again, this was attributed to the level of staff turnover at the remote health services. A high level of satisfaction remained in regard to the POCT training sessions, resources and training instructors. Greater than 90% of respondents indicated they had a better understanding of the POCT device after the training session. This was a particularly noteworthy finding as many health professional staff stated they had used the i-STAT device previously in other states of Australia. These results validated that the methods developed for the NT POCT Program were robust enough to withstand a significant expansion of the program, even within this remote and challenging environment.

A further two studies conducted and co-authored by this author provide additional results on POCT operational effectiveness of specific POC tests in the remote NT. The full citation for each of these studies is provided below:

> **Spaeth, B**, Shephard, M & Schatz, S 2014, 'Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care', *Rural and Remote Health*, vol. 14, no. 4, p. 2849.
>
> **Spaeth, B** & Shephard, M 2016, 'Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's Northern Territory', *Point of Care*, vol. 15, no. 1, pp. 30-4.

The first study investigated the clinical and operational effect of POCT for HbA1c in remote Indigenous communities within the NT POCT Program (Spaeth, Shephard & Schatz 2014). As outlined in the study, operational effectiveness was measured through comparing the timeliness of POCT for HbA1c to the laboratory method using a 'before and after' cohort study design. Timeliness was assessed in terms of HbA1c result turnaround time (TAT) and time taken for the HbA1c result to be discussed with the patient (time to consultation) both when the laboratory was used and after POCT was introduced. As outlined in the study, the average HbA1c result TAT for POCT was significantly shorter (6 minutes) than the TAT of the laboratory (42 hours). The time to consultation was also significantly reduced from an average of 24 days when the laboratory was used to less than 15 minutes in all but three cases after POCT was introduced. In the remaining three cases, the time

to consultation of POC HbA1c result was still earlier than the average laboratory time to consultation of HbA1c results.

As highlighted in the introduction of this thesis, information on laboratory TAT is limited. This was further validated by the literature review of this thesis which identified only one study which compared the patient waiting time for glucose and HbA1c by POCT to the waiting time for patients managed by the hospital in rural Thailand (Kulrattanamaneeporn, Wongboonsin & Kost 2009). Therefore, the study by this author is the first to provide quantitative data comparing the TAT of POCT versus laboratory testing in Australia in a remote location. This study also provides novel results comparing the time to consultation of pathology results conducted by POCT versus the laboratory. Outcomes related to the clinical effectiveness of HbA1c POCT in this study will be discussed separately within the section on assessment of POCT clinical utility.

The second study provides results on the positive acceptance of INR POCT conducted within the NT POCT Program (Spaeth & Shephard 2016), both through an increasing volume of INR testing within the Program over time and four patient case studies which highlight the clinical as well as operational and cultural effectiveness of INR POCT in this remote setting. The patient case studies demonstrate how INR POCT enabled the coagulation status of a patient to be monitored in the remote community, either at their local health facility or in their home. Prior to POCT being available, patients either had to travel or relocate to the nearest town with a pathology laboratory.

As identified in the literature review, the only studies to investigate the use of POCT for INR in rural or remote locations were those from the POCT in GP Trial, however, the POCT in GP Trial did not differentiate outcomes between urban, rural and remote locations. Also, the POCT in GP Trial focussed on POCT clinical utility rather than operational impact and did not provide individual patient case studies. Therefore, the study presented by this author is the first to provide results on operational effectiveness of POCT for INR specifically in remote settings. Again, the outcomes of clinical effectiveness in this study will be discussed separately.

3.4.2 Assessment of Ongoing Analytical Quality

Assessing ongoing analytical effectiveness is essential to ensuring that POC test results remain safe and appropriate for clinical interpretation across the life of the POCT device and a POCT program. As such, most POCT guidelines recommend analytical quality be monitored and assessed regularly through quality testing to ensure POC test results are able to meet benchmarks for analytical quality;

a task which is generally the responsibility of the POC Coordinator. Three co-authored studies included in this thesis provide the methods and results for monitoring ongoing analytical quality of POCT (conducted by this author) within the remote NT POCT Program. The full citation for these studies is provided below in chronological order:

> Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Lingwood, A, Loudon, J, Rigby, J & Daniel, V 2014, 'Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program', *Point of Care*, vol. 13, no. 1, pp. 6-11.
>
> Shephard, M, **Spaeth, B**, Motta, L & Shephard, A 2014, 'Point-of-care testing in Australia: Practical advantages and benefits of community resiliency for improving outcomes.', in G Kost & C Curtis (eds), *Global Point-of-Care - Strategies for Disasters, Complex Emergencies, and Public Health Resilience*, American Association of Clinical Chemistry Press, Washington DC, pp. 527-35.
>
> **Spaeth, B**, Shephard, M, Auld, M & Omond, R 2017, 'Immediate pathology results now available for all remote Northern Territorians', in L Coleman (ed.), *14th National Rural Health Conference*, Cairns, Queensland.

The first study provides results for the ongoing analytical quality for years one to four of the NT POCT Program with the methods and processes for conducting and recording quality control results also provided (Shephard, M, Spaeth, Mazzachi, et al. 2014). As outlined by this study, the analytical quality of the i-STAT device was comparable to that obtained by laboratory analysers; a novel and significant finding due to the challenging conditions experienced in the remote NT and the fact that POCT is conducted by non-technically trained personnel.

The next study provides a summary of ongoing analytical quality within the NT POCT Program across the first five years of the program, this time focussing specifically on POC tests for acute care (Shephard, M, Spaeth, Motta, et al. 2014). Again, this study demonstrates the acceptable long-term analytical quality of acute care tests conducted within the NT POCT Program. This study also highlighted that Remote Area Nurses and AHWs were capable of conducting POCT to a high analytical standard.

The third study provides results on analytical quality of POCT in the NT POCT Program across a period of significant expansion POCT services (Spaeth et al. 2017). During this rollout of the i-STAT device,

the analytical quality of POC test results was closely monitored to ensure the high level of quality was maintained. As outlined in the study, the analytical quality of the POC test results remained acceptable despite a significant expansion of POCT in this remote and challenging setting and many newly trained remote health professionals using the i-STAT device.

It is important to note that quality control testing has been the core element of quality surveillance and that EQA or proficiency testing has only recently been introduced to the NT POCT Program. A mentioned in the introduction, EQA was not initially included in the NT POCT Program due to the high costs of this material as limited funds were available for POCT in the remote NT. EQA testing has now been introduced due to the NT DoH recontracted the Flinders University ICPOCT in 2016 with an increased budget to include this material.

Collectively, these three studies demonstrate the rigorous quality testing framework developed by this author has ensured the analytical quality of POCT in the NT Program has been sustained across almost ten years of testing including a period of significant expansion of POCT in 2015-2016.

As evidenced by the literature review, very few studies report on the methods or results for monitoring ongoing analytical quality post initial implementation of POCT for acute care in remote primary health care settings. Therefore, these studies provide the first evidence for acute POC tests being able to achieve and maintain high levels of analytical quality in remote primary health care settings. This is essential criteria for POCT, particularly for acute care tests, to ensure results are accurate, precise and reliable for patient management.

3.4.3 Assessment of Clinical Effectiveness

The primary aim of POCT is to improve patient outcomes through delivering rapid pathology results at the site of patient care which, if acted upon clinically in a timely manner, can enable immediate changes to clinical management. As such, the WHO states that medical devices should be appropriate, accessible and improve patient care (World Health Organization 2011). Anecdotally, POCT is thought to improve patient outcomes through delivering rapid diagnostic test results which then lead to rapid changes in patient treatment and management. However, evidence for the clinical effectiveness of POCT is equivocal. This was highlighted in the literature, where the POCT in GP Trial provided the most comprehensive assessment of POCT in GP settings in urban, rural and remote locations, and found the clinical effectiveness of POCT was variable with medication

compliance improved for all, and therapeutic control improved for only some, of the chronic diseases investigated.

The literature review also highlighted that no previous studies had investigated the use of POCT for acute care in a rural or remote primary health care settings. Three studies included in this thesis aimed to address this gap in knowledge. A further two studies provide evidence for the clinical effectiveness of POC tests for chronic diseases specifically in remote locations. This author was the primary author on four of the five co-authored studies and developed the methods and provided most of the data analysis for all five studies. The full citation for these studies is provided below:

> Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Lingwood, A, Loudon, J, Rigby, J & Daniel, V 2014, 'Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program', *Point of Care*, vol. 13, no. 1, pp. 6-11.
>
> **Spaeth, B**, Shephard, M & Schatz, S 2014, 'Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care', *Rural and Remote Health*, vol. 14, no. 4, p. 2849.
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> **Spaeth, B** & Shephard, M 2016, 'Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's Northern Territory', *Point of Care*, vol. 15, no. 1, pp. 30-4.
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> **Spaeth, B**, Shephard, M, Auld, M & Omond, R 2017, 'Immediate pathology results now available for all remote Northern Territorians', in L Coleman (ed.), *14th National Rural Health Conference*, Cairns, Queensland.
>
> **Spaeth, B**, Shephard, M & Omond, R 2017, 'Clinical Application of Point-of-Care Testing in the Remote Primary Health Care Setting', *Quality in Primary Care*, vol. 25, no. 3, pp. 164-75.

The first 2014 study highlighted the clinical effectiveness of the NT POCT Program through describing two patient case studies, one acute and one chronic, where POCT provided a defined clinical benefit to the patient (Shephard, M, Spaeth, Mazzachi, et al. 2014). The acute case described how a POC test for Troponin I identified a non-ST elevation myocardial infarction (non-STEMI) in an elderly male tourist, enabling the immediate initiation of treatment and transfer to a tertiary hospital. The second case described how an Indigenous woman with a history of rheumatic heart disease (RHD) was able to have her coagulation status closely monitored using POCT for INR. Prior

to the availability of POCT, this patient's INR was not monitored as regularly as it should have been as INR testing was only available by the laboratory which was over 200kms from her remote community.

A further study audited HbA1c testing conducted for patients with established diabetes both before and after POCT was introduced in the remote NT (Spaeth, Shephard & Schatz 2014). As discussed earlier, this study also compared the timeliness of HbA1c testing conducted by the laboratory and by POCT in a remote primary health care setting. The clinical effectiveness of POC HbA1c testing was demonstrated through a significant improvement in glycaemic control in patients with established diabetes (reduction in HbA1c of 2.7%) after the introduction of POCT ($p<0.001$). POC HbA1c tests were also conducted much closer to the recommended frequency (3 monthly testing) for patients with poorly controlled diabetes.

The next study provides evidence for the clinical (and operational) effectiveness of INR POCT within the NT POCT Program through four patient case studies (Spaeth & Shephard 2016). The first case study described how INR POCT improved a patient's time within therapeutic range (TTR) through increasing the patient's self-motivation as INR tests could now be conducted in a timelier manner and enable immediate changes to treatment compared to when the laboratory was used. The second case highlighted how INR POCT provided rapid identification of a patient's widely fluctuating INR results, enabled her coagulation status to be stabilised within the recomeneded therapeutic range and minimised the patient's risk of adverse events such as a stoke or internal bleeding. The third case described how INR POCT enabled an Indigenous man with RHD to remain in his remote community with family whilst still having his coagulation status monitored regularly. Prior to INR POCT being available at his local remote health service, this patient had to travel 500kms by road to have his INR test conducted by the nearest laboratory; a journey that was often not possible when roads were cut off due to flooding, and which meant his coagulation status was not monitored as closely as it should have been. The last patient case described how INR POCT enabled the rapid identification and early treatment of a dangerously high INR level for an Indigenous patient with severe RHD, thus assisting in preventing serious complications such as blood clots and bleeds. Together these cases highlight the clinical and cultural benefits of INR POCT specifically in this remote setting.

The fourth study included a single patient case to demonstrate how POCT produced a defined clinical benefit to an acutely ill paediatric patient in a remote location. This case described how POCT

for electrolytes allowed a child with vomiting and diarrhoea to be monitored closely and receive informed rehydration treatment to be safely stabilised in a remote primary health care service. The significant delay in laboratory testing was also highlighted by this case as results for a specimen sent to the laboratory during the patient's initial presentation were reported back to the treating doctor two days after the patient had stabilised with the assistance of POCT.

The final study provided the most detailed examination of clinical effectiveness within the remote NT POCT Program (Spaeth, Shephard & Omond 2017). As outlined in the introduction to this thesis, this study was made possible through a grant awarded by the Emergency Medicine Foundation. At the same time as this grant was awarded, the NT DoH provided the funding for the rollout of i-STAT devices to all remote health services in the Territory. For this reason, a RCT was not possible as all remote health services in the NT now had access to the POCT device. Other remote locations in Australia experience significantly different rates of disease and acute presentations and, therefore, could not be used as a control group. The author of this thesis was a principal investigator for this Emergency Medicine Foundation study and conceived the original study design. Clinical effectiveness was investigated through an audit of all patient presentations that met the selection criteria for three common acute presentations in six remote health services over a six-month period. As outlined in the study, the three presentations included patients presenting with chest pain and no ST-elevation detected by ECG, patients with acute renal failure who had missed a dialysis session and patients with acute diarrhoea with symptoms suggestive of dehydration. As outlined in the study, these acute conditions were chosen due to the high prevalence of cardiac disease, kidney disease and acute infectious disease in the remote NT.

A total of 200 patient cases met the selection criteria. More than one-third of patients with chest pain (48 of 147) would have been unnecessarily evacuated to the nearest tertiary hospital if POCT for troponin I was not available on-site. POC troponin testing also enabled the identification of three patients with ACS that would not have been otherwise identified, thus, significantly improving the outcome of these patients by providing a rapid diagnosis of non-STEMI and enabling the early initiation of treatment and a medical retrieval. For chronic renal failure patients who had missed one or more dialysis sessions (n=28), POCT identified four patients with dangerously high potassium levels and enabled immediate treatment to be initiated with each patient recording a reduced potassium level (measured by POCT) prior to evacuation. POCT identified stable potassium levels in a further ten patients, allowing them to remain in the community to receive dialysis and not be unnecessarily evacuated. POCT for electrolytes enabled 40% of patients with acute diarrhoea (10

out of 25) to receive informed rehydration therapy prior to a medical retrieval. The remaining 15 patients, 60% were treated safely on-site through the use of POCT until their electrolyte levels had stabilised.

To further highlight the clinical utility of acute POCT within the remote health services, a patient case was presented for each of the three common acute presentations. The first case described how a patient with symptoms not typical of myocardial infarction received a diagnosis of non-STEMI due to the POC troponin I test, allowing immediate clinical management to be initiated and a medical retrieval to be prioritised for this patient, thereby significantly improving the outcome for this patient. In the second case, POCT for potassium enabled an Indigenous female with chronic renal failure to attend a family funeral in a remote community, thus providing a cultural as well as clinical benefit for this patient. The final case involved a patient a history of chronic obstructive pulmonary disease (COPD) and heart disease who presented with an acute case of diarrhoea and a cough. POC electrolyte results identified this patient was significantly dehydrated and enabled informed rehydration therapy until her electrolyte results had stabilised. Also, POCT for troponin I and blood gases assisted in ruling out an acute cardiac event and exacerbation of COPD for this patient.

Collectively, these studies provide new knowledge for the clinical effectiveness of POCT for acute and chronic care in remote primary health care settings. The patient cases within these studies provide real examples of how POCT has produced a defined clinical benefit to the patient and also highlight some of the cultural benefits of POCT. While the literature review identified several studies on the use of acute POCT in tertiary care settings, the only study to provide case studies were those provided in a magazine article on mobile emergency care (Fuller 2008). Also while several studies provided evidence for the clinical effectiveness for INR POCT in rural and remote locations, none provided specific cases studies to highlight how POCT resulted in a defined clinical benefit to the individual patient. Prior to POCT being available in the remote NT health services, it was not uncommon for patients to be transported by air to one of the major centres for the sole reason of having a pathology test conducted by the laboratory to rule in or rule out an acute condition (Braund et al. 2016). Hence, POCT can prevent unnecessary dislocation from traditional homelands through ruling out or stabilising acute conditions and, thus, avoiding the unnecessary stress of being transported to a foreign environment.

3.4.4 Assessment of Cost Effectiveness/Economic Impact

While the primary aim of POCT is to deliver an improvement in clinical outcome, the cost effectiveness of a POCT program must also be considered to determine its long-term sustainability. This is particularly the case as the cost of POCT is compared to laboratory-based testing, which takes advantage of greater economies of scale and is, therefore, often perceived as more cost-effective. However, in rural and remote locations, the cost of laboratory-based testing is increased due to the extended distance pathology specimens are required be transported to reach a centralised laboratory. As such, POCT is anecdotally thought to reduce the costs associated with pathology in rural and remote locations. However, as highlighted by the literature review, results on cost-effectiveness of POCT in rural and remote settings are varied. For chronic disease, the POCT in GP Trial found POCT significantly reduced the costs to patients and their families. However, the per-patient cost to the health system was higher for almost all POC tests investigated. In contrast, a study on use the of POCT for diabetes management in rural Thailand found POCT was significantly more cost-effective than using the laboratory (Kulrattanamaneeporn, Wongboonsin & Kost 2009). For acute care, the literature review identified a study which found that POCT produced a cost saving through reducing patient transfers and increasing discharges in one hospital in rural New Zealand (Blattner, Nixon, Dovey, et al. 2010), though no previous studies were found to have investigated the cost benefit of acute POCT in a remote primary health care setting.

Two co-authored studies included in this thesis address this gap in knowledge by providing results on the cost effectiveness of POCT in the remote primary health care sector. The author of this thesis was a primary author and assisted in the data collection and analysis for both studies. The full citation of these studies is provided below:

> **Spaeth, B**, Shephard, M, Auld, M & Omond, R 2017, 'Immediate pathology results now available for all remote Northern Territorians', in L Coleman (ed.), *14th National Rural Health Conference*, Cairns, Queensland.
>
> **Spaeth, B**, Kaambwa, B, Omond, R & Shephard, M 2018, 'Economic Evaluation of Point-of-Care Testing in the Remote Primary Health Care Setting of Australia's Northern Territory', *ClinicoEconomics and Outcomes Research*, (accepted 12 March 2018).

The first study included an audit of all patient cases in the Top End of the NT where a POC troponin test had been conducted on the i-STAT device over a six-month period (Spaeth et al. 2017). The

audit was performed by a medical registrar with assistance of this author. The POC troponin I test was found to have prevented 80 unnecessary medical retrievals and provided reassuring results in a further 474 patient cases through ruling out a cardiac event, resulting in cost savings of $640,000 and $3.8 million respectively. While this audit provided only a basic estimate of POCT cost effectiveness, it formed the premise for a more rigorous study to be conducted.

The most recent study presented in this thesis provides an in-depth economic evaluation of POCT in the remote NT (Spaeth et al. 2018). This study was conducted alongside the clinical effectiveness study within the grant awarded by the Emergency Medicine Foundation. As previously mentioned, this study coincided with the expansion of the NT POCT Program to all remote health services in the remote NT and, as such, a RCT was not possible. Therefore, a decision analytic simulation model was used to conduct an economic evaluation, with the support of a health economist and this author collecting all data and assisting with data analysis. As outlined in the clinical effectiveness section, three common acute presentations were investigated. The costs associated with using POCT combined with standard practice (using clinical signs, symptoms and protocols) were compared to normal practice alone. Cost savings were determined from unnecessary medical retrieval avoided through the use of POCT. From the 200 patient cases identified, 60 medical evacuations were avoided due to on-site POCT. The costs and time associated with the POCT arm and usual care arm in the models were determined using time in motion analyses. These analyses were conducted by health professionals with expertise and recent experience with the three acute presentations both with and without the use of POCT and results were analysed by this author. POCT was found to be more expensive than usual care due to the extra time and resources required. However, the cost of POCT was significantly outweighed by the cost savings POCT produced through preventing unnecessary medical retrievals. An audit of electronic patient information systems in the NT was then used to calculate the prevalence of each acute presentation in the NT and modelling was used to extrapolate the results from the six remote health services to provide a NT-wide estimate of cost savings. This study determined that POCT was estimated to provide a cost saving of more than $20 million dollars per annum to the NT health sector and thus provide substantial evidence for the cost effectiveness of POCT in the remote primary health care sector.

As identified in the literature review, unnecessary medical evacuations avoided by POCT was also used as an outcome measure in the study by Blattner, Nixon, Dovey, et al. (2010) based in a rural New Zealand hospital where cost savings were measured in terms of reductions in medical transfers and an increase in the number of discharges by POCT. However, the clinical setting of the New

Zealand study differs significantly from the study conducted in the remote NT of Australia. Firstly, the New Zealand study was conducted in a regional tertiary hospital, whereas the Australian study was conducted in remote primary health care services. Also, the New Zealand hospital was a two to four hour journey by road to the nearest major hospital and had seven on-site doctors and ten acute beds. In comparison, remote health services of the NT are located up to 1000 kilometres from the nearest tertiary hospital, generally do not have a doctor on-site and emergency care is provided by off-site, on-call RMPs. The methods used to determine cost effectiveness were also different. The New Zealand study used a 'before and after' study design in which doctors were required to record the diagnosis and patient plan pre- and post POCT results. The remote NT study used decision making by a senior RMP with significant experience in making clinical decisions regarding medical retrievals, and was informed by clinical protocols with modelling used to determine cost savings. In addition, the study by this author is the first to provide complimentary data on emergency medical retrievals such as the time required, distance travelled and associated costs. As outlined within the literature review of the economic evaluation study, the only study in Australia to provide information on the cost of medical retrievals was one based in Queensland that focussed on inter-hospital transfers rather than retrievals from remote communities (O'Connor et al. 2009).

As such, the study conducted and co-authored by this author provides new information related to the use of POCT in emergency medical retrievals and demonstrate the significant cost savings POCT can deliver in remote primary health care settings in Australia.

3.5 Sustainability of Point-of-Care Testing

The effectiveness of a new POCT program is generally not realised immediately after implementation. Long-term sustainability of POCT is a crucial objective and measure of success for a POCT program. Maintenance of an intensive level of support services, as well as regular audits of defined outcome measures, is essential to ensure long-term sustainability of a POCT program, particularly in challenging settings such as rural or remote locations. In Australia, the rural and remote health care sectors are highly variable, particularly in Indigenous settings, where the patient population and health workforce are highly transient and reactive action from government often changes health care priorities. As such, it is important to provide continuous evaluation of program efficacy in these settings.

As identified by the literature review, the majority of POCT programs based in a rural or remote location were relatively short pilot programs with only initial results on POCT outcomes provided. The POCT in GP Trial was the largest RCT of POCT conducted across urban, rural and remote GPs globally. However, the POCT in GP trial was conducted over a period of just 18 months and, therefore, the enduring challenges for sustainability of POCT in this primary care setting was not investigated in any depth. The literature review did identify two long-term POCT programs; these were the ICCNet and QAAMS programs, established for 17 and 20 years respectively (Shephard, M et al. 2017b; Tideman et al. 2014). The ICCNet included POCT for cardiac markers as one component of a wider cardiac care program (Tideman et al. 2014) and, therefore, published studies on ICCNet program have provided only limited information on the results of POCT implementation and evaluation in this network. Only one published study on ICCNet specifically discussed the sustainability of POCT, but this was simply an opinion piece describing how an online POCT training module for remotely located POCT operators had reduced costs (St John et al. 2015). However, as discussed in the literature review of this thesis, the methods for this training system were not described or tested for their suitability. The QAAMS Program provided an evidence-based case model of a POCT service that has been regularly audited and has been sustainable in the long-term, however, it uses POCT for HbA1c and urine ACR for diagnosis and management of diabetes and for the detection of early kidney disease respectively, but does not include any POCT for acute care. In addition, the QAAMS Program is conducted specifically in Indigenous health services. While a high proportion of these services are located in rural or remote locations, QAAMS studies have provided limited information on the specific challenges experienced by POCT in remote settings as they have

focussed more specifically on challenges for POCT in the Indigenous health care sector. The only study related to the QAAMS Program to provide specific methods to address the challenges for POCT in rural or remote locations was co-authored by the author of this thesis, the full citation for this study is provided below:

> Shephard, M, Halls, H, McAteer, B, Mazzachi, B, Motta, L, **Spaeth, B** & Shephard, A 2013, 'Management challenges for point-of-care coordinators in delivering training and competency programs', *Point of Care*, vol. 12, no. 2, pp. 84-5.

This editorial outlined the specific challenges for POC Coordinators in delivering POCT training to rurally and remotely located health professionals. Also described in this study are the methods developed by this author and co-workers to address the challenges in delivering POCT in isolated locations. At the time this study was conducted, this author was the Coordinator of the NT POCT Program and the Device and Quality Manager for the QAAMS Program. As outlined in this paper, there are a unique set of challenges faced by POC Coordinators in delivering POCT programes in remote and isolated locations, for example, the high turnover of staff which has previously been discussed. This study highlights that there are additional challenges experienced in training remotely located health professionals. These include the level of education of remote health professional staff which may vary considerably and, therefore, one form of training will not suit all staff. The workload of staff working in remote locations is also often greater and more unpredictable than their urban counterparts, which creates challenges in organising training sessions. There are also environmental challenges such as fluctuations in power and extreme weather causing problems with phone and internet communication. Several methods to combat these challenges are provided by this editorial. These include a wide range of electronic and hardcopy training resources being made available to enable access to training materials in all conditions. In addition, various methods for attending and completing training should be made available to allow for differences in the level of health professionals' education. To enable the POC Coordinator to focus on delivering and maintaining the high workload of providing POCT training required in remote locations, the POCT competency assessment process and reminders for competency updates can be automated. This editorial, therefore, provides new knowledge in the field of POCT by offering insights and methods to ensure the sustainability of POCT training in rural and remote settings. This author has also provided additional contributions to the literature in relation to the role of the POC Coordinator in the form of an invited book chapter titled *Stakeholder perspectives on point-of-care testing*. The

section of the chapter subtitled *A POCT Coordinator Perspective* provides the personal experiences of this author in managing a remotely located POCT network and is provided in Appendix C.

A new training strategy for POCT conceived, designed and initiated by this author is also described in this editorial (Shephard, M et al. 2013). This novel approach to training involved a re-design of the face-to-face POCT training presentation into a format that could be delivered remotely using computer-based screen-sharing software. This method allowed training to be delivered remotely even to locations with poor internet speeds, such as those in the remote NT. This author provided the original re-design of training for two POCT programs, the QAAMS Program and the NT POCT Program, which significantly improved the efficiency of POCT training (Shephard, M et al. 2013). This novel POCT training method provided additional benefits over the previous pre-recorded training videos which were available on the website or DVD as they enabled trainer and POCT operator interaction and provided a means of also assessing practical competency during the training session. In the NT POCT Program, the ability to assess practical competency for POCT is particularly important for acute care POCT devices due to the clinical significance of critically-ill patient results.

To further address the gaps in knowledge related to the long-term sustainability of POCT programs in remote locations, this author has also co-published one book chapter and two studies based on research conducted on the NT POCT Program. These include (in chronological order):

> Shephard, M, **Spaeth, B**, Motta, L & Shephard, A 2014, 'Point-of-care testing in Australia: Practical advantages and benefits of community resiliency for improving outcomes.', in G Kost & C Curtis (eds), *Global Point-of-Care - Strategies for Disasters, Complex Emergencies, and Public Health Resilience*, American Association of Clinical Chemistry Press, Washington DC, pp. 527-35.
>
> Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Lingwood, A, Loudon, J, Rigby, J & Daniel, V 2014, 'Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program', *Point of Care*, vol. 13, no. 1, pp. 6-11.
>
> **Spaeth, B**, Shephard, M, Auld, M & Omond, R 2017, 'Immediate pathology results now available for all remote Northern Territorians', in L Coleman (ed.), *14th National Rural Health Conference*, Cairns, Queensland.

A peer-reviewed book chapter co-authored by the author of this thesis titled *Point-of-care testing in Australia: Practical advantages and benefits of community resiliency for improving outcomes* outlined further challenges in managing remotely located POCT networks, and provided strategies to increase community resilience and improve outcomes related to POCT. As outlined in a section of the book chapter subtitled *Toward Building a Sustainable and Resilient Workforce Capacity*, this author identified that untrained POCT operators were producing significantly more pre-analytical errors than trained POCT operators. Using a hidden function on the connectivity system of the i-STAT device, this author employed a strategy to 'lock-out' untrained operators from using the POCT device to prevent such errors from occurring, with the error rate decreasing from 15% to 8% after this strategy was introduced. As previously mentioned, this author has made additional contributions to the literature on the use of POCT connectivity systems which further discuss the advantages of POCT connectivity in managing remotely located operators (Appendix A).

The study titled *Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program* described a novel method of providing feedback on POCT use to the remotely located health services to assist with the management and sustainability of POCT in remote settings. This author developed the POCT Feedback Report (conceived, designed and initiated by this author) after learning the managers of remote health care services experienced difficulties in identifying local issues with POCT due to the high rates of staff turnover. As described within this study, the POCT Feedback Reports were designed to provide the following key statistics on POCT use at each remote health service:

- Number of POC tests and errors conducted by each trained operator;
- Description of the POCT errors obtained and how to avoid these errors;
- The participation rate for quality testing procedures; and
- Reminders for any routine actions required by the remote health service staff such as training updates for POCT operators and cleaning/maintenance procedures for the POCT device.

The Feedback Reports ensured that any problems with POCT were identified early with feedback on how to prevent the issues from reoccurring. In support of the effectiveness of the Feedback Report, this study reported that:

> *"*there was unanimous agreement from health centre managers that monthly feedback reports assisted in monitoring the use of the i-STAT device in their health centre*".*

Evidence to support this latter statement was also provided in the subsequent study titled *Immediate pathology results now available for all Northern Territorians*. This study examined the effectiveness of the POCT Feedback Reports through a survey of health service managers (conducted by this author) to determine their level of knowledge of on-site POCT conducted at their local service before and after the Feedback Report was implemented. Survey responses indicated health service manager satisfaction increased from less than 27% before to more than 60% after the Feedback Reports were introduced regarding their knowledge of on-site POCT usage. A high proportion of health service managers indicated the Feedback Reports were informative (77%) and were useful in assessing the effectiveness of POCT use at their health service (86%). The development of the POCT Feedback Report provides an original contribution to knowledge in the field of POCT which has now been adopted in several other POCT programs managed by the ICPOCT and operating in geographically isolated locations.

In addition to the Feedback Report survey, this study also provided the methods and strategies employed for the large-scale rollout of the i-STAT POCT device to every remote health service in the NT. The rollout began in October 2015 and saw the number of remote health services with an i-STAT device double from 36 to 72. As discussed in the paper, several measures were put in place to ensure the i-STAT rollout occurred in a coordinated and streamlined manner, and that the NT POCT Program remained sustainable. This included appointing a POC Rollout Coordinator (experienced member of the NT POCT Management Committee) to oversee the rollout of i-STAT devices in close collaboration with the NT POCT Program Coordinator (this author). Secondly, the Program Coordinator developed two new approaches to manage POCT consumable ordering, as this process was deemed to be one of the main challenges for newly enrolled remote health services. Firstly, new information on average POCT cartridge usage was added to the POCT Feedback Reports to provide each health service with a guide on the number of cartridges to order, which also acted as a reminder to the health service manager to order POCT stock; a task that was often overlooked during their busy work schedule and meant at times no POCT stock was available at the remote health services. Secondly, this author developed a method for ordering and distributing quality

control samples to ensure all remote health services were testing the same lot number each month to streamline the monitoring of POCT analytical quality.

This author presented the methods and results on the i-STAT rollout at the 14th National Rural Health Conference in Cairns in March 2017. The findings of this study were particularly applicable to the conference audience, with many health professionals and policymakers attending from the rural and remote health sector in Australia and internationally. As a result of the presentation, this author received an invitation from the National Rural Health Alliance to provide a short editorial on the challenges of pathology testing in remote locations (Spaeth 2017). The National Rural Health Alliance is the peak body working to improve the health and wellbeing of people living in rural and remote Australia. The article titled *'Simply' better access to pathology diagnostics is not so simple* was published in the 59th edition of the Partyline magazine and is provided in Appendix D.

The challenges identified by this research are likely to be generalisable to similar isolated settings. As such, the novel methods developed by this author are likely to be valuable in addressing the barriers to sustainability of POCT models in other remote settings.

All of the studies presented in this thesis thus far have been conducted in rural or remote Australia and have provided extensive evidence for the operational, analytical, clinical and economic effectiveness as well as the sustainability of POCT in these settings. Finally, to demonstrate the robustness of the methods developed by this author, a study demonstrating the transferability of these methods to an international setting is provided.

3.6 Translation of Point-of-Care Testing

As discussed, it is vitally important to develop sustainable methods for implementation and management of a POCT program to ensure it delivers the benefits for which it was introduced. The ultimate test of the robustness of a POCT system/network is to translate its methods and processes to a different POCT program (in terms of settings, location and tests) and to determine if they are sufficiently robust to be transferred to that alternative setting. The final study included within this thesis demonstrates how the methods developed for the remote NT POCT Program (by this author) were used to implement a POCT program into a rural location in Pakistan for the detection of anaemia. The full citation for this study is provided below:

McCormack, T, Ayub, R, Aziz, F, Motta, L, **Spaeth, B** & Shephard, M 2017, 'Point-of-care testing facilitates screening and treatment for anaemia in women and children in rural Pakistan', *Australian Journal of Rural Health*. doi:10.1111/ajr.12395

This study provides the methods and results of a POCT program for haemoglobin (Hb) to screen for anaemia in women and children in rural Pakistan (McCormack et al. 2017). This research project originated from an international collaboration between the ICPOCT and the Head of the Health Professions Education College of the Al Nafees Medical College and Hospital, Islamabad, Pakistan. The ICPOCT was approached to collaborate on a research project to implement a POCT program using Hb to screen for anaemia in women and children in rural Pakistan, and to examine the clinical effectiveness of POCT for this purpose. There was a strong clinical need for POCT in this setting due to the poor diets and high rates of parasitic infection causing anaemia in this population. In addition, this rural mountainous region of Pakistan had poor access to even basic diagnostic services due to its limited accessibility. This author was invited to assist with the initial implementation of POCT in this rural setting due to her experience and expertise in managing remote POCT programs. In particular, this author's methods for providing POCT training to remotely located health professionals and monitoring the ongoing analytical quality of POCT in remote locations were used to implement and manage this POCT program. The locally-selected Pakistani health professional team who were chosen to perform POCT included a senior general practitioner who coordinated the study and 22 of her third-year medical students. This author was not closely involved with examining the clinical effectiveness of POCT in this setting, but did work collaboratively with other members of the research team to establish the research design and perform data collection and analysis.

As outlined in this study, POCT provided an effective means to screen for anaemia in this isolated location by providing a rapid diagnosis of anaemia. As such, POCT ensured there was no loss to follow-up as those identified with anaemia could be administered treatment immediately based on their Hb result measured by POCT. This multifaceted intervention was deemed effective, as indicated by a statistically significant increase in Hb results from baseline (post POCT) and a decrease in the prevalence of anaemia in this isolated location. In addition, the POCT device was determined to have sound analytical quality throughout the length of the research project (6 months).

This study provides evidence of the transferability of the research methods developed by this author to other isolated locations. The literature review in this thesis confirms the originality of this study as no studies investigating the use of POCT for Hb in a rural or remote setting were identified.

The next chapter of this thesis, the linking statement, will demonstrate how each of the studies discussed in the contextual statement build upon one another to inform each phase of POCT program establishment, specifically in a rural or remote location, from initial evaluation and implementation through to assessing the outcomes and finally program translation.

CHAPTER 4 LINKING STATEMENT

As outlined in the previous chapter, the studies in this thesis provide methods and results on each stage of POCT implementation and assessment, with specific focus on rural and remote locations. As demonstrated in the contextual statement, a number of publications cover several of these stages. Therefore, this chapter will link each study based on the phase of POCT implementation on which it is principally focussed. A summary of the flow of the studies according to its prominent focus is provided in Table 16.

A linking statement is provided between each study to highlight how each links to the next to ultimately build a significant evidence base for the use of POCT in rural and remote locations. A co-author contribution statement will also be provided to declare this author's contribution to each of the studies included in this thesis.

To avoid infringement of any copyright laws, and to comply with the University's higher degree requirements for a PhD by published works, the manuscripts are provided in the format in which they were submitted to journal (with editorial comments incorporated) prior to publication. As such, each study is presented in its final format prior to publication. This includes the reference lists for each study, which may not reflect the reference style in the body of this thesis.

To view the final published manscript, the Digital Object Identifier (doi) link or URL to each publication is provided within each of the linking statements, with the exception of the book chapter for with neither a doi nor URL is available.

Table 16 – Summary of how each published study addresses each stage of POCT implementation and evaluation.

Stage of POCT evaluation	Title of Publication	Study Description	Citation
Initial evaluation of analytical quality	*Assessment of the Nova StatSensor whole blood point-of-care creatinine analyzer for the measurement of kidney function in screening for chronic kidney disease*	Initial evaluation of the analytical quality of new POCT device in a controlled setting (laboratory-based).	(Shephard, M et al. 2010)
	Assessment of a point-of-care device for measuring creatinine in a community screening program for chronic kidney disease	Evaluation of analytical quality of the redesigned POCT device in the setting of intended use (rural farming).	(Spaeth, Shephard, Shephard, et al. 2015)
	Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory	Evaluation of analytical quality a POCT device in the setting of intended use (remote Indigenous).	(Spaeth, Shephard, McCormack, et al. 2015)
POCT Program Implementation	*Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program*	Methods and initial results for implementation of a POCT program in remote Northern Territory of Australia.	(Shephard, M et al. 2012c)
Evaluation of operational and clinical effectiveness	*Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care*	Results on timeliness and clinical effectiveness of POCT for HbA1c compared to laboratory-based testing.	(Spaeth, Shephard & Schatz 2014)
	Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's NT	Evidence for operational and clinical benefits of INR POCT in remote primary health care services in the NT.	(Spaeth & Shephard 2016)
Evaluation of clinical effectiveness	*Clinical Application of Point-of-Care Testing in the Remote Primary Health Care Setting*	Evidence for the clinical effectiveness of acute POCT in remote primary health care services in the NT.	(Spaeth, Shephard & Omond 2017)

Evaluation of economic impact	*Economic Evaluation of Point-of-Care Testing in the Remote Primary Health Care Setting of Australia's Northern Territory*	Economic evaluation of acute POCT provides first evidence regarding cost effectiveness of POCT in remote primary health care services in the NT.	(Spaeth et al. 2018)
Sustainability of POCT program/ model	*Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program*	Evidence for ongoing analytical quality, operational and clinical effectiveness of the NT POCT Program four years after its initial implementation.	(Shephard, M, Spaeth, Mazzachi, et al. 2014)
	Management challenges for point-of-care coordinators in delivering training and competency programs	Outlines the challenges experienced by POC coordinators and describes strategies (some developed by this author) to address challenges in delivering POCT training to remotely located operators.	(Shephard, M et al. 2013)
	Point-of-care testing in Australia: Practical advantages and benefits of community resiliency for improving outcomes	Provides examples of the strategies employed for POCT in rural and remote locations to increase community resilience and improve outcomes in the long-term.	(Shephard, M, Spaeth, Motta, et al. 2014)
	Immediate pathology results now available for all remote Northern Territorians	Demonstrates stability of analytical quality, as well as operational and clinical effectiveness, during a period of significant expansion of the NT POCT Program. Provides additional methods to ensure the long-term sustainability of POCT in remote settings.	(Spaeth et al. 2017)
Translation of POCT model	*Point-of-care testing facilitates screening and treatment for anaemia in women and children in rural Pakistan*	Demonstrates the translation of POCT methods and systems developed by this author to implement a community screening program using POCT for detection of anaemia in rural Pakistan.	(McCormack et al. 2017)

4.1 Pre-implementation of POCT

4.1.1 Study 1: Laboratory-based evaluation of POCT analytical quality

Shephard, M, Peake, M, Corso, O, Shephard, A, Mazzachi, B, **Spaeth, B**, Barbara, J & Mathew, T 2010, 'Assessment of the Nova StatSensor whole blood point-of-care creatinine analyzer for the measurement of kidney function in screening for chronic kidney disease', *Clinical Chemistry and Laboratory Medicine*, vol. 48, no. 8, pp. 1113-119. DOI 10.1515/CCLM.2010.238.

This study aimed to evaluate the analytical quality of a newly released POCT device measuring creatinine by capillary finger-stick sample for potential application to screen for CKD in at-risk populations. Analytical quality was measured through determining the imprecision, accuracy and linearity of the POCT device with results compared to a laboratory device validated against the IDMS-aligned reference method.

This author was responsible for conducting the imprecision analyses using three methods:

1) Within-run analysis (n=10) of three levels (low, normal and high) of QC material;

2) Between-day (n=20) of three levels (low, mid and high) of QC material; and

3) Between- device analyses of patient samples (n=98).

Results from these analyses indicated the POCT device did not meet imprecision goals for creatinine derived from biological variation data and also displayed a strong negative bias.

The linearity of the POCT device was assessed through testing samples across a range of creatinine concentrations with only minor deviations from linearity observed.

Accuracy was assessed by comparing the difference in patient creatinine results obtained on the POCT device to results obtained by the laboratory method using Bland-Altman difference plots. POCT device sensitivity, specificity and positive and negative predictive values were calculated by using the creatinine results obtained by POCT to determine if eGFR was correctly categorised as being above or below 60 mL/minute when compared to the laboratory method. These analyses were conducted before and after the POCT results were recalibrated to the IDMS-aligned method. However, the POCT device displayed poor correlation and a negative bias compared to the

laboratory method both before and after recalibration. The POCT device also demonstrated poor sensitivity compared to the laboratory method which would have resulted in a significant number of patients with abnormal renal function not being detected by POCT.

To summarise, this was the first study to provide an evaluation the Nova StatSensor POCT device in Australia using both capillary and venous samples. While the device was considered easy to use with highly desirable characteristics for use in screening for CKD (as previously discussed), this analytical evaluation determined its analytical performance to be not acceptable for routine patient testing. The results of this evaluation were provided to the manufacturer of the StatSensor (Nova Biomedical) to make improvements to the device.

This study demonstrates the importance of evaluating the analytical performance of a POCT device *before* implementation and outlines the methods used for POCT device evaluations. If the POCT device is able to demonstrate acceptable analytical performance in this evaluation stage, it can move to the next phase of evaluation which is to determine its analytical performance in the clinical setting of intended use.

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B. CO-AUTHORSHIP DETAILS (To be completed by the candidate and co-authors)

In accordance with Clause 20.5 and Clause 8 of Appendix F of the RHD Policies and Procedures, a candidate must sign a declaration that the thesis does not contain any material previously published or written by another person except where due reference is made in the text or footnotes. There can be no exception to this rule. Material produced jointly by a candidate and their supervisors or others can be included in the narrative of the thesis only if it is the original work of the candidate. To ensure compliance with the Australian Code for the Responsible Conduct of Research (2007), if the thesis involves the original work of the joint authors other than the candidate, this work must be fully acknowledged in exactly the same way as the work of other authors. A candidate is required to obtain permission from any co-authors to include their work in the thesis.

Please note. A copy of this page will be provided to the Examiners.

1. **Publication Details:** Assessment of the Nova StatSensor whole blood point-of-care creatinine analyzer for the measurement of kidney function in screening for chronic kidney disease, Published in Clinical Chemistry and Laboratory Medicine, 2010;48:1113-9.

Section of the thesis where the publication is referred to: Throughout the entire thesis

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Prof Mark Shephard, Michael Peake and Timothy Mathew worked collaboratively on the development of the research design and providing a first draft of the manuscript with input and comment from co-authors.
Oliva Corso and Brooke Spaeth worked collaboratively on the collection and analysis of data, with supervision provided by Prof Mark Shephard and Timothy Mathew. All authors assisted with the analysis of data and editing the final manuscript.

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Assessment of the Nova StatSensor Whole Blood Point-of-Care Creatinine Analyzer for the Measurement of Kidney Function in Screening for Chronic Kidney Disease

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Running Title: Assessment of Nova StatSensor Creatinine Analyser

ABSTRACT

Background: Point-of-care testing for creatinine using a fingerprick sample and resultant estimated glomerular filtration rate has potential for screening for chronic kidney disease in community settings. This study assessed the applicability of the Nova StatSensor creatinine analyser for this purpose.

Methods: Fingerprick samples from 100 patients (63 renal, 37 healthy volunteers; range 46 to 962 µmol/L) were assayed on two StatSensor analysers. Lithium heparin venous plasma samples collected simultaneously were assayed in duplicate using the isotope dilution mass spectrometry-aligned Roche Creatinine Plus enzymatic assay on a Hitachi Modular P unit. Method comparison statistics and the ability of the StatSensor to correctly categorise estimated glomerular filtration rate above or below 60 mL/min were calculated pre and post alignment with the laboratory method.

Results: StatSensor 1 creatinine results (y) were much lower than the laboratory (y = 0.75x + 10.2, average bias -47.3, 95% limits of agreement -208 to +113 µmol/L). For estimated glomerular filtration rates above or below 60 mL/min, 100% and 87% of results respectively agreed with the laboratory estimated glomerular filtration rate (79% and 96% post alignment). StatSensor 2 statistics were similar. The 95% limits of agreement between StatSensor creatinine results were -35 to +34 µmol/L.

Conclusion: Isotope dilution mass spectrometry alignment of the StatSensor will identify most patients with estimated glomerular filtration rate <60 mL/min, but there will be many falsely low estimated glomerular filtration rate results that require laboratory validation. Creatinine results need improvement.

Non standard abbreviations:

eGFR: estimated glomerular filtration rate

CKD: chronic kidney disease

IDMS: isotope dilution mass spectrometry

POCT: point-of-care testing

KEY: Kidney Evaluation for You

NIST: National Institute of Standards and Technology

CLSI: Clinical and Laboratory Standards Institute

MDRD: Modification of Diet in Renal Disease

KEEP: Kidney Early Evaluation Program

ACR: urine albumin:creatinine ratio

INTRODUCTION

Chronic kidney disease (CKD) has a prevalence of approximately 16% and 13% in Australian and American environments respectively (1,2). The disease is usually silent and progressive, and end stage renal disease is placing increasing burdens on health care budgets, with increasing numbers of patients requiring dialysis (3). Early signs of chronic kidney disease include proteinuria, increased blood pressure and reduced glomerular filtration rate (GFR) (4). GFR (eGFR) can be estimated using laboratory measurements of serum creatinine, and considerable international efforts have been made to align creatinine results to isotope dilution mass spectrometry (IDMS) equivalent standards (5). In addition, simplified equations to convert serum creatinine results to eGFR based on age, sex, and ethnic background have now been adopted (5-7).

Although efforts to align the calibration of laboratory creatinine estimations are well-advanced (8), there can be valid reasons for measuring creatinine in non-laboratory situations. These include screening programs for chronic kidney disease to facilitate the early detection and follow-up of at-risk patients. Recently Kidney Health Australia conducted a targeted community-based program for CKD risk called KEY (Kidney Evaluation for You). This pilot program was the first program for CKD risk assessment undertaken in the primary health care setting in Australia (9). The KEY study used the i-STAT point-of-care testing (POCT) analyser (Abbott Point of Care Inc, New Jersey, USA) for measuring creatinine, with subsequent calculation of eGFR. However, the i-STAT device required a venous whole blood sample of approximately 100 µL, which is less ideal than a fingerprick sample for a screening situation. In addition, i-STAT has been reported to produce higher creatinine results than the Roche enzymatic creatinine assay (Roche Diagnostics Australia, Sydney, Australia) (10).

A recently released point-of-care device from Nova Biomedical (Massachusetts, USA) that measures creatinine using just 1.2 µL of whole blood and converts creatinine results to eGFR has been actively promoted to fill a niche in the POCT market. We evaluated the performance of this device against

the IDMS-aligned Roche enzymatic creatinine assay and assessed the potential use of the Nova device for detecting silent kidney disease in the community. The results of this study are also relevant for radiology patients using potentially nephrotoxic contrast media (11) and in other POCT environments.

MATERIALS AND METHODS

Ethics approval

Ethics approval to conduct this study was obtained from the Flinders Clinical Research Ethics Committee (application number 222/08).

Patient samples

One hundred subjects (48 males and 52 females) participated in the study; 63 were patients attending either the renal clinic or dialysis clinic at the Renal Unit, Flinders Medical Centre (FMC) and 37 subjects were healthy volunteers.

Capillary whole blood specimens were obtained from each subject and immediately analysed in singlicate on two Nova StatSensor Creatinine devices using the same reagent strip lot number. A venous whole blood specimen anticoagulated with lithium heparin (Greiner blood tube, Greiner Labortechnik GmbH, Cat No 456083) was obtained from each subject at the same time and sent to the pathology laboratory at Flinders Medical Centre, Adelaide, South Australia. In the laboratory, the venous whole blood sample was centrifuged (4500g for 5 mins) and a plasma sample aliquoted for duplicate laboratory analysis.

Test method

The Nova Biomedical StatSensor Creatinine meter measured creatinine on 1.2 µL of whole blood in 30 seconds. The sample was added to a reagent strip which was inserted into the device prior to

sample application. In the reagent strip, creatinine is converted to hydrogen peroxide in an enzymatic cascade involving creatininase, creatinase and sarcosine oxidase. The signal generated from H2O2 was detected amperometrically. Calibration was factory-encoded into the reagent strip.

Fingerprick analyses were conducted according to manufacturer directions by a non-laboratory operator trained by Nova Biomedical.

Comparison method

Creatinine was also measured in the laboratory by assaying plasma from each patient in duplicate using the IDMS-aligned Roche Creatinine Plus enzymatic assay (Cat No 1775685) on a Hitachi Modular P unit. The performance of this assay has been validated versus both the IDMS reference method and international reference materials (SRM 967) (12-15).

Imprecision

Imprecision (coefficient of variation, CV%) for creatinine measurement on the Nova StatSensor device was assessed in three ways. Within-run and day-to-day imprecision were calculated using repeated analysis (n=10 and 20 respectively) of three levels of Nova StatSensor quality control material (Cat No 43921-3; QC lot numbers 5008340241, 5008100242 and 5008344243 for within-day and 5009037241, 5009037242 and 5009043243 for day-to-day). Between-device imprecision was calculated from the difference between results obtained on the same samples analysed on the two Nova devices (using the equation $s=\sqrt{(\sum d^2/2n)}$, where s=standard deviation, d=difference between individual results on the 2 devices and n=number of duplicates [98 in this data set] and CV% =s/m x100 where s=standard deviation and m=mean creatinine concentration).

Linearity

Linearity of the Nova analysers was assessed by increasing the creatinine concentration of a base pool of lithium heparin anticoagulated venous whole blood (58 µmol/L) by 1000 µmol/L using a concentrated solution of creatinine prepared from National Institute of Standards and Technology

Standard Reference Material (NIST SRM) 914a (NIST, United States Department of Commerce), By mixing the base pool and the spiked sample in various ratios, whole blood samples were prepared in which the base pool was supplemented with 100, 250, 500, 750 and 1000 µmol/L of creatinine. All samples were assayed on both Nova 1 and Nova 2 analysers, and linearity assessed using Clinical and Laboratory Standards Institute (CLSI) EP6-A guidelines (16) (see statistical analyses).

Accuracy

The accuracy of creatinine results on each Nova StatSensor device was compared to the mean of duplicate creatinine results from the IDMS-aligned laboratory method using Passing Bablok linear regression analysis (17). Differences between results were graphed against the Roche enzymatic assay using a modified Bland Altman difference plot (18).

Estimated GFR (eGFR) on the Nova StatSensor, calculated automatically from the measured creatinine using the Modification of Diet in Renal Disease (MDRD) equation (factor 186), was also plotted against eGRF from the laboratory method, calculated by the laboratory information system (LIS) from the measured creatinine using the standardised MDRD equation (factor 175). The ability of the Nova StatSensor to correctly categorise eGFR above or below 60 mL/min was then assessed by calculation of sensitivity, specificity, positive and negative predictive values.

After alignment of the Nova StatSensor results to the laboratory creatinine method, this process was repeated, now using an eGFR factor of 175 for the Nova StatSensor.

Statistical Analyses

Statistical analyses, including assessment of linearity, were performed using the statistical package Analyse-it (clinical laboratory version 2.21).

RESULTS

Imprecision

Within-run and day-to-day imprecision averaged 3.3% and 8.9% respectively at 100 µmol/L creatinine and 2.8% and 5.3% at 600 µmol/L creatinine for the two StatSensor analysers (Table 1). For the laboratory assay, year-long imprecision (approximately 1200 QC data points) was 1.9% and 1.4% at similar low and high concentrations of creatinine. The Roche enzymatic assay imprecision was consistent with data reported during the use of this method to develop the IDMS-aligned 175 MDRD equation (14).

Between-device imprecision was 7.8% (all concentrations, n=98), 7.8% for creatinine <150 µmol/L (n=62), and 6.2% for creatinine >150 µmol/L.

The StatSensor creatinine day-to-day imprecision did not meet either the desirable or minimum analytical goal for imprecision derived from biological variation criteria (CV < 2.2% and 3.2% respectively)(19), or the criteria required to keep the analytical error in eGFR calculations below 10% (5). The laboratory assay met both these requirements.

Linearity

Minor deviations from linearity were observed and are shown in parenthesis after the addition of 100 (-3.9%) , 250 (5.4%), 500 (5.5%), 750 (2.0%) and 1000 (-3.3%) µmol/L creatinine to a base pool of blood containing 58 µmol/L creatinine. The CLSI EP6-A linearity protocol measures the degree to which a curve (polynomial line of best fit) approximates a straight line.

Initial Method Comparison

Creatinine concentrations in the samples tested ranged from 46 to 962 µmol/L by the laboratory method. Table 2 summarises the method correlation statistics for the Nova StatSensor device versus the IDMS-aligned Roche enzymatic method, split by creatinine concentration.

Using a factory based calibration, StatSensor 1 (y) produced slightly lower results than the IDMS-aligned Roche enzymatic assay (x) for 62 samples with creatinine concentrations < 150 µmol/L (y = 0.96x -3.5, average bias -7.3, 95% limits of agreement -36 to +21 µmol/L). For 100 samples spanning the full concentration range, the StatSensor results were much lower (y = 0.75x +10.2, average bias -47.3, 95% limits of agreement -208 to +113 µmol/L). Patients on dialysis had significantly lower StatSensor creatinine results than the Roche enzymatic assay, as shown in Figure 1A. Similar findings have been reported at a recent conference (20-22), with interference from creatinine and urea described in one abstract (20), while the effect of haematocrit was ruled out as a cause of discordant results in another study (21)

Because of the underestimation of creatinine, eGFR results from StatSensor 1 were incorrectly categorised as > 60 mL/min for 7/53 patients (false normal results). There were no false abnormal results (eGFR < 60 mL/min) (Figure 2A and Table 3).

StatSensor 2 had very similar summary statistics, indicating a consistent factory calibration and analytical performance for the two instruments (n=98 pairs, average bias between StatSensors 0.7 µmol/L, two samples had insufficient volume for assay on both devices). However, as illustrated in Figure 3, for *individual* samples there was more variation in results than expected between the two POC analysers (95% limits of agreement -35 to +34 µmol/L for all samples and -16 to +17 µmol/L for samples with laboratory creatinine < 150 µmol/L).

Correction of Observed Method Bias

Using the Passing Bablok slope and intercept factors, the significant overall negative bias observed across the full creatinine concentration range with the factory-calibrated Nova 1 device was corrected using a reciprocal recalibration equation: Nova (recalibrated) = [Nova (factory calibration) x 1.3333] – 13.53 µmol/L. Method comparison statistics post recalibration are provided in Table 2.

StatSensor 1 eGFR results were then recalculated using the 175 MDRD equation and replotted against the IDMS-aligned laboratory eGFR (Figure 2B). Once Nova StatSensor 1 was recalibrated to the laboratory assay, eGFR ≥ 60 mL/min was correctly identified versus the laboratory assay for 37/47 patients (79%). There were 10 false abnormal results. eGFR < 60 mL/min was correctly identified for 51/53 patients (96%). There were 2 false normal results (Table 3).

Both before and after recalibration, however, we were concerned by the number of StatSensor creatinine results showing poor agreement with the laboratory method (Figure 1). Pre-dialysis results from one patient were omitted from graphs and statistical calculations because of very inconsistent results (lab 541,538: Nova, factory calibration 186,154 µmol/L).

DISCUSSION

Screening programs for early detection of CKD are increasing important because the burden of the disease continues to rise globally and many risk factors such as hypertension, smoking and obesity can be readily modified (3). In the United States, the Kidney Early Evaluation Program (KEEP) provides such a national screening agenda (23). As part of KEEP, creatinine (and eGFR) is measured at a central laboratory and results are returned to patients at a later date. Point-of-care testing for creatinine confers particular advantages for the CKD screening process as participants can be provided with immediate feedback on their kidney function during their community assessment. In Australia, the recent KEY study combined POCT for creatinine (and calculation of eGFR), glucose, haemoglobin A1c, cholesterol, and urine albumin:creatinine ratio (ACR) with family history, blood pressure and measurement of height, weight and body mass index as well as an exit interview with a renal nurse to provide an integrated on-site approach to targeted community-based CKD risk assessment (9). POCT was considered pivotal to the success of KEY, with greater than 96% of

participants stating POCT was convenient and helped them understand their results better (9). In the KEY study, creatinine was measured on an i-STAT device which proved useful and robust in this setting. However, for large scale risk assessment in settings such as pharmacies or workplaces, capillary whole blood is the sample of choice for creatinine measurement.

The Nova StatSensor device, which is simple to use and can measure creatinine using a fingerprick sample, has considerable potential for use in this niche but its analytical performance is of paramount importance in deciding its suitability for screening. Based on the results of this evaluation, agreement with laboratory creatinine results did not meet expectations, especially using the factory-based calibration. The device exhibited a significant negative bias at high creatinine concentrations, with wide limits of agreement compared to the well-established Roche enzymatic assay. The reason for some unusual divergences from laboratory creatinine results and falsely low results for patients undergoing dialysis requires further investigation. Imprecision (8.9%) exceeded established criteria at creatinine concentrations <150 μmol/L). For detecting eGFR less than 60 mL/min, the Nova StatSensor recorded a 13% (7/53) false normal rate, meaning these patients who had Stage 3 CKD would be missed.

Once Nova StatSensor 1 was recalibrated to the IDMS-aligned Roche enzymatic Hitachi assay, the number of false normal results decreased to 4% (2/53), however 21% (10/47) of results were now incorrectly classed as abnormal (ie eGFR < 60 mL/min). For community based programmes and hospital use, we consider that with recalibration this instrument will identify most patients with eGFR < 60 mL/min, but there will be many falsely low eGFR results that will require laboratory validation and contribute to unnecessary stress among patients.

Throughout the evaluation period, some further problems were experienced with the StatSensor method. These included poor reproducibility with certain batches of quality control material (not used in the imprecision studies) and instability with different reagent strip lot numbers.

In summary, the Nova StatSensor did not measure creatinine as well as expected, and we believe that the assay needs urgent improvement. Using the factory calibration, 18% of creatinine results below 150 umol/L differed by more than 20umol/L from the Roche enzymatic assay, and 62% of results above 150 umol/L differed by more than 20%. Many samples had large differences in creatinine results compared to the IDMS-aligned laboratory method (Figure 1), and this is concerning given international efforts to standardise creatinine results (5). Despite this, it could still be useful as a screening test for CKD in community and other settings, as the risk of missing CKD Stage 3 with recalibration of the instrument was < 5% in this study.

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Conflict of interest: The authors have no conflict of interest to declare.

Table 1. Nova StatSensor day-to-day method imprecision (n=20)

QC	Target	Acceptable range	Mean		SD		CV(%)		Range	
			Device 1	Device 2	Device 1	Device 2	Device 1	Device 2	Device 1	Device 2
Low QC	84	44 - 124	99.6	100.8	8.89	8.97	8.9	8.9	83 - 123	84 - 123
Mid QC	173	115 - 230	199.6	195.5	17.31	16.09	8.7	8.2	157 - 237	158 - 232
High QC	531	398 - 663	605.4	601.0	32.65	31.28	5.4	5.2	543 - 665	532 - 668

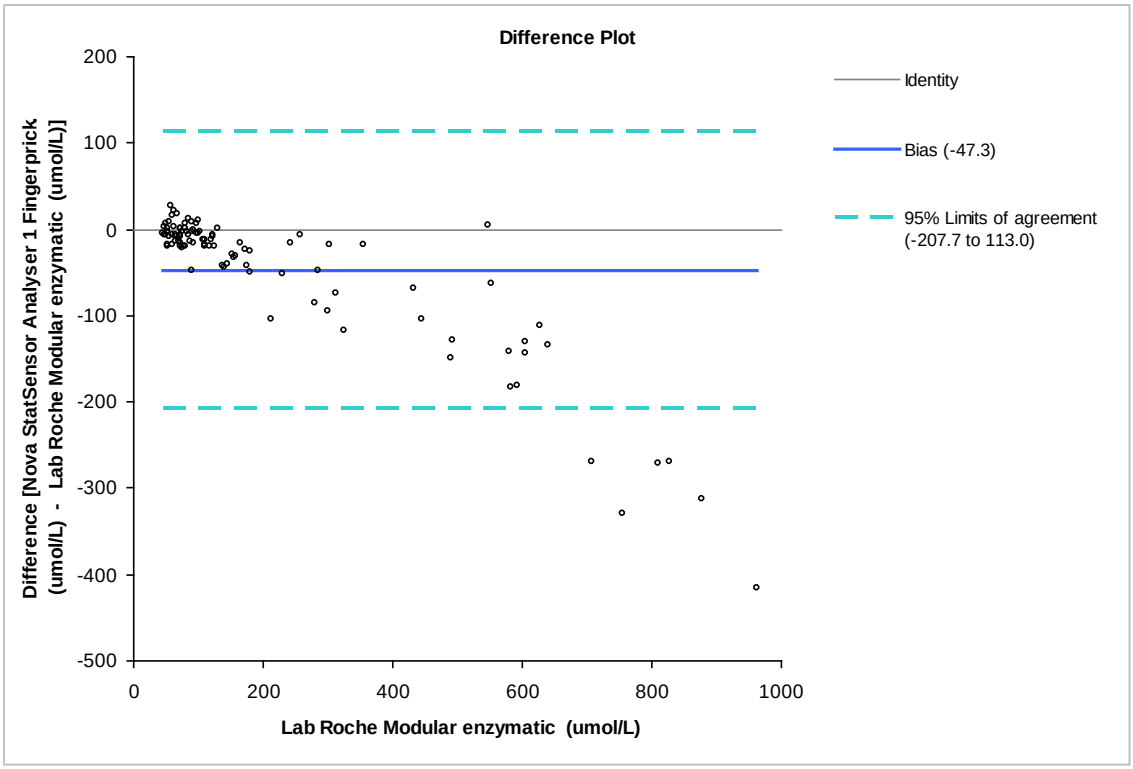
Creatinine units were µmol/L.
Devices 1 and 2 are two separate Nova analysers.
Acceptable range is that stated by the manufacturer.

Table 2. Method correlation statistics for the Nova (y) vs the IDMS-aligned Roche enzymatic creatinine method (x) before and after IDMS alignment.

Nova (y)	Creatinine Concentration (μmol/L)	PB Slope (95% CI)	PB Intercept (95% CI)	r	Mean (x) (range)	Mean (y) (range)	Mean bias (95% CI)	95% Limits of agreement	n
Factory Calibration									
Nova 1	<150	0.96 (0.82 to	- 3.5 (-14.5 to 7.5)	0.83	82.6 (46 to 144)	75.2 (32 to 131)	- 7.3 (-11.0 to - 3.6)	-35.9 to 21.2	62
Nova 2	<150	0.92 (0.77 to	2.4 (-9.1 to 12.8)	0.84	82.6 (46 to 144)	75.9 (31 to 125)	- 6.7 (-10.3 to - 3.1)	-34.8 to 21.3	62
Nova 1	All	0.75 (0.70 to	10.2 (6.2 to 17.4)	0.97	217.0 (46 to 962)	169.6 (32 to 566)	- 47.3 (-63.6 to -	-207.7 to 113.0	100
Nova 2	All	0.74 (0.69 to	14.0 (8.0 to 20.5)	0.97	209.8 (46 to 962)	163.4 (31 to 545)	- 46.5 (-63.6 to -	-213.7 to 120.8	98
After Recalibration									
Nova 1	<150	1.31 (1.12 to	- 19.9 (-36.0 to - 5.7)	0.83	82.6 (46 to 144)	86.8 (29 to 161)	4.2 (-0.2 to 8.7)	-30.1 to 38.5	62
Nova 2	<150	1.25 (1.08 to	- 12.3 (-27.4 to 0.3)	0.84	82.6 (46 to 144)	87.6 (28 to 153)	5.0 (0.8 to 9.3)	-27.5 to 37.6	62
Nova 1	All	1.00 (0.94 to	- 0.4 (-5.7-> 9.1)	0.97	217.0 (46 to 962)	212.6 (29 to 741)	-4.3 (-14.5 to 5.9)	-105.2 to 96.5	100
Nova 2	All	0.99 (0.93 to	4.5 (-3.7 to 12.7)	0.97	209.8 (46 to 962)	204.3 (28 to 713)	-5.5 (-16.4 to 5.3)	-111.3 to 100.3	98

Figure 1. Plot showing differences between Nova StatSensor 1 and laboratory Roche enzymatic creatinine results.

A. Nova StatSensor factory calibrated



B. Following laboratory recalibration of the Nova StatSensor 1

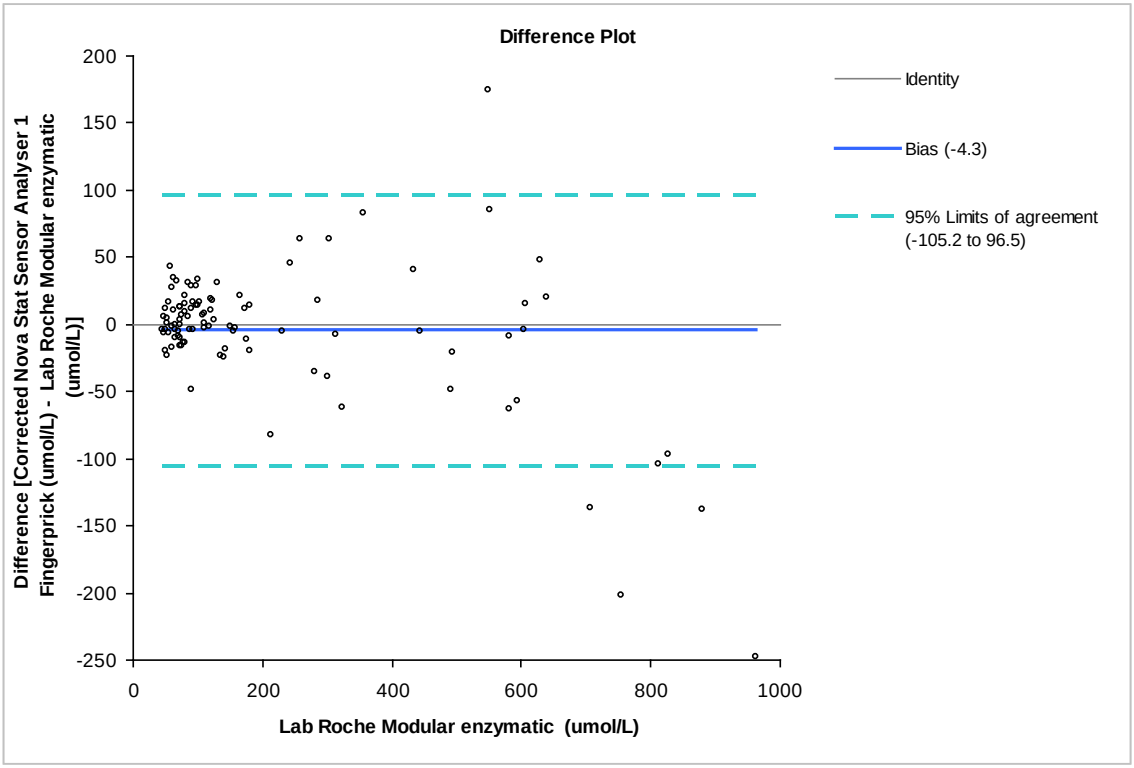
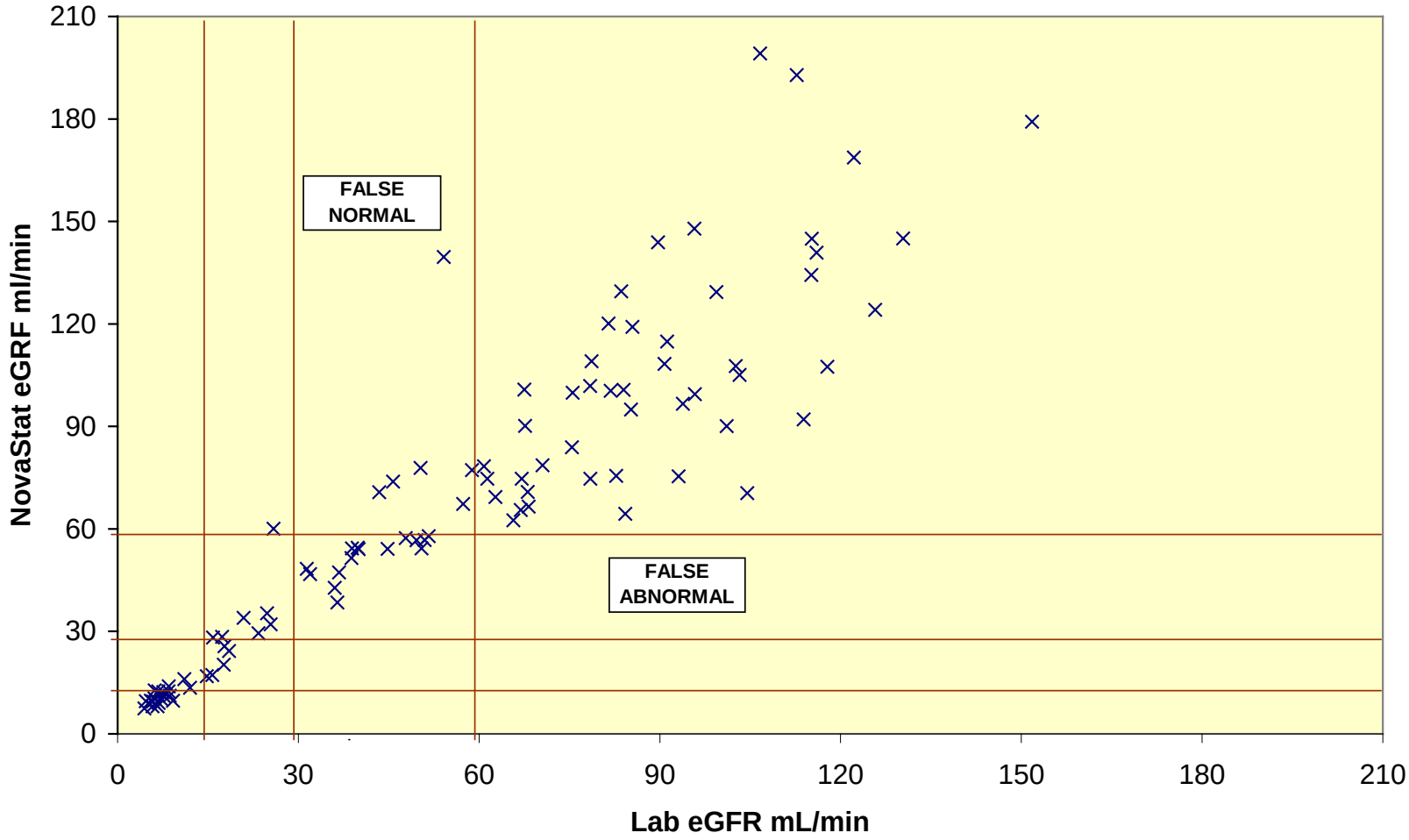


Figure 2. Plot of eGFR results from Nova StatSensor 1 versus the laboratory Roche enzymatic method

A. Nova StatSensor factory calibrated



B. Following laboratory recalibration of the Nova StatSensor 1

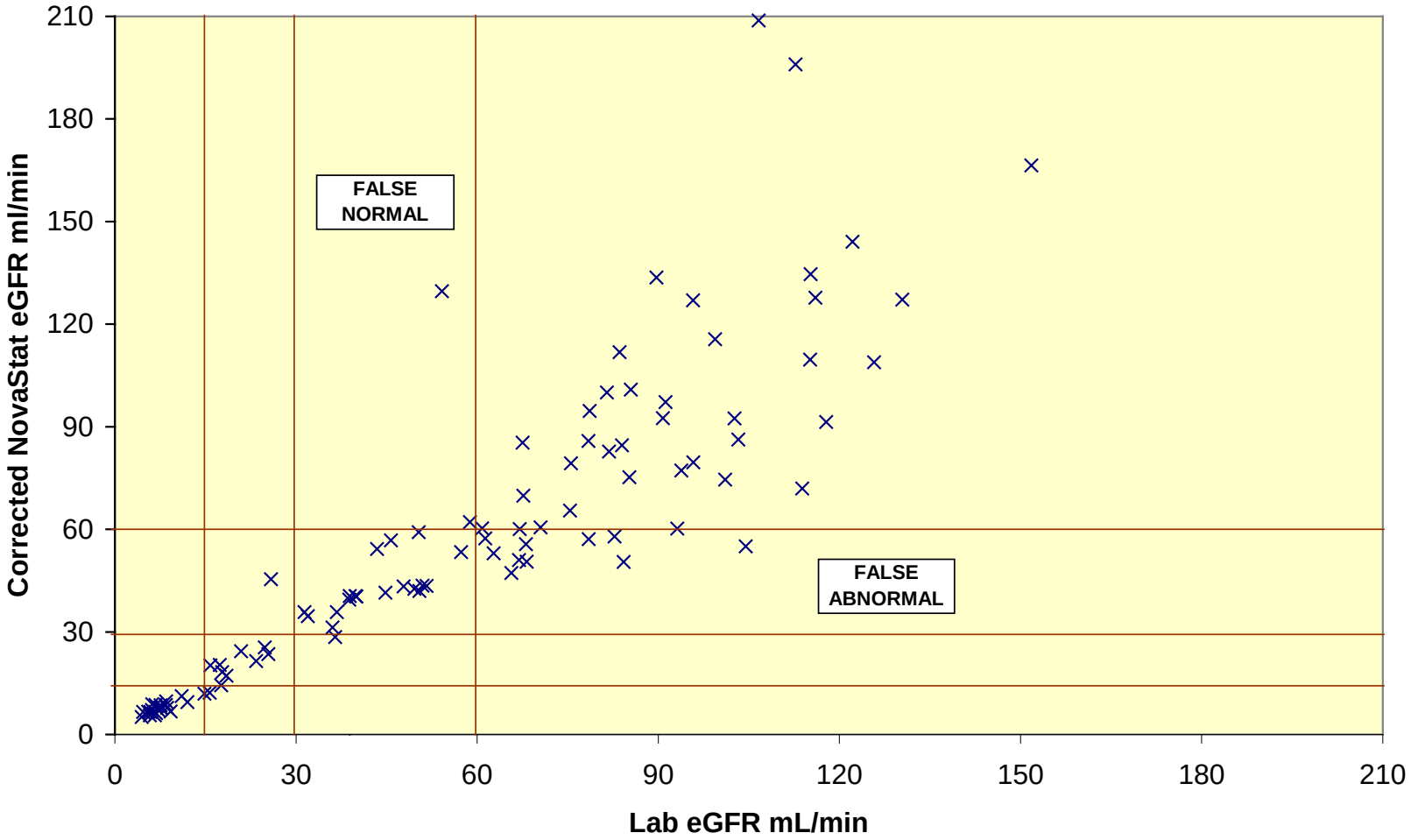


Figure 3. Difference between creatinine results on individual patient samples, when measured on both Nova StatSensor devices.

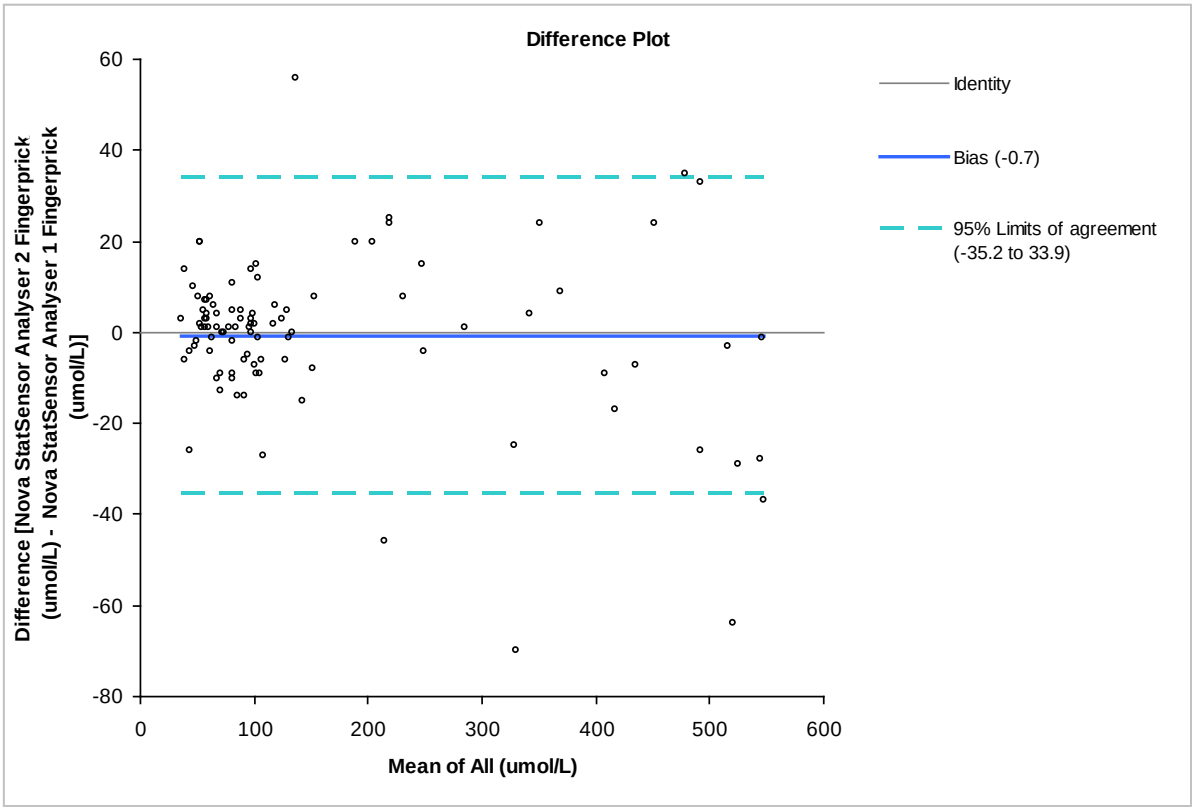


Table 3. Predictive values for Nova StatSensor versus Roche Hitachi enzymatic assay using an eGFR cut-off value of 60 mL/min to detect reduced kidney function

Device	Calibration	Sensitivity (%)	Specificity (%)	PV (+ve test) (%)	PV (-ve test) (%)
Nova 1	Factory calibration	86.8	100.0	100.0	87.0
Nova 2	Factory calibration	82.4	100.0	100.0	83.9
Nova 1	Post lab recalibration	96.2	78.7	83.6	94.9
Nova 2	Post lab recalibration	92.2	78.7	82.6	90.2

Positive test (reduced kidney function) eGFR < 60 mL/min; negative test eGFR >= 60 mL/min

4.1.2 Study 2: Evaluation of POCT analytical performance in setting of intended use – rural community screening

Spaeth, B, Shephard, A, Shephard, M & Mathew, T 2015, 'Assessment of a point-of-care device for measuring creatinine in a community screening program for chronic kidney disease', *Medical Research Archives*, no. 3, pp. 1-6. Available at: <http://www.journals.ke-i.org/index.php/mra/article/view/132>.

The next study aimed to re-evaluate the analytical performance of the Nova StatSensor creatinine device after modifications had been made by the device manufacturer based on the information provided by the first study. This time the POCT device was evaluated within a clinical setting of intended use; a community CKD screening program in a rural farming town with a population at risk of CKD.

Venous and capillary blood samples (n=109) were tested in duplicate on two StatSensor devices (by this author) with a venous sample also sent to the laboratory for measurement on a device with a method traceable to the IDMS reference method.

Analytical performance was assessed through calculations of accuracy and between-device imprecision with all analyses conducted by this author. Accuracy was assessed by comparing POCT results to the laboratory method with correlation and mean difference calculated using Passing-Bablok linear regression and Bland-Altman difference analyses respectively. The eGFR results from each StatSensor device were also used to stage CKD risk (stages 1-6 according to the level of kidney function/kidney damage) compared to the laboratory method.

Results for imprecision indicated the performance of the POCT device had not improved from the initial study with the POCT device now demonstrating a significant positive bias resulting in an underestimation of calculated eGFR and the misclassification of CKD risk in more than 40% of patients on both POCT devices. A statistically significant difference between creatinine results on each StatSensor device was also detected ($p<0.001$). Therefore, the analytical performance of the StatSensor device remained unacceptable despite the manufacturer's purported improvements to the device test method.

This study was the first to evaluate the Nova StatSensor creatinine device in a clinical setting in Australia using both capillary and venous blood samples. The results of both evaluations of the Nova StatSensor device are consistent with other studies evaluating analytical quality using venous whole

blood samples (Haneder et al. 2012; Korpi-Steiner, Williamson & Karon 2009; Kosack et al. 2015). In contrast, several studies considered the StatSensor to have acceptable analytical performance, however, many of these studies failed to compare POCT analytical performance to goals for analytical quality or to an IDMS-aligned laboratory method. Many of the studies used only a small number of patient comparisons or repeat tests for calculations of accuracy and imprecision, therefore limiting the outcomes of these studies.

This study again highlights the importance of rigorous evaluations of POCT device analytical performance. This study was undertaken in a clinical setting where it was intended to be routinely used, however, POCT was performed by a trained medical scientist (this author) and may not accurately reflect device performance when used by non-technical trained staff. For this reason, it is recommended to evaluate analytical quality under 'real-life' conditions to assess how the POCT device will perform in the clinical setting.

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1. **Publication Details:** Assessment of a Point-of-Care Device for measuring creatinine in a community screening program for chronic disease, Published in the Medical Research Archives, 2015;3:1-6.

Section of the thesis where the publication is referred to: Throughout the entire thesis

Candidate's (Brooke Spaeth) Contribution to the publication:

Research Design: 25%

Data Collection and analysis: 70%

Writing and editing: 50%

Outline your (the candidate's) contribution to the publication:

Prof Mark Shephard and Timothy Mathew worked collaboratively on the development of the research design with input from other co-authors. Brooke Spaeth conducted the data collection and analysis with assistance from Anne Shephard.
Brooke and Mark provided the first draft of the manuscript with editing from Anne and Timothy.

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ASSESSMENT OF A POINT-OF-CARE DEVICE FOR MEASURING CREATININE IN A COMMUNITY SCREENING PROGRAM FOR CHRONIC KIDNEY DISEASE

Brooke Ann Spaeth, Anne K Shephard, Mark DS Shephard, Timothy H Mathew

ABSTRACT

Background: Chronic kidney disease (CKD) is a major contemporary global health problem. Creatinine measurement for the calculation of estimated glomerular filtration rate is an important component of assessing CKD risk. A point-of-care test for creatinine using capillary sampling is required as part of a screening assessment.

Objectives: Evaluate the analytical performance of a modified point-of-care testing method for whole blood creatinine (Nova Biomedical StatSensor whole blood creatinine analyser) relative to a laboratory method.

Design and methods: Conduct a patient comparison study between the point-of-care testing and laboratory methods in a rural community setting. Calculate measures of imprecision and assess the ability of the POCT method to determine staging of CKD compared to the laboratory.

Results: Between-device imprecision averaged 8.8%. The StatSensor devices showed a positive bias of approximately 14% for whole blood creatinine measurement compared to the laboratory method, leading to more than 40% of community patients being staged differently for CKD risk with approximately 25% more abnormal results.

Conclusions: The StatSensor whole blood creatinine point-of-care device remains analytically unsound for use as a screening device for CKD.

Key Words: chronic kidney disease; point-of-care testing; creatinine; estimated glomerular filtration rate.

BACKGROUND

The burden of chronic kidney disease (CKD) continues to increase both in Australia and throughout the world [1- 6]. A recent article highlighted the evolving importance of chronic kidney disease – "from subspecialty to global health problem" [1]. CKD is often described as a 'silent' disease due to its asymptomatic nature. In Australia, approximately 10% of adults presenting to their family practice have CKD and 80% have at least one risk factor for CKD [7]. Kidney Health Australia, in partnership with Flinders University International Centre for Point-of-Care Testing, has undertaken targeted screening in primary care settings for members of the general population considered at high risk for CKD through an initiative called KEY (Kidney Evaluation for You) [8]. The screening strategy incorporates the use of point -of-care testing for markers of risk including blood creatinine, urine albumin:creatinine ratio (ACR), and blood pressure [9]. Creatinine measurement provides an estimate of the glomerular filtration rate (eGFR), which can be used to stage CKD [10-12]. The Abbott i-STAT device (Abbott Point of Care, Princeton, NJ, USA) has been the device of choice for point-of-care creatinine measurements in KEY due to its analytical reliability [5]. However the i-STAT requires 60 µL of venous whole blood to measure creatinine. For patient convenience, a POC device that uses capillary (fingerprick) whole blood would provide a more practical option for primary-care based CKD screening. In 2010, we evaluated the Nova StatSensor (Nova Biomedical, Waltham, MA, USA) hand- held POC device for creatinine, which used 1.2 µL of capillary whole blood and provided a creatinine (and associated eGFR result) in 30 seconds. However, its analytical performance did not meet specifications for both precision and accuracy [13]. The manufacturer of the device subsequently made amendments to the device designed to improve its analytical performance characteristics. We re -evaluated the modified device in a rural community setting as part of the KEY program and the findings of this study are reported here.

DESIGN AND METHODS

Setting

The device evaluation was conducted as part of a community screening event held by Kidney Health Australia for citizens over the age of 50 years from the rural farming town of Kyabram, 200 kilometres north of Melbourne, Victoria, Australia. The surrounding community has a population of approximately 12,000 people, of which 2% are of Aboriginal descent [14].

Patient Samples

Venous and capillary whole blood samples were collected from 111 community participants (35 male, 76 female, mean age 68 years). After consent was obtained, a venous whole blood specimen was collected into a lithium heparin anticoagulant tube and sent to the nearest laboratory (Monash, Melbourne, Victoria) for analysis of plasma creatinine. A capillary specimen was then obtained and immediately analysed on two StatSensor creatinine analysers (Nova Biomedical, USA) using the same reagent strip lot number.

Test method

To perform the point-of- care test for creatinine, the reagent strip was inserted into the analyser prior to sample application. Calibration information is encoded within this strip. Whole capillary blood was then applied to the reagent strip and the creatinine result was displayed in 30 seconds. Finger-prick analyses were conducted according to manufacturer instructions by a trained medical scientist (BS). Quality Control testing was performed at the beginning and at the end of each day of screening using the manufacturer's recommended quality control material.

Comparative laboratory method

Venous whole blood samples were sent to the laboratory and measured on a Beckman UniCel® DxC800 Synchron (Beckman Coulter, Australia) using the Jaffe rate method to determine the

concentration of creatinine. This method is traceable to the isotope dilution mass spectrometry (IDMS) reference method.

Accuracy

The point -of-care creatinine result on each StatSensor analyser was compared to the creatinine result from the laboratory method using Passing Bablok linear regression analysis. Differences between results were plotted against the laboratory method using Bland Altman difference analysis. Estimated GFR on the StatSensor (using CKD-EPI equation) was also plotted against eGFR from the laboratory method [15]. The staging of CKD using the StatSensor eGFR was then compared to the laboratory staging of CKD.

Statistical Analyses

Statistical analyses were performed using the statistical package Analyse-it for Microsoft Excel (clinical laboratory version 2.21).

RESULTS

Imprecision

Between device imprecision (calculated from matched patient results from each StatSensor device) was 8.8% (capillary blood, creatinine range 50 to 212 µmol/L, n=109).

Method comparison

Creatinine concentrations in samples tested by the laboratory ranged from 48 to 168 µmol/L (mean 83 µmol/L). Table 1 summarises the method correlation statistics for StatSensor devices 1 and 2 versus the laboratory (Jaffe) method.

Table 1 - Method correlation statistics for the StatSensor versus the laboratory method.

Device	PB[a] Slope	PB[a] Intercept	r[b]	Mean Laboratory Creatinine (µmol/L)	Mean StatSensor Creatinine (µmol/L)	Mean Bias (µmol/L)	95% limits of Agreement (µmol/L)	n
StatSensor 1	1.21	0.71	0.81	83	99	16.4	-12.1 to 44.8	109
StatSensor 2	1.18	-4.02	0.84		93	10.1	-16.2 to 36.4	109

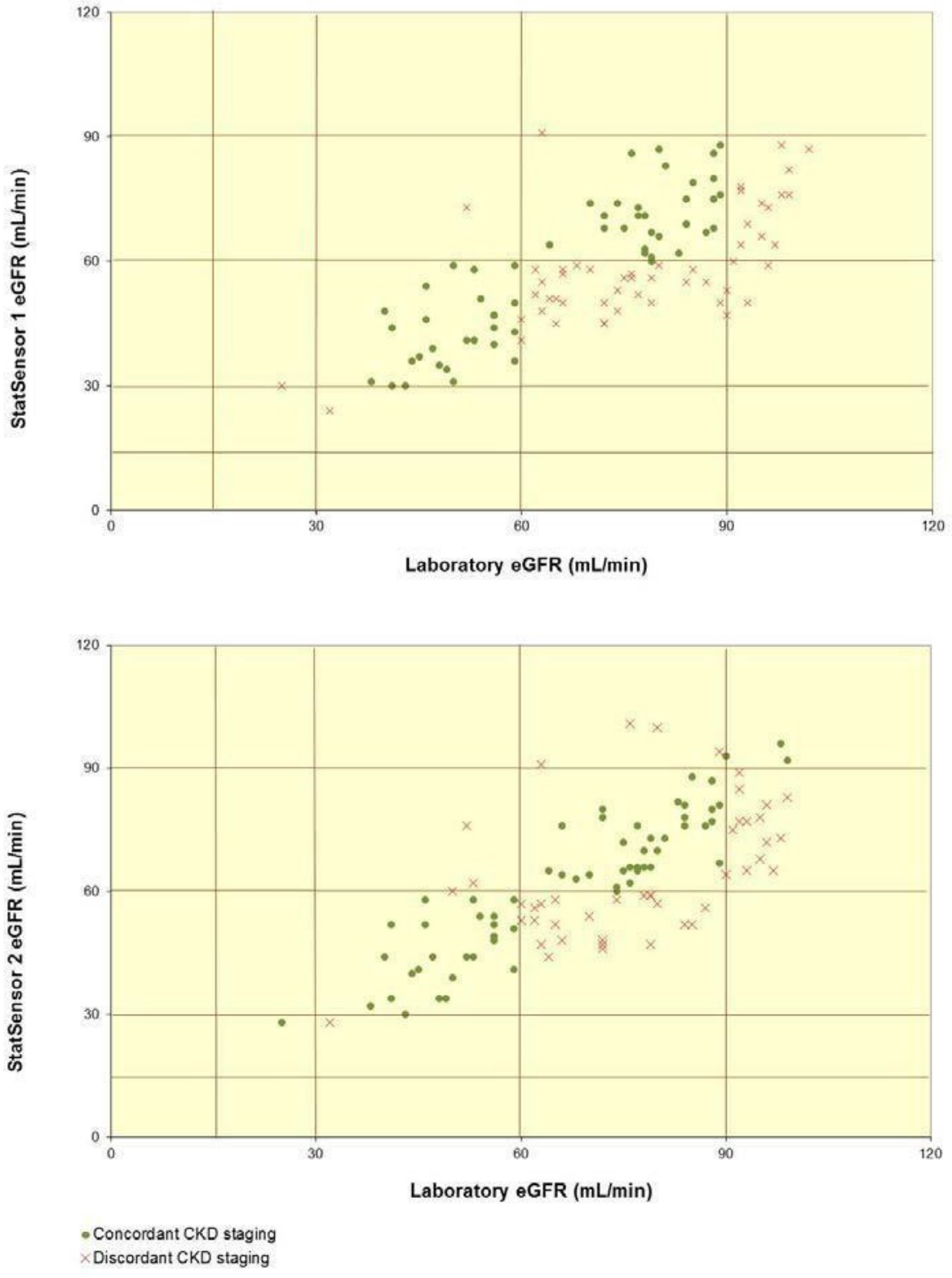
[a] PB = Passing Bablock linear regression.

[b] r = correlation coefficient.

Both StatSensor analysers produced higher results than the laboratory method (average bias 13.7%) and there was a statistically significant difference between creatinine results on the two analysers (paired t test $p<0.001$).

Due to the over estimation of creatinine values with the StatSensor (and therefore an underestimation of eGFR values [EKD-EPI]), 48% of patients were staged differently for CKD with StatSensor 1 and 41% with StatSensor 2 (see Fig. 1) compared to the staging of CKD from laboratory results. There were 31% more (34 participants) abnormal results (eGFR <60) with StatSensor 1 and 21% (23 participants) more abnormal results with StatSensor 2 compared to laboratory results. One patient (0.9%) with StatSensor 1 and three patients (2.8%) with StatSensor 2 had normal eGFR results (>60) from StatSensor testing but abnormal eGFR on laboratory testing (see Fig. 1).

Fig 1: Plot of eGFR (mL/min) for Nova StatSensor 1 and 2 versus laboratory method.



DISCUSSION

With the global prevalence of CKD continuing to escalate, the need for simple, minimally invasive screening tests for identifying CKD risk is becoming increasingly important. An analytically sound whole blood creatinine measurement that can be performed using finger-prick sampling would be most useful in this context. The StatSensor creatinine analyser fits many of the criteria for a screening device, given it is hand- held, requires a small sample volume, is battery operated and has the onboard capacity to automatically convert creatinine concentration to an eGFR value. However, in a previous evaluation of this device conducted in a hospital environment, we found its analytical performance was poor. The results of the current study, conducted in a rural primary care setting, indicate that the modified StatSensor devices still do not meet analytical specifications. Between-device imprecision had not improved (7.8% in the original evaluation and 8.8% in the present study) and creatinine results varied significantly between the two analysers. Based on this current study the StatSensor device is unsuitable for use as a screening tool in routine practice.

CONCLUSIONS

Despite the efforts of the company to improve the performance of the device, the findings of this study indicate the StatSensor whole blood creatinine device remains analytically unsound for use as a screening device for CKD.

SOURCES OF SUPPORT THAT REQUIRE ACKNOWLEDGEMENT:

Nova Biomedical provided devices, reagents and quality control materials to support the point-of-care testing conducted in this project and provided financial support for laboratory analysis of venous samples.

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4.1.3 Study 3: Evaluation of POCT analytical performance in the setting of intended use – remote primary health care

Spaeth, B, Shephard, M, McCormack, B & Sinclair, G 2015, 'Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory', *Pathology*, vol. 47, no. 1, pp. 91-5. DOI 10.1097/Pat.0000000000000202.

The third analytical evaluation was conducted in the setting of intended use (remote primary health care services) with all POCT conducted by personnel who would operate the device if routinely implemented (remote area nursing staff). This study assessed the analytical performance of the HemoCue WBC DIFF which measures a total and 5-part differential WBC count. As outlined in the contextual statement, while several studies had previously evaluated this POCT device and found it to have acceptable analytical quality, this study was the first to evaluate the device in a remote primary health care setting using both capillary and venous samples. Moreover, this evaluation occurred in an environmentally challenging location and in a primarily indigenous community in Australia's remote NT.

Accuracy was determined by comparing WBC DIFF results from both capillary and venous whole blood samples on 53 patients to the results of a laboratory method measuring WBCs on venous whole blood samples. Passing-Bablok and Bland-Altman analyses were performed by this author to determine the correlation and mean difference between POCT and laboratory results.

The analyses indicated that both capillary and venous POCT results correlated well with laboratory results for all WBC types, except for monocytes. However, results from capillary blood samples demonstrated a negative bias for neutrophils and a positive bias for lymphocytes. Poor performance was observed for monocytes and eosinophils, however, all results for these cells types were either very low or zero. A limitation of this study is the samples tested by the laboratory travelled for between 12 and 24 hours over a distance of more than 2000kms before they were tested. This may have affected the integrity of the samples tested by the laboratory, and hence, the comparison results. However, this study did identify a significant pre-analytical issue with the pathology service delivery using the laboratory system as 11% of pathology reports for WBC from this remote location were returned with comments indicating the specimens did not reach the laboratory in time (<36 hours) for accurate measurement. Note these results were not used in the accuracy analysis.

HemoCue WBC DIFF device imprecision was determined by repeat analysis of three blood samples with low, normal and high numbers of total WBC (testing and analysis conducted by this author). The imprecision for all WBC types was acceptable, except for monocytes and eosinophils, where again only very low or zero results were obtained for these cell types.

Interviews of key staff involved in the evaluation stated the HemoCue WBC DIFF device was easy to use and clinically useful due to the high rates of chronic and acute infections in this setting. The POCT device was determined to be suitable for use in remote primary health care settings, however, it was recommended that results from capillary specimens should be interpreted with caution with venous sampling being the recommended sampling method.

Once a POCT device is determined to have acceptable analytical performance in the setting of intended use, systems and processes can be developed in preparation for its implementation for its routine clinical use.

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1. **Publication Details: Spaeth BA, Shephard MDS, McCormack B, Sinclair G,** Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory, Published in Pathology, 2015;47(1):91-95.

   Section of the thesis where the publication is referred to: Throughout the entire thesis.

   Candidate's (Brooke Spaeth) Contribution to the publication:

   Research Design: **90%**

   Data Collection and analysis: **70%**

   Writing and editing: **80%**

   Outline your (the candidate's) contribution to the publication:

Brooke Spaeth designed the research project with supervision from Mark Shephard. Brooke assisted with data collection and provided the main analysis of data. Brooke provided the first draft of the manuscript and approved the final version. Mark Shephard supervised research design, assisted with data analysis and provided edits to the final version of the manuscript.
Beverley McCormack provided the data collection and edits the final version of the manuscript.
Dr Gary Sinclair assisted with the collection of data and provided edits to the final version of the manuscript.

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Evaluation of HemoCue white blood cell differential counter at a remote health centre in Australia's Northern Territory

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Sir,

The total white blood cell (WBC) count and differential is a frequently ordered pathology test to detect infection, inflammation or as part of a full blood count or complete blood count in a routine health assessment.1 Differentiation of the number of white blood cells into subtypes (neutrophils, lymphocytes, monocytes, eosinophils and basophils) provides additional clinical information; for example, to distinguish between a potential bacterial, viral or parasitic infection.[2]

Traditionally the differential WBC count is measured by automated laboratory cell counters. The ability to measure a differential WBC count by point-of-care testing (POCT) would be useful in extra-laboratory (e.g., emergency departments and outpatient clinics) and primary care (e.g., general practices and Aboriginal Medical Services) settings where the convenience, accessibility, portability and immediacy of the POCT result would be advantageous.[3]

In 2008, HemoCue AB (Sweden) developed a POCT device for total WBC count. In 2012, this device was further refined to additionally provide a 5-part differential count. In this study we examined the

analytical performance characteristics and usefulness of the HemoCue WBC Diff counter in a remote Aboriginal medical service, where access to pathology services is difficult due to the geographical isolation from the nearest laboratory and the high burden of infection among its Aboriginal community members.

The study was implemented in a remote Indigenous com- munity in Australia's Northern Territory, located over 600 km from the nearest major town and laboratory service (Mt Isa, Queensland). The community has a population between 500 and 800 people, of which 94% are Aboriginal.[4] The Remote Health Centre is serviced by two Remote Area Nurses (RAN) and a visiting medical practitioner. During the wet season the community is frequently cut off via road due to flooding.

Ethics registration for this project was obtained in March 2013 from the Menzies School of Medicine Ethics Committee. Informed verbal consent was obtained from each patient routinely presenting to clinic with symptoms indicating a WBC count was needed. Patient participation in the study was voluntary.

A 10 mL sample of capillary or venous blood is loaded into a HemoCue WBC Diff microcuvette. The red blood cells are lysed and the WBCs stained with methylene blue. Thirty seven images are then taken of the stained WBCs using microphotographs, images are focused and mathematical algorithms classify and count cell types. Total WBC and a 5-part differential count are displayed in less than 5 min. The measuring range for the total WBC count is 0.3–30 x 10^9/L. The analyser is small, lightweight and portable (size 190 160 160 mm, weight 1.3 kg). The analyser operates by batteries or by AC power adaptor and has external connectivity capability.

Venous whole blood samples sent to the laboratory were measured on a Sysmex XE-2100 analyser (Sysmex America, USA). Fluorescent labelling is used to measure the nucleus- plasma ratio of each individually stained cell, enabling differentiation and reporting of six WBC populations. The XE-Series utilises an adaptive cluster analysis system (ACAS) to separate cell populations into well-defined three-dimensional clusters. This study comprised 62 adult patients routinely presenting to

clinic with symptoms indicating a WBC differential count was needed. Each patient result was recorded using a unique code number to maintain confidentiality in the study.

The Flinders University International Centre for Point-of-Care Testing (ICPOCT) developed a training resource package and delivered on-site training to the clinical team at the health service. A RAN collected the venous sample to be sent to the laboratory and tested a small aliquot of the venous sample on the WBC Diff prior to dispatch to the laboratory. A fingerpick capillary sample was also taken at the same time from each patient and tested on the WBC Diff on-site. The venous sample was then sent via Mount Isa to the nearest accredited pathology laboratory in Brisbane some 2000 km from the remote community. The average transport time was between 12 and 24 h, while the turnaround time for the result to be reported to the treating doctor at the remote health service was between 4 and 7 days.

Results of POCT performed on both venous and capillary samples and comparative laboratory test results were entered into an Excel spreadsheet for subsequent statistical analysis. To assess accuracy, Passing–Bablok linear regression analysis (to calculate the slope, intercept and correlation coefficient) and Bland–Altman analysis (to calculate mean bias, 95% confidence intervals and mean % bias) were performed on the comparison patient data using the Analyse-It statistical software program (UK; http://analyse-it.com).

Three patient samples (with differing total white cell counts of 3.5 x 10^9/L, 11.5 10^9/L and 23.5 x 10^9/L, designated low, normal and high) were analysed 20 times each on the same day (and within 12 h of collection) to calculate within- day imprecision. For imprecision, the coefficient of variation (CV%) was calculated for each sample and compared to the analytical goals for each cell type set by the Royal College of Pathologists Quality Assurance Program Pty Ltd (RCPA QAP).

Of the 62 patients tested at the clinic, seven were excluded as venous samples did not reach the laboratory within their specified transport times and sample integrity could not be guaranteed. Two samples were excluded in the capillary comparison as an error relating to the image being out-of-

focus was obtained on the POCT device and a repeat sample could not be obtained. The remaining 53 matched sets of data were analysed for the capillary POCT versus laboratory comparison, while 55 matched sets of data were available for venous POCT versus laboratory comparison. The 62 patients comprised 32 males and 30 females, while the age range of the patient group was 19–83 years.

The results of the Passing–Bablok analysis are shown in Fig. 1. For both the capillary and venous whole blood comparisons, the correlation coefficient (r) was >0.75 for all cell types except monocytes. Results of Bland–Altman analysis for capillary and venous POC samples versus the laboratory method are shown in Table 1. The mean percentage difference between capillary (y) and venous (x) POCT results for each cell type was: total WBC 2.8%, neutrophils 2.6%, lymphocytes 12.5%, monocytes 4.2% and eosinophils – 10%. The results of within-day imprecision studies (*n* = 20) conducted on three patient samples with differing total WBC counts are summarised in Table 2.

Table 1 - Summary of Bland–Altman analysis, comparing capillary and venous POCT results with laboratory results

Cell type (x10^9/L)	Sample type	Number	Mean lab value	Range of values	Mean bias	95% confidence intervals	Mean % bias
WBC Count	Capillary	53	7.90	3.9 to 14.2	−0.38	-0.83 to 0.07	−4.8%
	Venous	55	7.80	3.6 to 12.9	−0.45	−0.73 to −0.16	−5.8%
Neutrophils	Capillary	53	4.60	1.3 to 7.7	−0.66	−0.97 to −0.35	−14.3%
	Venous	55	4.65	1.9 to 10.4	−0.46	−0.68 to −0.24	−9.9%
Lymphocytes	Capillary	53	2.47	1.3 to 4.1	0.39	0.26 to 0.53	15.8%
	Venous	55	2.28	1.2 to 3.8	0.12	0.02 to 0.23	5.3%
Monocytes	Capillary	53	0.54	0.1 to 1.3	−0.1	−0.17 to −0.03	−18.5%
	Venous	55	0.52	0.2 to 1.2	−0.11	−0.19 to 0.03	−21.2%
Eosinophils	Capillary	53	0.29	0 to 0.9	−0.043	−0.072 to −0.015	−14.8%
	Venous	55	0.30	0.1 to 1.1	0	−0.03 to 0.02	0.0%

Table 2 - Observed within-day imprecision for total WBC and their subtypes for three patient samples

Cell Type	WBC			Neutrophils			Lymphocytes			Monocytes			Eosinophils		
Sample (n=20)	L	N	H	L	N	H	L	N	H	L	N	H	L	N	H
Mean (x109/L)	3.4	10.5	23.5	2.8	4.8	20.3	0.2	4.9	2.0	0.2	0.74	0.9	0.2	0.09	0.2
SD	0.28	0.28	0.61	0.13	0.22	0.74	0.06	0.24	0.24	0.07	0.11	0.22	0.12	0.03	0.06
CV%	8.3	2.7	2.6	4.8	4.7	3.7	24.7	4.9	11.7	37.8	14.8	24.7	52.3	34.2	33.7

CV, coefficient of variation; H, high total WBC count; L, low total WBC count; N, normal total WBC count; SD, standard deviation.

For all total and differential cell counts with a mean cell number greater than 4 x 10^9/L, the imprecision was less than 5%. For cell counts with a mean cell number between 0.5– 4 x 10^9/L, the imprecision was less than 15%. For individual cell counts with cell numbers <0.5 x 10^9/L, the imprecision was greater than 20% in all cases.

High levels of imprecision were reported for monocytes and eosinophils due to the very low number of cells present; for example, a CV of 34% was reported but all repeat tests results were either zero or 0.1 x 10^9/L. The basophil count was not included in the data analysis as none of the patient samples had a basophil count above 0.1 x 10^9/L (>1%).

The analytical performance characteristics for the total WBC and differential cell counts were generally acceptable, except for monocytes. The results for basophils were not reported in this study due to low cell numbers in the samples tested. Basophils and monocytes counts are commonly imprecise, even for automated laboratory analysers,[5] due to the relatively low numbers of cells present and similarities between monocytes and other cells that may interfere with the count (such as abnormal or atypical lymphocytes). Poor performance of monocyte counts on the HemoCue WBC Diff has also been reported previously in peer-reviewed publications in the Netherlands and United States.[6–8]

This device evaluation was performed in one of the most remote and challenging environments for POCT in Australia. Observed differences between POCT and laboratory results may result in part from long transport/turnaround times for venous samples to reach the laboratory (2000 km away). Supporting this premise, 11% of venous samples collected did not reach the laboratory in time to be accurately measured (>36 h).

A limitation of this study was that there were very few acute patient presentations at the remote health service with low (<4 10^9/L) or high (>11 10^9/L) total WBC counts and therefore we cannot comment authoritatively on the accuracy of the HemoCue WBC Diff at these levels.

The RAN performing the HemoCue tests commented that the analyser was ‘easy to use’ and the

clinician involved commented that the 'levels of imprecision observed would not change clinical judgement'.

The logistical difficulties in transporting pathology samples from remote communities to the nearest pathology laboratory can often compromise the integrity of the sample, and lead to a patient's results being suppressed. Being able to perform tests at the point of patient care (providing it is of equivalent analytical standard) can improve the operational effectiveness of pathology testing delivery. The ability to measure a total WBC and a differential count on-site in a remote community provides a convenient and accessible service for the patient and obviates the need for follow-up visits by the patient. It also has clinical benefits for patient care in terms of timeliness of results enabling more rapid initiation of treatment of infections. The HemoCue WBC Diff was shown in this study to be a user- friendly POCT device by its clinical stakeholders and has demonstrated generally sound analytical performance for total WBC and differential count (except for monocytes), making it a useful surrogate analyser for use in remote communities.

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The authors state that there are no conflicts of interest to disclose.

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Figure 1 – Comparison plots for the HemoCue capillary and venous samples versus laboratory method (Sysmex XE-2100)

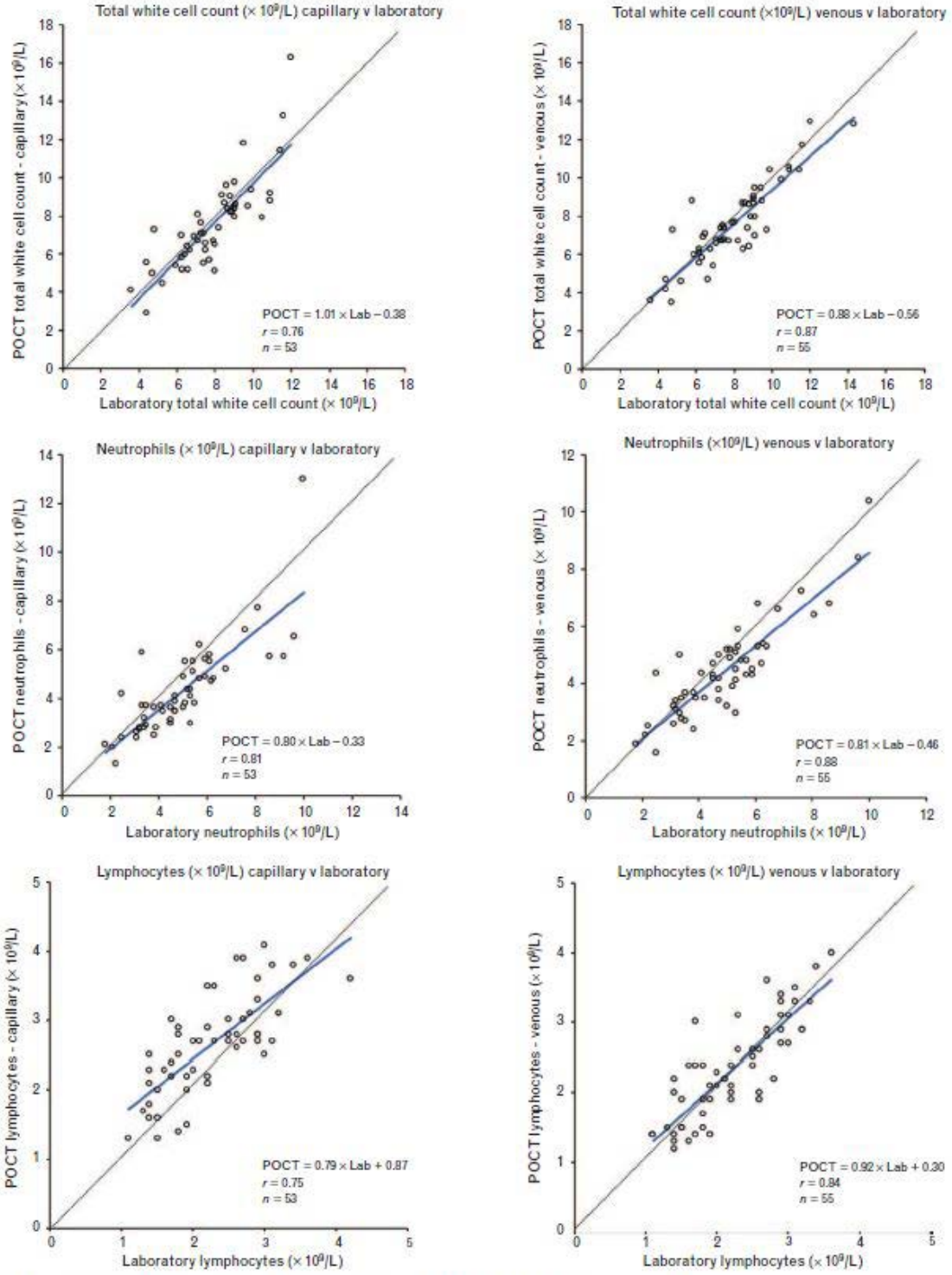
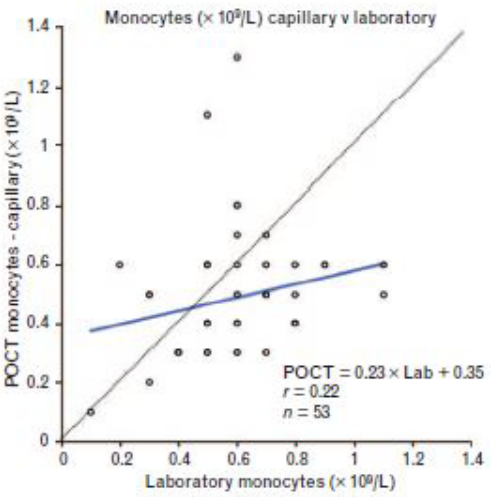
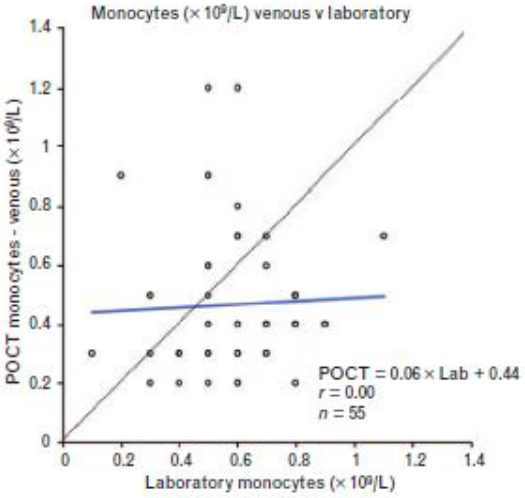
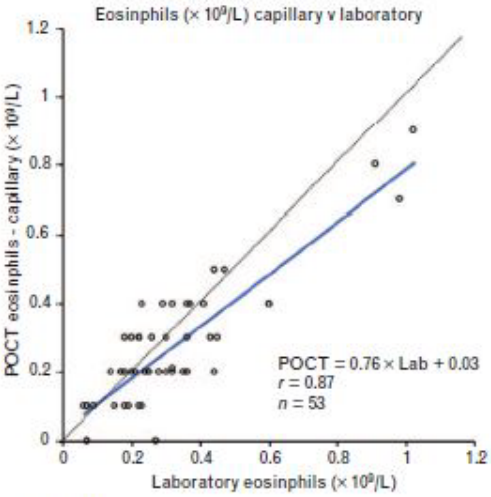
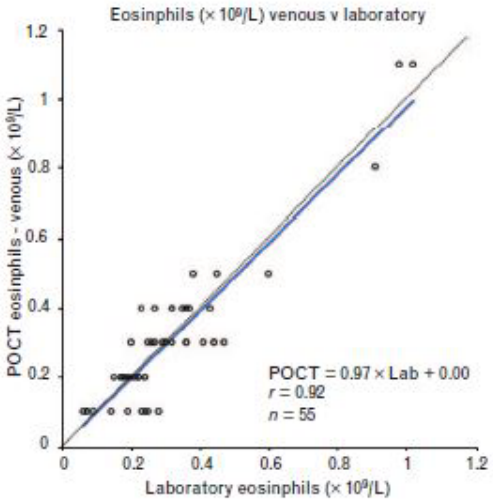


Figure 1 (continued)









4.2 Implementation of a POCT program

4.2.1 Study 1: Implementation of POCT program in a remote primary health care setting

Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Loudon, J, Rigby, J & Daniel, V 2012, 'Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program', *Australian Journal of Rural Health*, vol. 20, pp. 16-21. DOI 10.1111/j.1440-1584.2011.01243.x.

The next study describes the methods and process designed for implementation of the NT POCT Program for acute and chronic care in remote primary health care services of the NT using the Abbott i-STAT device. The reasoning for the POCT being implemented and the justification for the POCT device chosen was provided in the introduction to this thesis.

As outlined in the manuscript, and discussed in detail in the contextual statement, key processes for POCT training, quality management, surveillance of on-site POCT and governance were implemented and tailored specifically for the remote primary care setting.

Operational effectiveness was demonstrated by an increasing number of POC tests and a significant number of remote health professional staff completing POCT training in the first year of the Program.

A quantitative survey of remote health professional staff was conducted to determine the level of satisfaction with pathology services before and after the i-STAT device was introduced. This survey indicated levels of satisfaction with pathology testing increased after the introduction of POCT. Most notably, satisfaction with the timeliness of pathology testing increased significantly post implementation of POCT ($p<0.001$). As previously discussed, the modest response rate to the was, at least in part, attributed to the high rate of staff turnover (33%) at the remote health services in the first year of the Program.

The rate of staff turnover was determined to one of the greatest challenges for sustaining the remote NT POCT program in terms of maintaining operator training and ensuring quality testing procedures were adhered to in a timely manner. As highlighted in the discussion of this study, several approaches were implemented to address these obstacles (with the methods and results for

these novel approaches being included in later studies related to the sustainability of the NT POCT Program).

The survey of health professional also provided preliminary data on the operational effectiveness and clinical utility of the i-STAT device in the remote NT. For example, 95% of respondents indicated that POCT was more convenient than laboratory testing. Also, a significant number of respondents indicated the i-STAT had assisted in stabilising acutely ill patients (84%) and improved medication compliance for patients with chronic disease (58%). These findings formed the basis of further studies providing a more in-depth examination of operational and clinical effectiveness in this setting.

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1. **Publication Details:** Design, implementation and initial assessment of the Northern Territory Point-of-Care Testing Program, Published in the Australian Journal or Rural Health, 2012;20(1):16-21.

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Research Design: **70%**

Data Collection and analysis: **90%**

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Outline your (the candidate's) contribution to the publication:

Brooke and Prof Mark Shephard worked collaboratively on the development of the research design.
Brooke was supervised by Prof Mark Shephard in the data collection and analysis process.
Brooke completed the initial draft of the manuscript. Prof Mark Shephard provided major editing of the manuscript. Co-authors Beryl Mazzachi, Malcolm Auld and Steven Schatz provided minor edits to the draft manuscript and approved the final version.

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Design, Implementation and Initial Assessment of the

Northern Territory Point-of-Care Testing Program

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ABSTRACT

Objective: To improve pathology services in selected remote health centres from the Northern Territory (NT) through the implementation of a quality managed point-of-care pathology testing (POCT) service.

Design: Study of the efficacy of the POCT service after one year and qualitative survey of POCT device operators.

Setting: Thirty three remote health centres in the NT administered by the NT Department of Health.

Participants: Remote health centre staff at participating remote health centres.

Interventions: The introduction of the i-STAT device to perform on-site POCT.

Main outcome measure(s): Number of remote staff trained, volume of testing performed and satisfaction of POCT device operators.

Results: One hundred and sixty four (164) health professional staff were trained to perform i-STAT POCT during the first year of the program. A total of 2290 POCT tests were performed on the i-STAT. The volume of testing consistently increased across the year. Tests for international normalised ratio (INR) were the most frequently performed (averaging 70 tests per month). Stakeholder satisfaction with the i-STAT device was high, with a statistically significant improvement in satisfaction levels with pathology service provision being reported after the introduction of POCT. Greater than 80% of respondents stated POCT was more convenient than the laboratory service and assisted in the stabilisation of acutely ill patients.

Conclusions: The NT POCT Program has been operationally effective and well-received by staff working as i-STAT POCT operators in remote health centres. Retention of remote health centre staff is the most significant challenge to ensuring the program's long term viability.

Key Words: Remote, point-of-care, i-STAT, satisfaction, governance

'WHAT THIS PAPER ADDS' BOXES

What is already known on this subject?

- Access to pathology testing in remote Australia is limited.
- There is a high burden of morbidity and mortality among Indigenous Australians in remote locations.
- Point-of-Care Testing has proven useful in assisting the management of patients with chronic disease.

What does this study add?

- This study is the first demonstration of the effectiveness of Point-of-Care Testing in some of the most remote Indigenous communities in Australia.
- This program provides a model for the successful implementation of Point-of-Care Testing in other remote and challenging clinical settings.
- Remote health professionals reported a significantly high level of satisfaction with Point-of-Care Testing for servicing acutely ill patients.

- This Program highlights the innovative capabilities of a connected Point-of-Care Testing network and its usefulness in providing surveillance of pathology testing in very remote locations, allowing all aspects of on-location testing to be closely monitored as well as the generation of network-wide statistics for management purposes.

INTRODUCTION

Access to general laboratory services for remote health centres in the Northern Territory (NT) is often difficult due to the extreme geographic isolation of many of its communities and the extensive distances to the nearest hospital.[1] This remoteness causes resultant issues with the co-ordination and appropriate transport of pathology samples from these health centres to laboratories in Alice Springs and Darwin, and the turnaround time for return of results. These problems were exacerbated in 2007 by the collapse of regional air services which were the primary means of transporting pathology samples.

As a result the NT Department of Health (known at the time as Department of Health and Families) decided to consider using point-of-care pathology testing (POCT) as an alternative and practical solution for the provision of pathology services for remote health centres in the Territory.[2]

In July 2008, the NT Department of Health contracted the Community Point-of-Care Services (CPS) unit at Flinders University to develop a collaborative framework by which POCT for acute and chronic care tests could be conducted safely on the i-STAT (Abbott Diagnostics) point-of-care analyser within selected rural and remote communities in the Territory. The Flinders CPS unit has had wide experience in the delivery of community-based POCT models in Aboriginal medical services and general practices across Australia for the past 15 years.[3-6]

The NT POCT Program commenced in August 2008, following the implementation of a training program for health professional staff, a competency assessment process, a quality management program and selected support services, which are essential elements to a sustainable POCT program.[7] This report briefly discusses the implementation of the program and describes the results of a stakeholder satisfaction survey conducted at the end of the program's first year.

METHODS

Governance

The NT POCT Management Committee was established to oversee and manage the program. The Committee comprised three members of the Flinders CPS unit (including the chairperson) and six members of the NT Remote Health Branch. The Flinders CPS unit prepared training resources comprising a training manual, posters and a DVD, conducted an initial training workshop series for POCT device operators, maintained a competency register of trained operators and a device asset register of all POCT devices in field use, managed the central data station for the i-STAT through which de-identified patient data and quality data were captured electronically from the field devices and monthly summary reports on field usage were prepared, and implemented a quality management framework to track the analytical performance of the i-STAT devices. The NT Remote Health Branch team ordered and dispatched i-STAT reagents and consumables to each health centre and co-ordinated the delivery of mobile field training and competency assessment.

Heath services enrolled in NT POCT Program

Thirty three (33) remote health centres managed by the NT Department of Health and three Aboriginal Community Controlled Health Services (ACCHS) overseen by Aboriginal Medical Services

Alliance of the Northern Territory (AMSANT) were enrolled in the NT POCT Program during its first year (Figure 1).

POCT Devices

The i-STAT 300 analyser (Abbott Point of Care, Doncaster, Australia) is a hand-held, portable, battery-powered POCT device weighing 520g. Single use, disposable cartridges are inserted into a slot at the base of the device where the test is measured by the generation of electrical signals (voltage, current and resistance). Four cartridges types that measure different pathology test profiles on the i-STAT were selected for use in the program. The Chem8+ cartridge measures electrolytes, total CO2, urea, creatinine, glucose, ionised calcium and haemoglobin on 95 µL of venous whole blood in two minutes. The PT/INR cartridge measures international normalised ratio (INR), a marker of clotting time for patients on warfarin therapy on 20-45 µL of capillary whole blood in five minutes. The CG4+ cartridge measures blood gases and lactate on 95 µL of venous whole blood in two minutes. The Troponin cartridge measures cardiac troponin I (cTnI) on 17 µL of venous whole blood in 10 minutes.

Monitoring of operational effectiveness

At the completion of each month, the Flinders CPS unit prepared management summaries for the NT POCT Management Committee from data extracted from the central data station which included the number of valid tests performed (patient, quality and total, split by location and operator), the number of test errors (by location, type of error and operator), and a summary of participation in quality management processes (by location and device).

Assessment of Satisfaction with POCT using the i-STAT

In July 2009 a questionnaire was distributed to all remote health centre staff using the internet-based software program Survey Monkey (www.surveymonkey.com). The questionnaire was designed to

determine satisfaction levels among device operators from the NT POCT Program, with the results used to assess the viability of the POCT program and inform Government policy in this area. The questionnaire contained a series of short statements or questions, with respondents rating their level of agreement or disagreement with the statement or question according to a 5-point Likert scale.[8] Participants were given equal opportunity to agree or disagree with each statement or question. All respondents completed the questionnaires anonymously. Results of the questionnaire was automatically calculated by Survey Monkey and analysed. Before and after results were analysed using the Stata 9.0 software program (StataCorp, College Station, Texas, USA).

RESULTS

Governance

The NT POCT Management Committee met 12 times during the first year of the program's operation. One hundred and sixty four (164) health professional staff were trained and received competency certificates during its first year. Seventy five (75) staff (comprising 54 nurses/Aboriginal Health Workers), 12 chronic disease co-ordinators, one doctor and 8 Remote Health Branch staff) were trained during initial training workshops. Eighty nine (89) personnel (comprising 76 nurses/Aboriginal Health Workers, 3 chronic disease co-ordinators, 4 doctors and 6 Remote Health Branch staff) were trained during 46 opportunistic field visits to remote health centres and/or sessions held in Darwin or Alice Springs by Remote Health Branch staff. During the first year of the program, 54 (33%) remote health centre staff either left the NT or moved internally to a health centre not in the program.

Operational Effectiveness

A total of 2290 POCT tests (1754 patient and 536 Quality Control) were performed on the i-STAT during the first year of the program. The volume of testing consistently increased across the first 12 months as operators became more confident with the device and its clinical use (figure 2). INR tests were most frequently performed (representing 48.6% of all tests conducted and averaging 70 tests per month), followed by Chem8+ tests (30.7%, 45 tests per month), cTnI (13.5%, 20 tests per month) and CG4+ (7.1%, 10 tests per month). For trained operators in the program the cartridge error rate observed in the first year of the program was 7.3%.

i-STAT Satisfaction Questionnaire

A total of 39 respondents completed the i-STAT questionnaire (representing a 31% response rate from the 127 operators who were sent the questionnaire). This low response rate is largely explained by the high rate of remote health staff attrition during the first year, with many of the operators being unable to be contacted or located due to their movements interstate.

Table 1 summarises the satisfaction with pathology services before and after POCT was introduced to the remote health centres. There was a statistically significant increase in satisfaction levels post POCT for all i-STAT tests and for the timeliness of acute care POCT results ($p < 0.001$, Fishers exact chi-squared test).

Table 2 summarises responses relating to the general use of the i-STAT.

Seventy two percent of respondents agreed that POCT on the i-STAT had improved the pathology service available to their patients. When asked in what ways this improvement had occurred at their health centre, greater than 80% of replies stated that POCT was more convenient than the laboratory

service and assisted in the stabilisation of acutely ill patients. Twenty one percent believed POCT had assisted in improving compliance with taking medication (figure 3).

DISCUSSION

Point-of-care testing (POCT) has come of age in Australia over the past 5 years, with the continued expansion and growth in the national Quality Assurance for Aboriginal and Torres Strait Islander Medical Service (QAAMS) POCT Program for diabetes management[3-6], the undertaking of a national trial of POCT in general practice[9-12], and the development of state-wide POCT models in South Australia and Queensland.[13-15] POCT has a particular niche in rural and remote Australia, where the provision of laboratory services is often limited by difficulties with transport of pathology samples and satisfactory turnaround around time for results. In an Indigenous setting, POCT confers the additional advantages of convenience, immediacy of result, and the negation of a follow-up visit, which is often difficult due to other social and cultural priorities.

The NT POCT Program arose as a result of the recent collapse of the NT regional air service and a pressing need to improve access to pathology services for its remote health centres which cater for an almost exclusive Indigenous clientele. The partnership between the NT Department of Health and the Flinders University Community Point-of-care Services unit was seeded in early 2008 and the NT POCT Program commenced in August that year.

The evidence base accumulated during the first year of operation has shown that the NT POCT Program has been operationally effective and generally well-received by health professional staff working as POCT operators of the i-STAT device in remote health centres. A pool of over 160 health professional staff were trained and received competency certificates as qualified POCT operators, thereby building significant POCT workforce capacity in the Territory. The volume of i-STAT testing

increased steadily across the first year. The low cartridge error rate was within the anticipated error rate of less than 10% and indicated that trained operator competency levels were sound. Stakeholder satisfaction with the i-STAT device was high, with a statistically significant improvement in satisfaction levels with pathology service provision being reported post the introduction of the i-STAT. Its clinical utility in assisting with the stabilisation of acutely ill patients was verified. Evidence for its clinical effectiveness and quality of testing will be the subject of further papers.

Staff turnover in remote health services is a constant problem, making health programs difficult to sustain.[17-18]. Eighty percent of staff responding to the i-STAT questionnaire also indicated that they believed staff turnover was the principal factor in impeding sustainability of the program. This is supported by the finding that 33% of operators trained left the NT or moved internally to a different health centre outside of the program during the first year. A particular challenge for the program has been to maintain levels of training and competency, analytical quality and participation in quality testing in the face of such staff turnover. At the commencement of the program, a pool of Chronic Disease Co-ordinators from both Central Australia and the Top End were trained with the aim of acting as a mobile POCT team to assist site operators with training, quality management procedures and general support. This strategy did not have the desired result due to competing time commitments of this highly skilled group. Since that time, we have deployed a mobile team of POCT trainers under the direction of the Professional Practice Team within the NT Remote Health Branch. We are also delivering face-to-face training sessions for Primary Health Centre Managers and Aboriginal Health Workers working in these centres. Training is now available through the NT Department of Health Intranet site to enable training and competency assessment to be undertaken 24 hours a day, 7 days per week. We are also providing monthly Feedback Reports the Primary Health Centre Managers to assist in the closer surveillance of volume and quality of i-STAT testing in each

service. Collectively, these measures have addressed many of the early challenges faced by the program.

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SUMMARY OF TABLES AND FIGURES:

Figure 1. General location of remote health centres participating in the NT POCT Program.

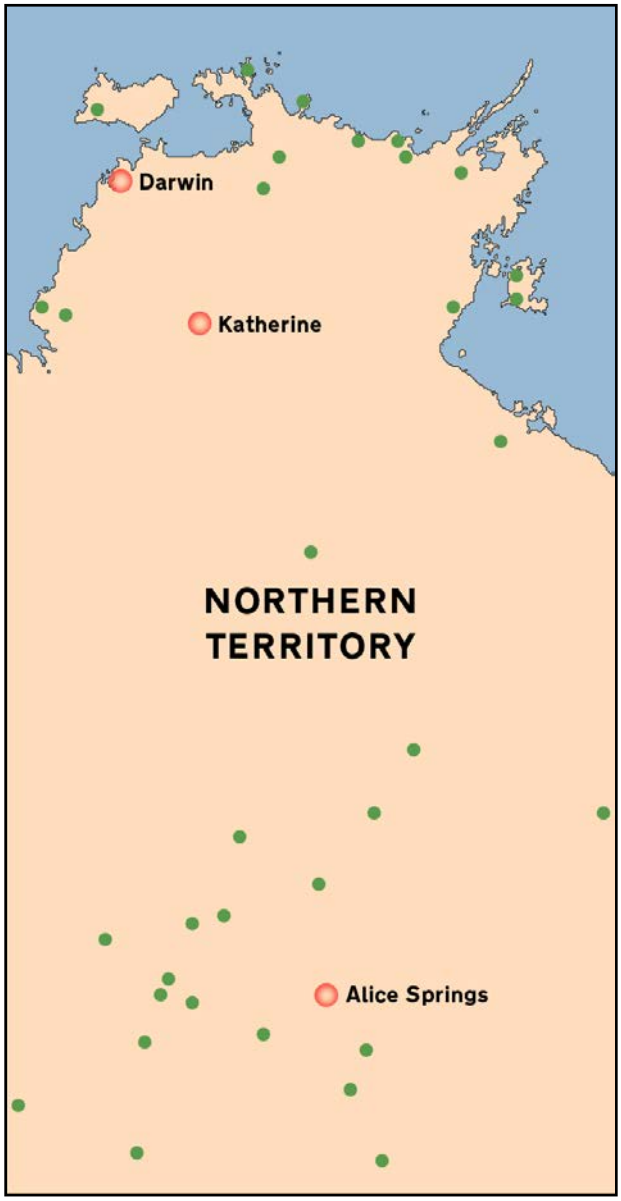

Figure 2. Volume of i-STAT testing across the first year of the NT i-STAT Program (August 2008 to July 2009).

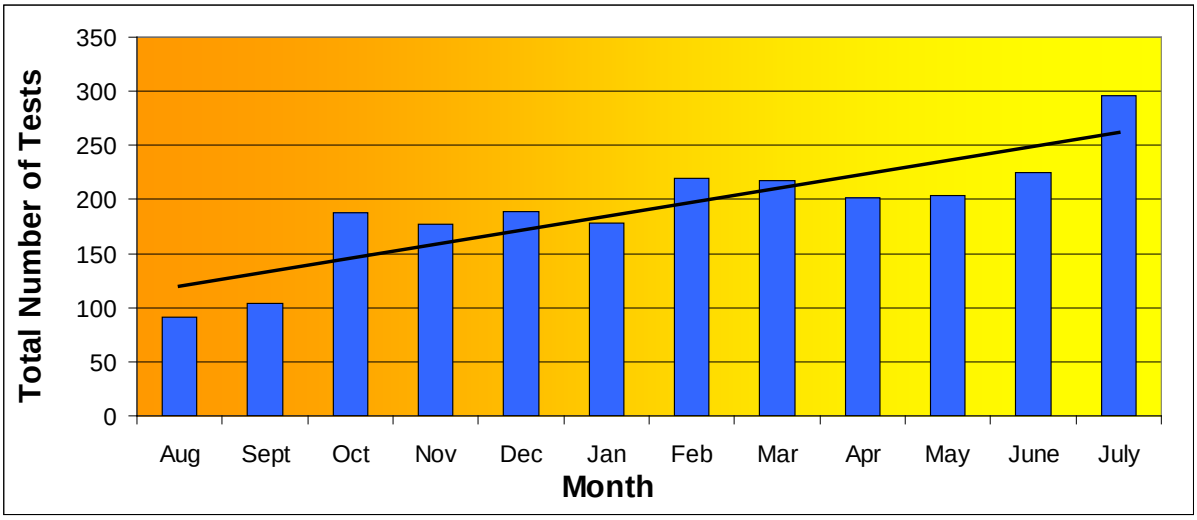

Figure 3. Responses to open questions on the i-STAT device.

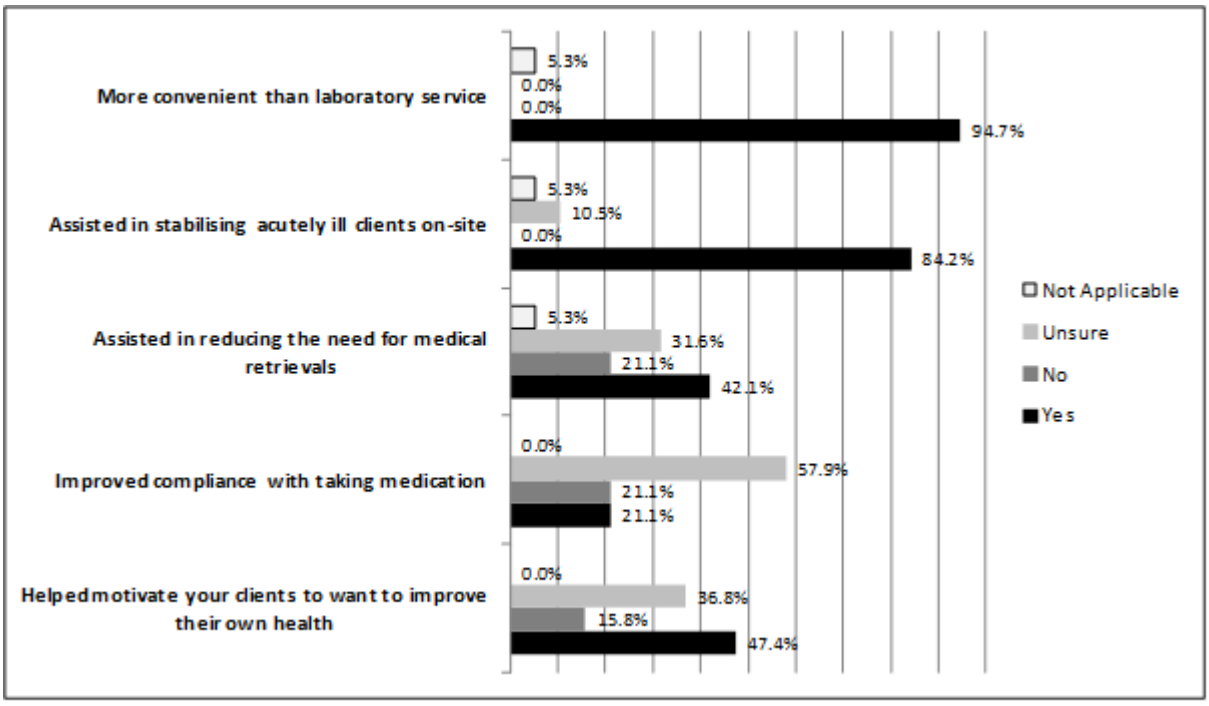

Table 1. Responses to questions relating to satisfaction with pathology services before and after introduction of the i-STAT device in the NT POCT Program

Focus of topic or question	Response					
	Unsatisfied †		Unsure		Satisfied‡	
	n	**%**	n	**%**	**n**	**%**
Satisfaction with INR by lab before	10	42%	3	12%	11	46%
Satisfaction with INR by POCT after	0	0%	0	0%	25	100 %
Satisfaction with cTnI by lab before	12	52%	4	18%	7	31%
Satisfaction with cTnI by POCT after	0	0%	1	4%	22	96%
Satisfaction with electrolytes by lab before	8	34%	3	13%	13	54%
Satisfaction with electrolytes by POCT after	0	0%	1	4%	25	96%
Satisfaction with blood gases by lab before	10	42%	7	29%	7	29%
Satisfaction with blood gases by POCT after	0	0%	4	16%	21	84%
Satisfaction with timeliness of lab for acute tests before	12	48%	6	24%	7	28%
Satisfaction with timeliness of POCT for acute tests after	0	0%	1	4%	25	96%

†*Unsatisfied = sum of 'very unsatisfied' and 'unsatisfied' responses*

‡ *Satisfied = sum of 'satisfied' and 'very satisfied' responses*

Table 2. Responses to questions relating to general aspects of the i-STAT program

Focus of topic or question	Response					
	Disagree†		Unsure		Agree‡	
	n	%	n	%	n	%
Topic: Program management and training and support services						
Management providing appropriate level of support for i-STAT	1	3%	2	7%	29	90%
Management providing appropriate level of training for i-STAT	1	3%	2	7%	28	90%
i-STAT manual has been instructive and appropriate	0	0%	1	3%	31	97%
i-STAT poster set has been instructive and appropriate	2	6%	3	10%	27	85%
i-STAT DVD has been instructive and appropriate	2	6%	8	25%	22	69%
Topic: Quality management						
Understand the need to perform QC testing on i-STAT	2	8%	0	0%	24	92%
Topic: Overall community acceptance						
Clients are satisfied with i-STAT POCT	1	3%	8	25%	23	72%
Topic: Personal comments on i-STAT						
Comfortable and confident with i-STAT	1	4%	3	10%	25	86%
Confidence in accuracy of i-STAT test results	0	0%	4	14%	25	86%
i-STAT POCT acceptable alternative to lab	0	0%	2	7%	27	93%
Enjoyed responsibility for i-STAT testing	1	3%	4	14%	24	83%

†*Disagree = sum of 'strongly disagree' and 'disagree' responses*

‡ *Agree = sum of 'agree' and 'strongly agree' responses*

4.3 Assessment of POCT – Clinical and Operational Effectiveness

4.3.1 Study 1: Assessment of HbA1c clinical and operational effectiveness in a remote setting

Spaeth, B, Shephard, M & Schatz, S 2014, 'Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care', *Rural and remote health*, vol. 14, no. 4, p. 2849. Available at: <www.rrh.org.au/journal/article/2849>.

This study was the first in this body of work to provide results on the clinical and operational effectiveness of the NT POCT Program. At the time this study was conducted, only anecdotal evidence was available for the timeliness of POCT compared to laboratory testing in remote locations. As such, the study addressed this gap in knowledge. This author conceived the study design, collected a majority of the data, provided the data analysis and wrote the first draft of the manuscript.

To demonstrate operational effectiveness, the turnaround time (TAT) for HbA1c results and time to consultation (for the discussion of test results) with the patient was compared using the same cohort of 40 patients before (when the laboratory was used) and after POCT was introduced. The TAT of laboratory HbA1c results averaged 42 hours compared to 6 minutes for the POCT HbA1c results. Most notably, the average TAT for consultation was substantially shorter (<15 minutes) for all except three POC test results compared to the average time to consultation of laboratory test results of 24 days. For the remaining three POC tests, the doctor was not available to see the patient immediately after the POC test result was obtained. In these cases, the doctor discussed the result with the patient after 3, 6 and 14 days (still less than the average laboratory time to consultation).

Clinical effectiveness was demonstrated through significant reductions in HbA1c levels, indicating improved glycaemic control, after the introduction of POC HbA1c testing. In this analysis, 181 patients with three or more POC HbA1c tests in a 16-month period had a significant reduction in HbA1c level from 9.2% to 8.8% ($p=0.013$). The further analysis of a subgroup of 40 patients who showed the most significant reduction in HbA1c after POCT was introduced (2.7% reduction, $p<0.001$) showed a modest increase in HbA1c of 0.3% when the laboratory was used (for an equivalent time period) prior to POCT being available. The frequency of POC HbA1c testing (average of 4.2 tests in 15 months) in this subgroup was also more closely aligned with recommendation of

3-monthly testing for poorly controlled diabetes compared to when the laboratory was used (average of 2.7 tests in 15 months).

This study highlighted the clinical and operational effectiveness of POCT using a cohort of patients. The effects of POCT on individual patients is outlined in the next study through several case studies which highlight how POCT benefits the lives of people living in remote locations in real-time.

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B. CO-AUTHORSHIP DETAILS (To be completed by the candidate and co-authors)

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1. **Publication Details:** Point-of-care testing for haemoglobin A1c in remote Australian Indigenous communities improves timeliness of diabetes care, Published in the Rural and Remote Health Journal, 2014;14:2849

Section of the thesis where the publication is referred to: Throughout the entire thesis

Candidate's (Brooke Spaeth) Contribution to the publication:

Research Design: **90%**

Data Collection and analysis: **80%**

Writing and editing: **80%**

Outline your (the candidate's) contribution to the publication:

Steven Schatz provided the original data set.
Brooke Spaeth developed the research design and collection of additional data (patient and laboratory Information) with supervision from Mark Shephard.
Brooke completed the first draft of the manuscript.
Prof Mark Shephard and Steve Schatz provided edits to the manuscript and approved the final version.

☑ I confirm that the details above are an accurate record of the candidate's contribution to the work.

Name of Co-Author 1: **Prof Mark Shephard**_ Signed: MDShephard Date: 17 / 12 / 17

☑ I confirm that the details above are an accurate record of the candidate's contribution to the work

Name of Co-Author 2: **Steven Schatz**_ Signed: _____ Date: 14 / 8 / 2017

Point-of-Care Testing for Haemoglobin A1c in Remote Australian Indigenous Communities Improves Timeliness of Diabetes Care

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On behalf of the NT POCT Program Management Committee.

Sources of Support:

The Quality Assurance for Aboriginal and Torres Strait Islander Medical Services (QAAMS) Program is funded by the Australian Government's Department of Health and Ageing.

ABSTRACT:

Introduction: In remote Australia timely access to pathology results and subsequent follow-up of patients for treatment is very challenging due to the long distances to the nearest laboratory. Point-of-care testing (POCT) offers a practical solution for pathology service provision in such remote communities. Since 2008, POCT for haemoglobin A1c (HbA1c) has been conducted in remote Northern Territory (NT) health centres for diabetes management of Indigenous patients through the national Quality Assurance in Aboriginal and Torres Strait Island Medical Services (QAAMS) Program.

Methods: POCT HbA1c results performed on Indigenous diabetes patients in the NT from July 2008 to April 2011 was accessed via the Territory's electronic patient information system. Patients who had three or more HbA1c results performed by POCT across this period were assessed to determine their overall change in glycaemic control. An audit of 40 of these Indigenous diabetes patients (who exhibited a decrease in HbA1c levels of more than 1.5%) was undertaken to compare clinical and operational efficiency of POCT versus laboratory testing over an equivalent time period (15 months).

Results: No change in glycaemic control was observed when these patients received laboratory HbA1c testing prior to the introduction of POCT. Long turnaround times for receipt of results and follow-up consultation with patients were identified during this period, compared to immediate receipt and actioning of results using POCT. Frequency of HbA1c testing was higher with POCT than the laboratory.

Conclusions: This audit demonstrates that POCT can significantly improve the timeliness and clinical follow-up of pathology results in remote locations, while also reinforcing the clinical and cultural effectiveness of POCT and its critical role in assisting to improve diabetes management in Indigenous Australians.

Keywords: point-of-care testing, haemoglobin A1c, timeliness, diabetes, remote, Indigenous, QAAMS.

INTRODUCTION:

Indigenous Australians living in remote areas are twice as likely to have diabetes than Indigenous Australians living in non-remote areas[1]. The management of diabetes in remote locations has been historically difficult due to the limited access to resources at the health service level[2,3]. In Australia's Northern Territory (NT), remote health centres are, on average, 275 kilometres from the nearest laboratory (range 100-700 kilometres), making timely access to pathology results and subsequent follow-up of patients for treatment very difficult[4,5,6,7]. Point-of-care testing (POCT) offers a practical solution for pathology service provision in such remote communities. Through the national Quality Assurance in Aboriginal and Torres Strait Islander Medical Services (QAAMS) Program[8,9,10,11], POCT for haemoglobin A1c (HbA1c) has been conducted in remote Northern Territory health centres for diabetes management of Indigenous patients since 2008. Here we present the results of a clinical audit comparing the timeliness of HbA1c testing before and after POCT was introduced into these remote health centres.

METHODS:

Thirty remote health centres in the NT currently participate in the QAAMS Program through a partnership between the NT Department of Health and the Flinders University International Centre for Point-of-Care Testing. HbA1c POCT is performed on-site in the remote health centres using the DCA analyser (Siemens Healthcare Diagnostics), which uses 1 µL of capillary whole blood and provides a result in 6 minutes. Operators performing the tests (remote area nurses and Aboriginal Health Practitioners) undergo training and competency certification through the QAAMS Program.

An audit of the number of HbA1c results performed by POCT on Indigenous diabetes patients from July 2008 to April 2011 was undertaken by accessing the NT's Primary Care clinical Information System (PCIS).

Ethics approval to source this data was obtained through the NT Menzies School of Health Research (registration number: QAAR-2012-1823). Confidentiality of patient data was assured as only de-identified patient information was analysed for the audit. Only pathology results collected for routine patient care were analysed in the audit. The audit did not result in changes to patient's routine clinical care. The audit formed part of the NT POCT Management Committee's charter to investigate the clinical effectiveness of POCT being undertaken as part of the program on behalf of the Northern Territory Government's Department of Health.

Patients who had three or more HbA1c results performed by POCT across this period were assessed to determine their overall change in glycaemic control. A subgroup of these patients (who exhibited a decrease in HbA1c levels of more than 1.5%) underwent a more detailed clinical audit to compare selected parameters across a 15-month period before POCT was introduced (when HbA1c testing was performed by the nearest local laboratory) and the 15-month period after POCT had been introduced. The parameters examined in this 'before and after' dataset included:

- Change in glycaemic control (mean change in HbA1c ± SD);
- Turnaround time of result reporting (calculated by determining the time taken, in hours, between collecting the blood sample from the patient and the result being received from the laboratory or POCT device);
- Turnaround time for follow-up consultation and management of the patient (calculated by determining the time taken, in days/hours, between collecting the blood sample from the patient and the treating medical practitioner consulting with patient about their laboratory or POCT HbA1c result and initiating management;
- Number of HbA1c tests performed per patient.

Paired t tests were used to determine the statistical significance of change in glycaemic control and the number of tests performed per patient before and after POCT was introduced.

RESULTS

A total of 907 Indigenous diabetes patients had 1594 HbA1c tests performed by POCT at the participating remote NT health centres from July 2008 and April 2011. 181 patients (20%) had three or more HbA1c POC tests performed (range 3 to 8 tests) during this period, with the mean HbA1c in this group falling significantly from 9.2% (77 mmol/mol) ± 2.1 (at their first POCT measurement) to 8.8% (73 mmol/mol) ± 2.2 (at their most recent measurement) (paired t-test p=0.013).

Forty of the 181 patients showed a greater than 1.5% reduction in HbA1c from their first to their most recent point-of-care test over a mean period of 15 ± 6 months.

Table 1 compares the change in glycaemic control, turnaround times for result reporting and patient follow-up/management, and HbA1c testing frequency for this subset of 40 patients across an equivalent time period (mean 15 ± 6 months) before and after the introduction of POCT.

Table 1 - Comparison of the clinical and operational efficiency of POCT versus laboratory HbA1c testing for pathology service provision in remote health centres of the Northern Territory.

Parameter	**15 months Before POCT**	**15 months After POCT**
Mean (±SD) change in HbA1c % (mmol/mol); first to most recent result	9.5% (80 mmol/mol) ±1.6 to 9.8% (84 mmol/mol) ± 1.3	10.6% (92 mmol/mol) ±1.6 to 7.9%* (63 mmol/mol) ± 1.3
Mean TAT† for reporting of HbA1c result	42 (±30) hours	6 mins
Mean TAT for patient follow-up and consultation	24 (±15) days	Less than 15 minutes^
Mean (±SD) number of HbA1c tests/patient	2.7 tests (±1.7)	4.2 tests* (±0.8)

†TAT = turnaround time; ^There were three cases where doctor was not available to see the patient immediately with their POCT result. In these cases, patients were seen after 3, 6 and 14 days; statistically significant result p=<0.001(paired t test)*

DISCUSSION

The mean HbA1c within this group fell significantly by 2.7% (paired t-test p=<0.001) over the 15-month period post POCT, while there was minimal change in glycaemic control (+0.3%) when the local laboratory was used to monitor HbA1c prior to the introduction of POCT.

The mean turnaround time from sample collection to receipt of result was 2.3 days when the laboratory was performing HbA1c testing, but was just 6 minutes (that is, the time taken for the result to be available on the DCA device) after POCT was introduced.

Importantly, when the laboratory performed the HbA1c and the patient was required to return to the service for a follow-up visit, the mean time to consult with the doctor was 24 days in this remote setting, compared to an immediate consultation with the doctor during the same visit post POCT.

The mean number of HbA1c tests per patient was higher (by 1.5) following the introduction of POCT (p=<0.001), being more consistent with the clinical recommendations for optimal frequency of HbA1c testing for poorly controlled Indigenous diabetes patients (4 tests per year) [12].

The provision of pathology laboratory services in remote locations such as the Northern Territory of Australia is severely compromised due (i) to the region's geographic isolation and long distances between health centres and local laboratories and (ii) difficulties in being able to recall patients living in remote communities for follow up consultation and actioning of pathology results. For these reasons, the Northern Territory Government decided in 2008 to invest in the opportunity to integrate quality-assured POCT into pathology service provision for its remote health centres. Many remote communities now have access to POCT for both chronic disease care (through the QAAMS Program) and acute clinical care[13-14] (using the i-STAT POCT device [Abbott Point of Care, Melbourne, Australia]).

POCT provides many advantages as a mode of pathology service provision for Indigenous patients, including convenience and accessibility, increased sense of ownership of their blood samples, motivation to take control of their own health and improved relationship with their doctor[10]. For the treating medical practitioner, the ability to see the patient and enact changes of management/treatment 'on the spot' facilitates improved clinical care.

CONCLUSIONS

In previous prospective longitudinal studies relating to POCT in Indigenous settings, our work has shown that glycaemic control for Indigenous diabetes has improved following the introduction of POCT into rural and remote communities[10,15]. In this study, we have compared the clinical and operational efficiency of POCT versus laboratory testing over an equivalent time period (15 months) using a 'before and after' study design across remote health centres in the Northern Territory. This study design has enabled quantitation of the delays experienced in providing laboratory services and clinical actioning of laboratory results in the most remote and challenging health service setting in Australia. At the same time, this study reinforces the clinical and cultural effectiveness of POCT and its critical role in assisting to improve diabetes management in Indigenous Australians.

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B.S. analysed the data and wrote the manuscript. M.S. reviewed/edited the manuscript and contributed to discussion. S.S. sourced the data and reviewed the manuscript.

The authors would like to acknowledge the continuing contribution of the following members of the Northern Territory POCT Management Committee to the program's success and sustainability: Dr Vinod Daniel, Malcolm Auld, Amanda Lingwood, John Louden, Janet Rigby and Beryl Mazzachi.

4.3.2 Study 2: Assessment of INR clinical and operational effectiveness in a remote setting

Spaeth, B & Shephard, M 2016, 'Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's Northern Territory', *Point of Care*, vol. 15, no. 1, pp. 30-4. DOI 10.1097/Poc.0000000000000082.

This next study aimed to identify the clinical and operational effectiveness of POC INR testing in the remote NT using four individual patient case studies. This author collected the data, performed most of the data analysis and wrote the first draft of the manuscript.

The operational and clinical benefits of POC INR testing were found to include:

- Enabling remotely located patients on anticoagulation therapy to have their INR measured regularly in their community;
- Negating the need for patients on anticoagulation therapy to travel to hundreds of kilometres to obtain laboratory-based INR testing;
- Allowing immediate changes to anticoagulation medication;
- Increasing the frequency of INR monitoring for patients on anticoagulation therapy;
- Resulting in greater time within the therapeutic range (TTR) and to a level consistent with international clinical recommendations for (TTR); and
- Enabling rapid identification and stabilisation of widely fluctuating INR levels, therefore reducing the risk of adverse events.

Data on the ongoing analytical quality of INR POC testing in the NT POCT Program was also provided in this study, with imprecision for QC testing meeting the analytical goal for INR set by the Australian Government and matching the performance of laboratory-based INR testing.

In summary, this study is the first to provide results on the operational utility, clinical benefits and ongoing analytical quality of POC INR testing in a remote setting.

The next study provides evidence for the clinical effectiveness for the acute POC tests in the NT POCT Program.

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1. **Publication Details: Spaeth BA, Shephard MDS,** Clinical and Operational Benefits of International Normalized Ratio Point-of-Care Testing in Remote Indigenous Communities in Australia's Northern Territory, Published in *Point of Care*, 2016;15(1):30-34.

   Section of the thesis where the publication is referred to: Throughout the entire thesis.

   Candidate's (Brooke Spaeth) Contribution to the publication:

   Research Design: **90%**

   Data Collection and analysis: **90%**

   Writing and editing: **80%**

   Outline your (the candidate's) contribution to the publication:

Brooke Spaeth designed the research project, provided the collection of data and analysis of data with supervision from Mark Shephard. Brooke provided the first draft of the manuscript and approved the final version.
Mark Shephard supervised research design, assisted with data analysis and provided edits to the final version of the manuscript.

☑ I confirm that the details above are an accurate record of the candidate's contribution to the work

Name of Co-Author 2: **Prof Mark Shephard** Signed: MDShephard Date: 17 / 10 / 17

Original Article for: Point of Care

Submitted: November 2014

Clinical and operational benefits of INR Point of Care Testing in Remote Indigenous Communities in Australia's Northern Territory

Brooke Spaeth and Mark Shephard

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Sources of support that require acknowledgement: None

Conflict of Interest: None

Key Words: point-of-care testing, i-STAT, remote, clinical effectiveness, warfarin, International normalised ratio

ABSTRACT

Among Indigenous people of Australia's Northern Territory (NT), the prevalence of rheumatic heart disease is one of the highest in the world. Warfarin is a common anticoagulant used to treat this condition and to minimise risk of a cardiac event. International Normalised Ratio (INR) testing is used routinely to monitor the efficacy of warfarin therapy and to ensure a patient's INR remains within a tight therapeutic range.

Since 2008, the i-STAT point-of-care testing (POCT) device has been used to measure INR for patients on warfarin therapy in 32 remote health centres participating in the NT POCT Program. A training and quality program to support i-STAT INR POCT is delivered by Flinders University International Centre for POCT and offers flexible options for training including on-site workshops, interactive teleconference training, and training via e-learning.

Since 2008, more than 13,000 INR POC tests have been performed on over 900 patients. Two hundred and ninety eight patients have had five or more INR POC tests performed and 212 of these have had more than 10 serial INR tests. The volume of patient INR testing has increased every year of the program, from 853 in 2008 to 3332 in 2014 (representing a 291% increase in testing since the program's inception). The number of remote health staff trained as POCT device operators is now greater than 700. The between-site imprecision (CV%) from monthly INR Quality Control testing has averaged 6.3% over the past 6 years (range 4.6% to 7.6%). A clinical audit of patient cases has identified improved clinical outcomes and operational benefits through POCT.

INTRODUCTION

Rheumatic heart disease (RHD) is the most common form of heart disease affecting children across the world and is defined as permanent damage to the heart following acute rheumatic fever (ARF).[1] Australia's Indigenous population are up to eight times more likely than non-Indigenous Australians to be hospitalised for ARF and RHD, and nearly 20 times more likely to die due to complications caused by the disease.[2] In the Northern Territory (NT), the prevalence of RHD is 13 to 17 per 1,000 Aboriginal people across all ages, compared to under two per 1,000 non-Indigenous people living in the NT.[3]

Warfarin is a common anticoagulant used in Australia to treat Indigenous people with RHD and minimise their risk of stroke.[2] The measurement of the International Normalised Ratio (INR) test is used worldwide to monitor the blood clotting status of patients on warfarin.[2] A patient's INR should be kept within a tight therapeutic range (normally 2.5 to 3.5 for atrial fibrillation) to reduce their risk of adverse events, with over-anticoagulation (INR > 5), for example, causing a significant increase in a patient's risk of bleeding.[4] The time in therapeutic range (TTR) is now a recognised measure of the quality of warfarin anticoagulation management.[5-6] An Australian Government review of anticoagulation therapies in atrial fibrillation recommends that the TTR for INR measurement should be greater than 70%, while patients with a TTR less than 60% are considered to be poorly controlled.[7]

In Australia, laboratory specimens for coagulation tests such as prothrombin time and INR should be collected and stored within strict guidelines and samples should reach the laboratory within a maximum of 24 hours after collection. In the NT, Department of Health policies state that a patient with an INR between 5 and 9 should have their warfarin dose withheld and their INR measured again within 24 hours.[8]

In remote areas of Australia such as the NT, the ability to closely monitor a patient's INR status in a timely manner using the pathology laboratory is significantly challenged due to (i) the large distances (range 100 to 700 kilometres) involved in transporting patient blood samples from remote health centres to the nearest laboratory for INR measurement, (ii) the time delay in reporting the INR result back to the community and (iii) the difficulty in recalling the patient for a follow-up visit to obtain their INR result and change their dose of warfarin. In a recent study, Spaeth et al (2014) found the turn-around time for laboratory pathology results in the NT to be reported to the remote health centre was approximately 42 hours.[9] For these reasons, POCT for INR is now a well-accepted alternative to laboratory testing and is recommended widely for use in primary care settings.[10]

Since 2008, the NT Department of Health has partnered with the Flinders University International Centre for Point-of-Care Testing to deliver quality-assured POCT on the i-STAT device (Abbott Point of Care, Doncaster, Australia) through the Territory's remote health centre network.[11-12] This paper reports on the operational and clinical benefits of INR testing on the i-STAT in the NT POCT Program over the past six years.

METHODS

Participating Services

Currently, 32 remote health services conduct INR POCT as part of their participation in the NT i-STAT POCT program; these include 18 services from Central Australia and 14 services from the Territory's Top End region (Figure 1).

Training

Training for INR POCT (and on the i-STAT device generally) is provided by via range of flexible formats including face-to-face workshops, on-site training and self-directed learning. In April 2012, an

interactive training method was introduced using the GoToMeeting teleconference provider (www.gotomeeting.com.au), with regular sessions held each week to combat the high staff turnover that occurs in remote health services.[11] A package of training resources (including a training manual, step-by-step poster sets for testing, DVDs and interactive web-based videos) are also provided to each participating health centre.

Analytical Quality

Quality control (QC) testing for INR is conducted monthly at each participating health centre. Between-site imprecision, the key performance indicator of quality, was calculated for INR QC testing across each year of the NT POCT Program and for each lot number of QC material tested. Observed performance was also compared to the median and 90th percentile imprecision achieved by Australasian laboratories participating in the most recent testing cycle of the Royal College of Pathologists of Australasia's (RCPA) Haematology Quality Assurance Program (QAP) (www.rcpaqap.com.au). The analytical goal recommended by the Australian Government for INR in the POCT in General Practice Trial was used as the benchmark to assess whether analytical performance for this test was equivalent to laboratory standards.[13]

Assessment of Effectiveness of INR POCT

The operational effectiveness of INR POCT was monitored by the Flinders University International Centre for Point-of-Care Testing, by providing monthly summaries to both the NT POCT Program Management Committee and the Primary Health Centre Managers on the volume of i-STAT patient and QC testing being conducted at each remote health centre (split by operator and test).

To monitor clinical effectiveness, the i-STAT central data station was used to search for clinical cases where POCT for INR (and other test profiles) had resulted in an improved clinical outcome for patients on warfarin (as well as other acute and chronic clinical presentations).

To calculate the time within therapeutic range (TAT) the percentage of days in range were determined using the Rosendaal Method.[14]

Ethics registration for this study was obtained through the NT Menzies School of Health Research (registration number: QAAR-2012-1823). A separate research approval was obtained through the NT Government's Remote Health Quality and Safety Team for remote health centre staff to interview patients concerning their satisfaction levels within INR POCT.

RESULTS

Operational Effectiveness

Over the first six years of the program, 746 remote health centre staff were trained as i-STAT operators (164 in year 1, 73 in year 2, 131 in year 3, 138 in year 4, 111 in year 5 and 129 in year 6). Since GoToMeeting training was introduced (April 2012), the number of remote health centre staff completing training has increased by 27% (n=204).

The total volume of i-STAT patient INR testing has continued to rise steadily across each year of the program, reaching 3332 patient tests in year six and totalling 13,972 since the program started (Figure 2). This consistent increase in INR patient testing reflects the increased number of staff trained as i-STAT operators as well as the positive acceptance of INR POCT in remote communities.

Across the first six years of the NT POCT Program, ten lot numbers of INR QC material were tested with the average between-site imprecision being 6.3% (range 4.6% to 7.6%). The observed between-site imprecision of the i-STAT compared well with: i) the median (4.6%) and 90th percentile (8.1%) within-site measures of imprecision observed for laboratory-based INR testing in the most recent cycle of the RCPA QAP Haematology Program and ii) the goal set by the Australian Government for INR testing in the Point-of-Care Testing in General Practice Trial (10%).[13]

Clinical Effectiveness

The following four cases illustrate examples of the clinical (and operational) effectiveness of INR POCT in the NT.

Patient Case 1: This case involved a 46 year old male whose INR levels were monitored over a two year period from April 2008 to April 2010 by both laboratory (2008/09) and POCT (2009/10).

The patient had a history of RHD and had received coronary artery bypass graft and aortic valve repair in 2005 and was now on warfarin medication to reduce his risk of stroke. He also had been diagnosed with hypertension in 2010. His therapeutic range was an INR between 2.5 and 3.5.

Prior to the i-STAT device being available at the remote health centre, this patient was required to have his blood sent 500km to the nearest laboratory for INR measurement. Once the INR result was reported back from the laboratory, usually 2 to 4 days later, he would be phoned and have to return to the remote health centre to have his warfarin dose adjusted if necessary. As can be seen from the accompanying graph (Figure 3), when the laboratory was being used, this patient's INR was measured 6 times over a period of 333 days (average time between tests 67 days) with time in therapeutic range (TTR) of 31%. However, after the i-STAT was introduced, the patient had 24 INR tests performed over a period of 326 days (average time between tests 14 days) with a TTR of 74%, now within the goal for optimal INR control.

In summary, the availability of POCT for INR allowed this patient's warfarin therapy to be more closely and effectively monitored than when the laboratory was used, resulting in a significant improvement in the patient's TTR.

Patient Case 2: The second case involves a 42 year old female with a history of atrioventricular blockage, cardiac failure and congenital pulmonary stenosis. She also had a recent history of mental health issues including suicidal tendencies and feeling of self-worthlessness.

The patient presented at a remote health centre after being phoned by the clinic nurse to remind her that she was overdue for her next INR test and review of warfarin medication (current dose 5 mg). During examination, the patient was noted to have a bruise on her tongue. When the patient's finger was lanced for the INR test, bleeding could not be stopped and her INR result on the i-STAT was >8.

The nurse advised her to stop taking warfarin and to continue with minimum dose of 2mg over the coming days. The patient returned to the clinic seven days later for a repeat INR. Her INR result was now 1.3, indicating an overcorrection of INR (below this patient's INR therapeutic range of 2 - 3) and placing the patient at risk of thrombosis. The patient was recommenced on 4mg warfarin. When he patient next returned to the clinic, her INR was now 2.5.

POCT for INR in this patient identified widely fluctuating, clinically dangerous INR levels which were ultimately stabilised in this mentally unstable, non-compliant patient, whilst allowing her to remain in the community with her family.

Patient Case 3: This case involves a 58 year old male from a small remote community located over 500kms from the nearest pathology laboratory. During the wet season this community is often cut off from the outside world due to flooding. The patient had a history of hyperlipidemia, hypertension and type 2 diabetes and, in August 2013, experienced congestive heart failure. As a result he was commenced on warfarin therapy to reduce his risk of repeat cardiac episodes. His therapeutic range for INR was between 2.0 and 3.0.

The patient now attends his remote community health centre each week to have his INR monitored closely on the i-STAT device. The nurse who regularly performs the INR test asked the patient how he feels about the POC test. The patient commented that he "comes to the clinic to get his INR done every week to keep his blood right and help him keep well". He stated that he "can get his check done at the clinic and have his warfarin tablets in a dosette box so he knows exactly what medication

to take daily". The patient mentioned that having the opportunity to have his INR test performed at the health centre, usually weekly, "enables him to spend more time at home with family".

Prior to the i-STAT testing being available the patient was required to have his INR tested frequently at a regional hospital laboratory some 5 hour's drive away. After having his venous sample taken he had to wait for results and return to get his medications before heading home. Since being able to access POCT, he has expressed great satisfaction to be back in the community with his family and undertaking community activities such as attending community meetings, being involved with the local land council and able to visit other surrounding communities.

The availability of INR testing on the i-STAT at this remote health center has allowed this patient's warfarin therapy to be monitored on-site, enabling him to remain in the community and attending to his community duties without having to leave the community to have his INR measured by the regional pathology laboratory.

Patient Case 4: This case involves a 54 year old female who contracted ARF as a child and was diagnosed with severe RHD in 1979. The patient also had a history of atrial fibrillation and underwent mitral valve replacement surgery in 2010. Due to the severity of the patient's RHD, she is required to have benzathine penicillin G injections every 28 days to prevent reoccurrences of ARF. If the patient's INR results fall below the therapeutic range of 2.5 – 3.5, she must be administered clexane to prevent thrombosis.

The patient was visited at her home by the local Aboriginal Health Worker for her regular INR check and to have her medication dosette box restocked. Her INR result on the i-STAT was 1.2 indicating the patient was at risk of clotting. The on-call District Medicare Officer (DMO) was called to address this INR result. While investigating the patient's history, the DMO noticed the patient was having difficulty stabilising her INR despite frequent check-ups and taking her medication regularly. The patient had been on cephalexin for approximately four months for an infected wound on her leg

which had long cleared up. The DMO removed the cephalexin from the patient's regular medication as he felt it may have been interacting with her warfarin medication. He also recommended clexane be re-administered with the patient remaining on a high dose (10mg) of warfarin.

The patient presented at the clinic four days later to have her INR checked. The INR result was now 2.6, within the therapeutic range, and her warfarin medication was reduced to 8mg daily. The patient had her INR checked again in three days' time, with the INR result now being 3.9, slightly higher than the recommended therapeutic range and her warfarin dose was subsequently reduced to 7mg. The patient's INR was checked again five days later with an INR result of 3.3, now within the therapeutic range, and she has remained on 7mg warfarin daily.

POCT for INR on this patient identified a low INR result and enabled immediate clinical interaction and close monitoring of her INR over the following 12 days to stabilise the patient's INR to within her recommended therapeutic range.

CONCLUSION

In this most remote and challenging location for POCT, the i-STAT has significantly increased the timeliness and convenience of INR testing and increased patient safety while on warfarin therapy. The observed analytical performance for INR testing on the i-STAT remained consistent across each year of the program and met profession-based analytical goals for imprecision. POCT for INR has proven to be operationally effective (with an increased volume of testing recorded each year of the program), and clinically effective (producing significant improvements in TTR as well as more rapid stabilisation of fluctuating INR levels).

The main challenges for the program's sustainability continue to be the current lack of Medicare reimbursement from the Australian Government for the INR test on the i-STAT device. During the

next five years, it is the Management Committee's intention to expand the program to all remote health centres in the NT, allowing all patients in these remote locations to access this timely and convenient service and gain the benefits of immediate POC test results.

ACKNOWLEDGEMENTS

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Figure 1 – A map of the Northern Territory of Australia with the general location of remote health centres utilising POCT.

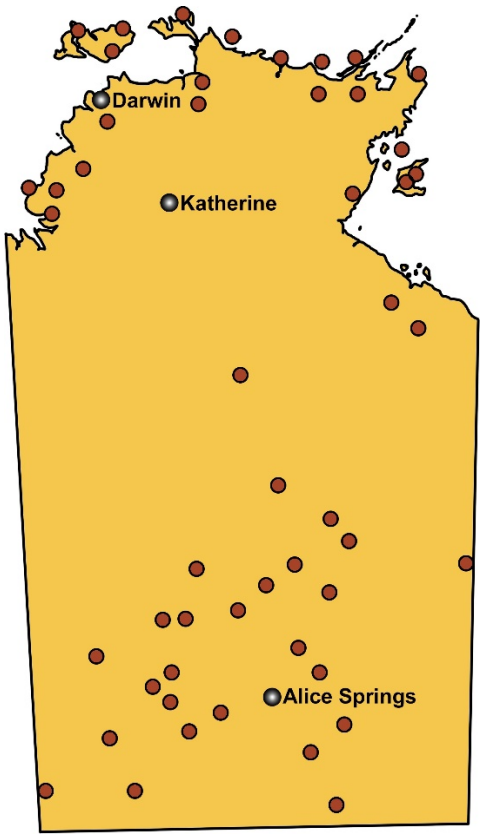


Figure 2 – Total number of patient INR tests conducted across each year since the commencement of the NT POCT Program.

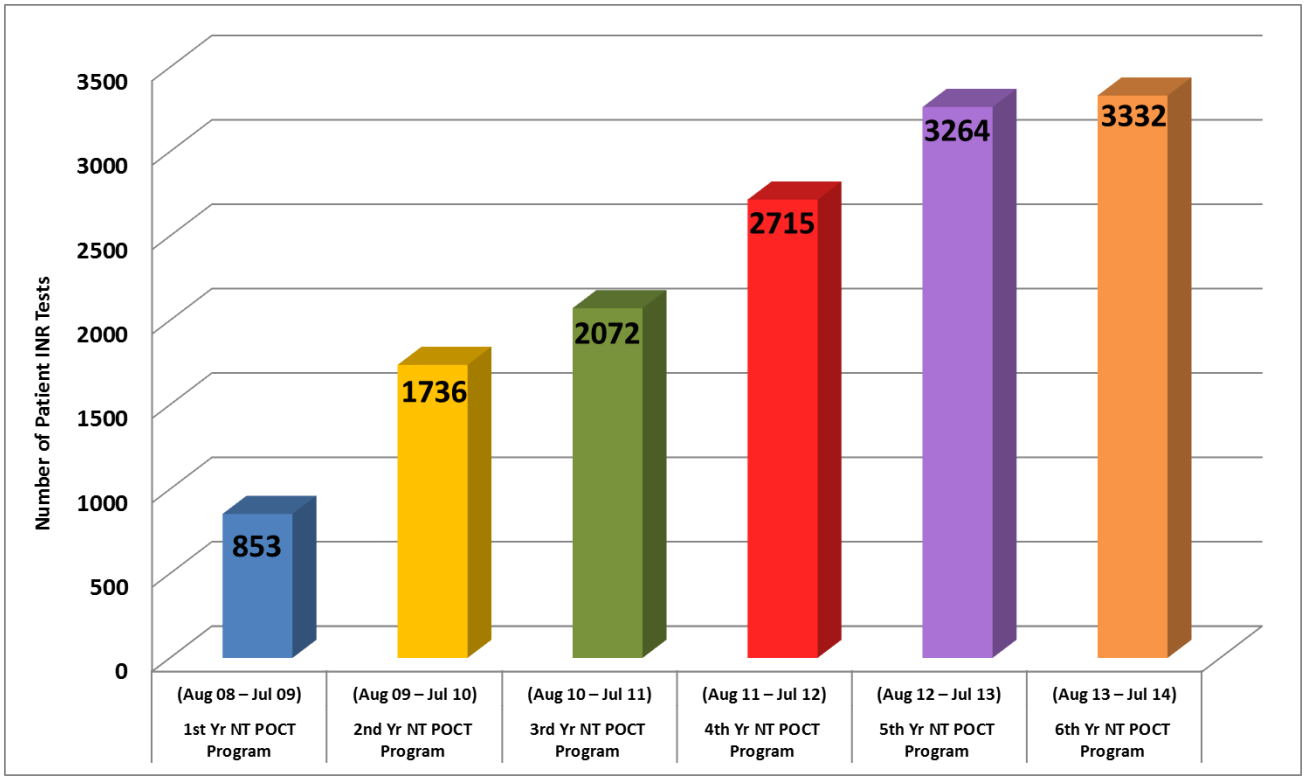
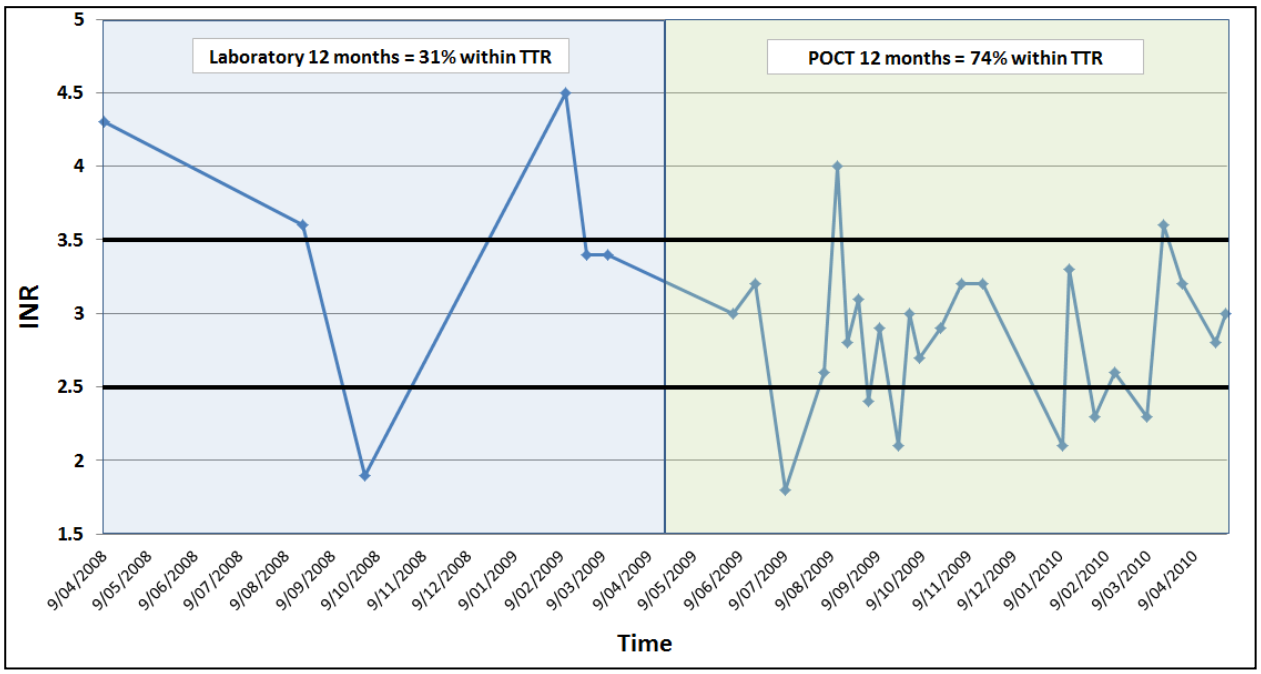


Figure 3 – Time within therapeutic range for patient case 1 before and after the introduction of INR POCT.



4.3.3 Study 3: Assessment of clinical effectiveness of acute POCT in a remote setting

Spaeth, B, Shephard, M & Omond, R 2017, 'Clinical Application of Point-of-Care Testing in the Remote Primary Health Care Setting', *Quality in Primary Care*, vol. 25, no. 3, pp. 164-75. Available at: <http://primarycare.imedpub.com/clinical-application-of-pointofcare-testing-in-theremote-primary-health-care-setting.php?aid=19705>.

As highlighted in the literature review of this thesis, no literature exists on the use of POCT for acute care in rural and remote primary health care setting. Therefore, this study provided the first evidence for the clinical effectiveness of acute care POC tests in this setting. This author conceived the study design, collected the majority of data, conducted most of the analysis and contributed to the writing of the manuscript.

For the reasons outlined in the contextual statement, a randomised control trial for this research study was not possible. As such, an audit of 200 patients presenting with three common acute presentations was conducted over a six-month period at six remote health services differing in population size and geographic location. These presentations included: patients with acute chest pain with no ST-elevation on ECG, patients with acute exacerbation of renal failure due to a missed dialysis session(s) and patients with acute diarrhoea and clinical signs of dehydration.

This study provided the first in-depth analysis of how POCT assisted in the triage of acutely ill patients. The audit demonstrated that POCT facilitated appropriate rapid diagnoses for a number of patients, enabling them to be stabilised on-site and, thus, preventing a substantial number of unnecessary medical evacuations for each acute condition (38% for patients with chest pain, 91% for patients who had missed a dialysis session and 10% with patients with acute diarrhoea). POCT also rapidly identified patients who required urgent aeromedical transfer to the nearest tertiary hospital emergency department. This rapid identification allowed medical retrieval services to be prioritised for the patient as well as enabling the early initiation of treatment. Three detailed patient cases were also provided in this study to demonstrate how POCT resulted in significant improvements in the patients' clinical outcomes. The cultural effectiveness of POCT in the remote NT was also highlighted by this study.

These findings are significant, as there is a high burden of acute patient presentations in the remote NT which often overwhelms aeromedical retrieval services. In these situations, patients with potentially acute or life-threatening illnesses are frequently forced to wait until a medical retrieval

plane becomes available which, in some cases, has resulted in the death of a patient (C Clohesy 2017, personal communication, 30 August).

The results of this clinical audit were subsequently used to determine the economic benefit of POCT to the NT health system in terms of cost savings through prevented unnecessary medical retrievals. The results of this evaluation are presented in the next study.

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1. **Publication Details: Spaeth B, Shephard MDS, Omond R,** Clinical Application of Point-of-Care Testing in the Remote Primary Health Care Setting, Published in *Quality in Primary Care,* 2017;25(3):164-175.

Section of the thesis where the publication is referred to: Throughout the entire thesis.

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Research Design: **80%**

Data Collection and analysis: **80%**

Writing and editing: **80%**

Outline your (the candidate's) contribution to the publication:

Brooke Spaeth designed the research project, provided the collection of data and analysis of data with supervision from Mark Shephard. Brooke provided the first draft of the manuscript and approved the final version.
Mark Shephard supervised research design, assisted with data analysis and provided edits to the final version of the manuscript.
Dr Rodney Omond assisted with research design and data analysis and provided edits to the final version of the manuscript.

☑ I confirm that the details above are an accurate record of the candidate's contribution to the work

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Clinical Application of Point-of-Care Testing in the Remote Primary Health Care Setting

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ABSTRACT

Background: Point-of-care testing (POCT) enables immediate pathology results to be used for timely clinical action during the patient presentation. While many benefits of POCT for chronic and infectious conditions have been well-documented, few studies have focussed on the clinical benefits of POCT for acutely ill patients in remote communities.

Aim: To determine the clinical effectiveness of POCT as a decision support tool for triaging acutely ill patients in remote Australia.

Methods: An audit examined three acute medical presentations (patients with acute chest pain, patients with acute exacerbation of renal failure due to a missed dialysis session(s) and patients with acute diarrhoea) at six remote health centres in the Northern Territory where POCT was routinely available. The main clinical outcome was the percentage (%) of patients with each acute presentation who did or did not require evacuation (as a result of POCT measurement).

Results: 200 patient cases met the selection criteria for the presentation types. Of 147 patients with chest pain, 126 patients were not evacuated due to on-site POCT for troponin I; from this latter group, 48 patients (38%) would have been evacuated if POCT was not available. Three of seven patients (43%) identified with non-STEMI through POCT would not have been evacuated if POCT was unavailable. Of 28 patients who missed dialysis sessions, 17 were evacuated, of which four (24%) had initial potassium results >6.5 mmol/L; all four received calcium gluconate/resonium medication and serial POCT with decreased potassium levels at evacuation. All 10 patients evacuated with acute diarrhoea received rehydration therapy prior to evacuation.

Conclusion: POCT enabled more informed triaging of acutely ill patients requiring evacuation to a tertiary hospital as well as ruling out the need for evacuation for patients who could remain in the community and be stabilised safely using POCT.

How this fits in with quality in primary care	
What do we know?	Current literature indicates that point-of-care testing (POCT) is able to provide improved detection and management of patients with chronic and infectious disease. Little information is available on the clinical benefits of POCT when used for acute care, particularly in the remote health setting.

What does this paper add?	This study provides quantitative evidence and illustrative case studies which highlight the clinical benefits of being able to conduct POCT for acute medical conditions in a remote primary care. For Indigenous Australians, there are also cultural benefits of acute POCT through stabilising a patient's clinical condition on-site and thereby enabling them to remain in community.

BACKGROUND

In Australia, general health status and life expectancy of people living in rural and remote areas is significantly lower than those in metropolitan or urban locations.[1] While there are many well-documented reasons for these disparities, geographical distance from the services and resources available in large metropolitan centres is a major factor.[2] For pathology services, most laboratories are generally located in large metropolitan centres close to a tertiary hospital. People living in these centres can generally expect to receive their pathology results on the same day or for emergency care within the hour.[3] For those living in rural or remote locations, the wait time for pathology results can range anywhere from 24 hours to 2 weeks.[4,5] In the case of an emergency a common option is to evacuate the patient to the nearest hospital to have the pathology tests conducted to assist in determining the patient's diagnosis.

Point-of-care testing (POCT) provides a means of obtaining immediately pathology results at the time of the patient presentation.[4] Furthermore, modern POCT devices are usually simple to operate,

even by non-laboratory trained staff, providing there are appropriate training and a support mechanisms in place.[6]

In the Northern Territory (NT) of Australia, a POCT network operates in 72 remotely located primary health care centres to provide immediate pathology results for both acute and chronic patient care.[7,8] The POCT device used in the program is the Abbott i-STAT (Abbott Point of Care, USA), which measures a range of pathology tests for emergency medical situations including electrolytes, urea, creatinine, cardiac troponin I, glucose, lactate, haemoglobin and blood gases. These tests can be performed on a venous sample of 100 µL or less), with results available in less than 10 minutes.

The NT POCT Program has been found to be operationally effective with high satisfaction rates reported by key stakeholders as well as an increasing volume of testing, analytically sound with POCT results achieving the same standards as Australian laboratories and is able to produce significant cost benefits through preventing unnecessary medical evacuations.[7,8,9,10]

While many clinical benefits of POCT in acute care have been previously examined in studies conducted in urban environments,[11,12,13,14] few studies have focussed on the clinical benefits to patients who live in remote communities. Here we describe the results of a study which investigated the clinical benefits of POCT for patients located in remote NT. This research was supported by a grant provided by the Emergency Medicine Foundation (Emergency Medicine Foundation Ltd).

AIM

The project intended to determine the effectiveness of using POCT as a decision support tool for triaging acutely ill patients in rural and remote Australia by auditing the clinical outcomes of three common acute medical presentations at selected remote health centres in the NT where POCT is available on-site to provide immediate access to pathology results.

METHODS

Ethics

Ethics approval for this project was obtained from the Human Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research (Application Number 2015-2469, approved September 2015).

Site Selection

Six remote health centres in communities with varying population sizes and locations were selected in attempt to eliminate any potential sources of bias. The health centres chosen comprised two large centres (servicing an Aboriginal population base of between 2000-3000 clients), two medium-sized centres (approximately 1000 clients) and two small centres (<500 clients). Two of the health centres were located in the Central Australian region and four were from the Top End of the Territory.

The participating remote health centres received on-going training and competency assessment for i-STAT POCT and conducted monthly quality control testing for continuing surveillance of analytical quality.

Clinical Presentations Included in the Study

Three common acute clinical presentations were investigated in the study: 1) patients with a primary presentation of acute chest pain (specifically those with a normal ECG who had clinical symptoms of non-ST elevation myocardial infarction [non-STEMI]); 2) patients with end stage renal disease (ESRD) with a primary presentation of chronic renal failure due to a missed dialysis session(s); and 3) patients with a primary presentation of acute diarrhoea with evidence of dehydration.

These clinical conditions were selected as the focus for this study because each relies heavily on pathology results to rule in or rule out the need for a medical retrieval or to determine the course of *in situ* patient management or treatment. For each of these conditions, there is a defined 'standard care' clinical protocol (with associated laboratory-based pathology testing) available through the Central Australian Rural Practitioners Association (CARPA) Standard Treatment Manual, with the evidence for the protocol provided in the compendium CARPA Reference Manual.[15,16,17] An alternate clinical pathway for those health services that have access to POCT (termed the 'POCT pathway' was developed by the investigator team for the study (including the Senior Rural Medical Practitioner [RO]). Figures 1 to 3 summarise these two alternate clinical pathways for each of the three medical conditions.

Patients with Acute Chest Pain (non-STEMI)

The detection of cardiac troponin is now an integral component of the differential diagnosis of acute coronary syndrome (ACS).[18,19,20] Cardiac troponin I (cTnI) is measured by the i-STAT using 17 µL of venous whole blood with results available in 10 minutes. Patients presenting at participating remote health centres with acute chest pain that were identified as having an ST elevation on ECG (ST elevation myocardial infarction or STEMI) are generally evacuated immediately from remote health centres and did not form part of this study. Thus, the focus of this study were patients presenting with acute chest pain without ST elevation on ECG (known as non-ST elevation myocardial infarction or non-STEMI). Patients were triaged according to the POCT decision pathway shown in Figure 1.

Patients with ESRD following a missed dialysis session

People living in remote NT have very high rates of kidney disease compared to urban Australians.[21] Patients requiring dialysis commonly present to their remote health centre feeling acutely unwell as a result of missing a scheduled dialysis appointment, often due to other cultural priorities[22,23]. The current clinical protocol for remote health centres with and without POCT recommends an

initial check of vital signs and an ECG as per Figure 2.[16] However, management differs thereafter in sites without and with access to POCT for potassium measurement, which can be measured using the i-STAT on 95 µL of venous whole blood with results available in 2 minutes. A high potassium level (along with creatinine) is a key indicator of renal failure and the decision to evacuate the patient or not is highly dependent on the POC potassium result at a cut-off of 6.5 mmol/L.[16]

Patients with Acute Diarrhoea

Acute diarrhoea is a particularly common acute medical condition observed in paediatric patients presenting to remote health centres in the NT.[24] It can be caused by a range of viral, bacterial or parasitic gastrointestinal pathogens and is often related to overcrowded living conditions and poor hygiene.[25] A major complication of acute diarrhoea is dehydration, which is assessed by calculating the degree of water deficit/loss and treated by carefully managing the rehydration of the patient. Blood potassium and sodium are important biochemical markers for the assessment and management of diarrhoea and associated dehydration respectively. The i-STAT measures both sodium and potassium on 95 µL of venous whole blood with results available in 2 minutes. The on-site turnaround of electrolytes by POCT potentially facilitates a more rapid and responsive rehydration of the patient.[12] Patients with acute diarrhoea (both adults and children) were triaged according to the POCT decision pathway shown in Figure 3.

Data Collection

The i-STAT Central Data Station (CDS), a centrally administered repository of all de-identified patient results captured electronically from each i-STAT device, was used to search for POC test results from the six selected health services which fitted the above selection criteria shown in Figures 1-3 and across the 6-month data collection period.

POC test results initially sourced from the CDS (n=417) included:

- Any troponin I results (positive or negative) (to capture any potential case of Acute Chest Pain without ST elevation on ECG)
- Sodium [Na] results <135mmol/L and/or potassium [K] results <3.2mmol/L (to capture any potential case of Acute Diarrhoea with resultant dehydration)
- Creatinine >200 µmol/L (eGFR of approximately 35 mls/min/1.73m^2) with a potassium result (of any concentration) also recorded (to capture any potential case of Chronic Renal Failure/missed dialysis session).

Clinical information on each patient who met one of the above 'test result' criteria was sourced from the Northern Territory's Department of Health Primary Care Information System (PCIS) to see if it could be included in (or excluded from) one of the three presentation types being investigated.

For each eligible patient case, the following demographic and clinical information was collected: Name of health service; patient identification number for each de-identified patient; age; sex; date of test; primary presentation; ECG result; medical history; POC test result(s); initial diagnosis; evacuated (Yes/No); staff time required to prepare for and perform the test (mins); time to diagnosis (mins); time to initiate treatment (mins); treatment/medication given at health centre; hospital diagnosis/outcome (if evacuated).

Outcome Measures for Clinical Effectiveness

The main clinical outcome measured in this study was the percentage (%) of patients with each acute presentation type who did or did not require evacuation (as a result of POCT measurement). A clinical advisor [RO] provided an independent clinical judgement on whether each patient would or would not have been evacuated to hospital should the results from the i-STAT device not have been available at the time. The clinical advisor is Senior Rural Medical Practitioner (RMP) with extensive experience in the decision making of patient evacuations. The clinical advisor also provides supervision and advice to other RMP staff in making the decision to evacuate patients.

The time to diagnosis (TTD) and/or time to treatment (TTT) [median ± interquartile range, IQR [mins/hrs] was also documented for each presentation type.

A number of patient cases where the POC test results had produced a defined clinical benefit to the patient were also recorded.

RESULTS

Patient Demographics

A total of 200 patient cases (average age 47 years; 51% males) met the selection criteria for the three presentation types. A summary of patient demographics based on each presentation type is provided in Table 1.

Patients Presenting with Chest Pain - Evacuated

Seven patients were evacuated with positive cTnI results and had a diagnosis of non-STEMI confirmed. Three patients were evacuated on the basis of a single cTnI result and four were evacuated after serial measurements. All patients received the recommended thrombolytic drugs (Clopidogrel, enoxaparin and aspirin) prior to evacuation. Troponin results on all 7 patients are summarised in Table 2. The clinical advisor determined that three patients (43%) would NOT have been evacuated if the i-STAT device was unavailable and this likely would have resulted in a poorer outcome for the patient.

A case study describing one of the 7 patients who was evacuated based on a positive troponin results is provided below.

Patient Case 1: A 54-year-old male with a history of ischaemic heart disease (IHD), including a non-STEMI three years prior and coronary artery bypass graft (CABG) surgery in the previous year, presented to his remote health centre at 10am. The patient complained of an epigastric burning

sensation for the past 6 hours which had been intermittent and worse when laying on his back. The patient had many other co-morbidities such as type 2 diabetes, dyslipidaemia and hypertension. On presentation the nurse noted the patient appeared bright and alert with no report of chest pain or any shortness of breath; he had been taking his regular medications as normal. The nurse's first impression was that the patient was experiencing reflux, and the patient was given 20mL of Gastrogel; however this did not relieve the patient's burning sensation. The nurse then sought to rule out any cardiac involvement and performed an ECG and cTnI test on the i-STAT device. The cTnI result of 0.25ng/mL (<0.08ng/mL = negative) was reported over the phone to the on-call cardiologist. The ECG trace was faxed to the cardiologist who noted inverted T-waves in V2 of the trace and made a diagnosis of non-STEMI. The patient was administered the appropriate cardiac drugs (Aspirin 300mg, Clopidogrel 300mg, and Clexane/Enoxaparin 80mg injection) and transferred to the nearest tertiary hospital via emergency evacuation. The estimated time of arrival for the evacuation team was 4 hours after the initial request and, during this time, the patient remained stable with no chest pain but hypertensive (BP 153/95 mmHg). Once the patient arrived at the hospital the decision to provide more extensive treatment was made and he was transferred to a different hospital with cardiac surgery facilities where he had a stent inserted. After his surgery the patient was noted to be 'doing well' and had a video-link cardiology review scheduled every 6 weeks from his home community. Approximately 8 months later the patient experienced a chest pain episode that worried him and presented at his remote health centre clearly concerned. A negative cTnI test and normal ECG trace were recorded and the patient was treated with Gastrogel for reflux which reduced the pain dramatically. The patient had a follow up cTnI test and ECG trace performed the next morning as a precaution, with both tests being negative.

During the study period, an additional 14 patients were also evacuated with negative troponin results (13 had an initial cTnI of ≤0.02 ng/mL and one patient had an initial result of 0.07 ng/mL).

Table 3 summarised the reasons for the evacuation of these patients with negative troponin results. Nine of the 14 patients were evacuated to have further investigations performed in hospital (outside of the remote health centres' capabilities). The clinical advisor noted that, of this group of 14 patients who had a negative troponin and were evacuated, all 14 would still have been evacuated if the i-STAT device was not available.

Patients Presenting with Chest Pain – Not Evacuated

Of the remaining 126 patients presenting with chest pain who were not evacuated, all had negative cTnI levels ≤0.04 ng/mL. Ninety seven (97) had a single cTnI result and 29 patients were ruled out after serial troponin measurements. The clinical advisor noted that, of this group of 126 patients not evacuated, 48 patients (38%) would have been evacuated if the i-STAT device was not available as cardiac involvement could not be ruled out without the cTnI POC test. Thirty one (31) of these 48 patients had a single cTnI test and 17 had serial cTnI testing to rule out cardiac involvement. All patients with negative troponin who were not evacuated had cTnI levels ≤0.04 ng/mL (that is; there were no patients with cTnI levels between 0.04 - 0.08 ng/mL who were not evacuated).

Patients with ESRD presenting after a missed dialysis session(s)

A total of 28 patients were identified as having chronic renal failure and having missed a dialysis session(s). The majority of patients in this group (n=20) came from two health services (one medium-sized and one large) who had a dialysis centre in the remote community. A summary of the data for the evacuated versus not evacuated group is summarised in Table 4.

Patients with ESRD presenting after a missed dialysis session(s) - Evacuated

Seventeen (60%) of patients were evacuated, all of which would still have been evacuated if the i-STAT results were unavailable. Four (24%) patients had an initial potassium > 6.5mmol/L; all of whom were treated on-site with Calcium Gluconate and/or Calcium Resonium. All four patients had

further monitoring of their potassium levels prior to evacuation, with all reporting a decreased potassium level by the time the evacuation team arrived. One of the 4 patients had 7 serial potassium measurements (ranging from 7.6 to 4.1 mmol/L) over a 6-hour period before an evacuation was possible (with the evacuation delayed due to high demand for evacuations at the time). The remaining 13 (76%) patients evacuated had an initial potassium < 6.5 mmol/L; however each of these patients had a confounding factor which necessitated their evacuation such as ECG changes, shortness of breath (SOB), fluid overload or sepsis.

Patients with ESRD presenting after a missed dialysis session(s) – Not Evacuated

A further 11 (40%) patients did not require an evacuation; 10 (91%) of these evacuations were specifically prevented due to having the i-STAT results available. A case study describing one of the 11 patients who were not evacuated is provided below.

Patient Case 2: A 60-year-old female of Indigenous descent presented to a remote health centre in the late afternoon having missed a dialysis session because she was visiting the remote community for a family funeral. The patient normally received dialysis in Darwin and wanted to know if there were any spare dialysis sessions in the community that she could attend to enable her to remain with her family for a few days. Upon presentation the nurse performed an ECG and measured electrolytes on the i-STAT tests. The ECG showed no abnormalities and the patient's potassium result was 5.5 mmol/L (reference interval 3.5 – 4.9 mmol/L). The nurse discussed the results with the on-site RMP who indicated the patient could not attend dialysis in the community as all the appointments were full; however, she was stable enough to remain in the community that day but needed to travel back to Darwin the next day for her normal dialysis session, to which the patient agreed.

The next afternoon the patient presented to the health centre again now feeling a little unwell and stating that she did not want to return to Darwin. The nurse performed a repeat ECG and

electrolytes on the i-STAT. The ECG trace was normal; however the potassium result was slightly higher than the previous day (5.8 mmol/L). The RMP was called and he asked for further information regarding the patient. The patient was not short of breath, had no weakness, confusion, nausea or vomiting and reported no chest pain. The RMP indicated that the patient could remain in the community for one more night. To ensure the patient would return for dialysis the next morning PATS transport was arranged. The patient was transported back to Darwin the next morning and had dialysis performed at the hospital as she had missed her scheduled appointment.

Patients Presenting with Acute Diarrhoea

A total of 25 patients were identified as presenting with acute diarrhoea (together with evidence of dehydration). Only 3 of 25 patients in this category were children, all of whom were evacuated.

Patients Presenting with Acute Diarrhoea - Evacuated

Ten of the 25 patients identified were evacuated, with three classified as having severe dehydration and seven classified with mild to moderate dehydration. The reasons for patients with mild to moderate dehydration being evacuated included further investigations for possible bacterial meningitis, acute gastroenteritis, acute renal failure, abdominal tenderness, pyrexia, and cerebrovascular incident.

All 10 patients received some form of rehydration therapy prior to evacuation. The clinical advisor indicated that 9 of the 10 patients evacuated would have still been evacuated without the i-STAT available. One patient was evacuated because they had evidence of renal failure (urea and creatinine elevated), which would not have been picked up without the i-STAT device available.

Patients Presenting with Acute Diarrhoea – Not Evacuated

The remaining 15 patients presenting with acute diarrhoea remained in the health centre for monitoring and treatment, with all receiving some form of rehydration therapy during on-site

stabilisation. The clinical advisor judged that two (13%) of the 15 patients would have required evacuation if the i-STAT was not available. One of these two patients was on haemodialysis at the time and the i-STAT enabled the patient's electrolyte results (including a potassium result of 4.9 mmol/L) to be monitored and an evacuation saved. In the second case, the i-STAT ruled out an evacuation of a patient with upper abdominal pain and diarrhoea. The electrolyte results allowed confirmation of safe treatment in the community for this patient who had a poor clinical history and uncertain diagnosis. A patient case is described below where the patient's electrolytes were titrated over three measurements and returned to normal, preventing an evacuation.

Patient Case 3: A 42-year-old male with a history of chronic obstructive pulmonary disease (COPD) and IHD presented to his remote health centre with a three-day history of diarrhoea and coughing. The nurse assessed the patient as having generalised mild tenderness and signs of dehydration. The on-call RMP then assessed the patient and confirmed his chest examination showed a probable chest infection. The RMP requested an ECG and asked the nurse to perform a cTnI, blood gas and electrolyte test on the i-STAT device. The ECG showed no major changes and the patient's blood gas and cTnI results showed no abnormalities; however, the electrolyte test revealed significantly low sodium and potassium levels of 129 mmol/L (reference interval: 138 – 149 mmol/L) and 2.9 mmol/L respectively. The RMP advised the patient be administered IV antibiotics for the chest infection and normal saline and 600mg of slow release potassium chloride for rehydration and reassessment in the morning. The next day the patient had a follow up i-STAT test performed which showed that his electrolytes had improved (sodium 134 mmol/L, potassium 3.5 mmol/L). The patient did not return until one week later where he was administered further antibiotics for his chest infection and had a follow up tests indicating his electrolytes had returned to normal (sodium 138 mmol/L, potassium 3.9 mmol/L).

For each presentation type, no adverse events were recorded for patients not evacuated in the 10 days following their initial presentation.

Time to Diagnosis and Time to Treatment

Table 5 summarises the TTD and TTT for patients presenting with each of the three acute presentations examined in this study.

The 'negative serial cTnI evacuated' group were diagnosed with other complications earlier and therefore had a shorter TTD, whereas the 'positive serial cTnI evacuated' group had to wait for repeat cTnI testing before a diagnosis could be made resulting in a longer TTD.

Of the patients who were not evacuated, only 26 of the 97 patients with a single cTnI tests and 11 of the 29 patients with serial negative cTnI results required treatment, with the median TTT of 15 minutes (±20 minutes) and 30 minutes (±45 minutes) respectively.

For the 28 patients presenting with chronic renal disease who missed a dialysis session, the median TTD was generally quicker for the evacuated group and the median TTT was similar for both groups.

Of the 15 patients who presented with acute diarrhoea/dehydration, the median TTD was similar for the evacuated and non-evacuated patient groups (approximately three quarters of an hour); however, four of the 15 patients not evacuated did not receive any treatment prior to discharge from the remote health centre. The time to treatment (TTT) was longer for the 'evacuated' group, which also had a very wide IQR.

DISCUSSION

In terms of the clinical benefits to patients located in remote Australia, POCT was shown to provide significant improvements in patient care, including the more informed triaging of patients requiring

evacuation to a tertiary hospital as well as ruling out the need for evacuation for patients who could remain in the remote community and be stabilised safely using the POCT device.

For patients presenting with chest pain (without evidence of ST-elevation of ECG) who were not evacuated, 38% (n=48) of this patient group would have been unnecessarily evacuated if the POC cTnI test was not available. These findings also demonstrate the cost benefits of POCT in preventing unnecessary medical evacuations which come at a high cost to the Northern Territory Government of $136.30 per minute flight time according to its Fees and Charges Manual.[26] Importantly, patients with a single positive cTnI test received the fastest combined diagnosis and treatment times of any group (40 minutes total); however there was significant variability around results. The patient with chest pain (case one) demonstrates how initially POCT allowed for the quick diagnosis and early treatment of this acutely ill patient prior to evacuation and then later how POCT also enabled the quick rule-out of cardiac involvement for this concerned patient.

In the group of patients with ESRD who had missed a dialysis session(s), POCT enabled the rapid determination of patients who required urgent treatment based on their high potassium levels, which is not always possible using ECG alone. Furthermore, in this group of patients, POCT allowed for the close monitoring and stabilisation of patient's potassium levels until dialysis was possible, reducing their risk of a cardiac event caused by high potassium. Patient case two described how POCT was able to assist in the monitoring of a patient who had missed a dialysis session so she could attend a funeral in her home community and spend time with her family, demonstrating a cultural benefit of POCT. If the POCT device was not present in this case, the patient's potassium level could not be measured and she would have been evacuated to hospital for assessment of her electrolytes and renal function.

In terms of the patients presenting with acute diarrhoea and signs of dehydration, POCT was able to quantify each patient's level of electrolyte deficit and allow for the gradual and informed titration

of electrolyte balance, which was evidenced by case three. In addition, patients with severe dehydration were quickly identified and correctly evacuated for further management of their acute condition.

A limitation of this study is that only three common acute medical presentations were examined and the clinical application of POCT was not investigated for every patient presentation. In addition, the study did not investigate the effects of unnecessary medical evacuations on patient/community (e.g. loss of productivity or social or emotional wellbeing of Indigenous patients).

While the focus of this study was to examine the clinical effectiveness of POCT for acute presentations through the correct triage of acutely ill patients, POCT also enabled many patients to remain in their community, rather than having to suffer the social and emotional trauma associated with dislocation from their families by having to undergo an evacuation for further investigation to a tertiary institution.

In terms of cost effectiveness, the significant cost saving achieved by the NT POCT Program have been reported previously, with savings to the NT Government in excess of $20 million per annum in prevented unnecessary medical retrievals.[10]

The clinical benefits of POCT for managing remotely located patients with chronic illnesses has been long established.[27,28,29,30] This study provides for the first time a quantitative evidence base for the clinical effectiveness of POCT in this acute clinical setting, where previously only anecdotal evidence existed. The innovative use of POCT for acute medical presentations is now firmly embedded within the remote health care framework in the Northern Territory, one of the most challenging clinical environments for the delivery of health care. Clinical staff working in these remote, low resource locations now have access to quality assured POCT equipment for use as a supportive tool to reassure clinical judgement and to enable better management of acutely ill patients.

CONCLUSION

POCT provides equity of access to pathology services to patients living in isolated locations, greater safety in acute care and timely clinical decision making. In these ways, POCT facilitates a closing of the gap in pathology service delivery that currently exists between regional/remote and urban settings.

This study provides health care policy makers with evidence that initial investment in POCT infrastructure, and the appropriate quality framework, provides real improvements to acute care provision and patient safety in remote locations, with associated benefits of long-term cost savings.

This acute care POCT model has significant potential for translation to other disadvantaged settings and low-resource countries.

In terms of future directions, opportunities exist to explore other POC tests and test profile to support a broader range of clinical decisions across the acute, chronic and infectious disease spectrums.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Figure 1 - Clinical pathway for patients with Acute Chest Pain (without ST elevation on ECG)

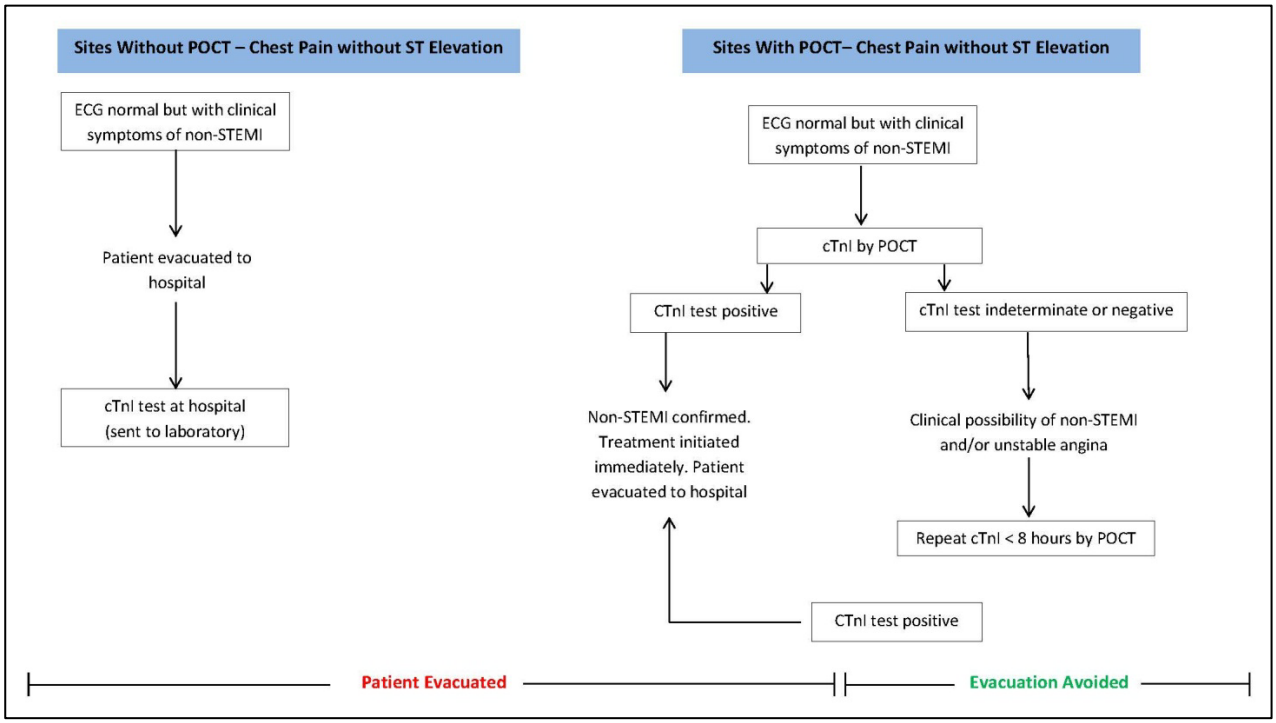


Figure 2 – Clinical pathway for patients with ESRD and missed dialysis session(s)

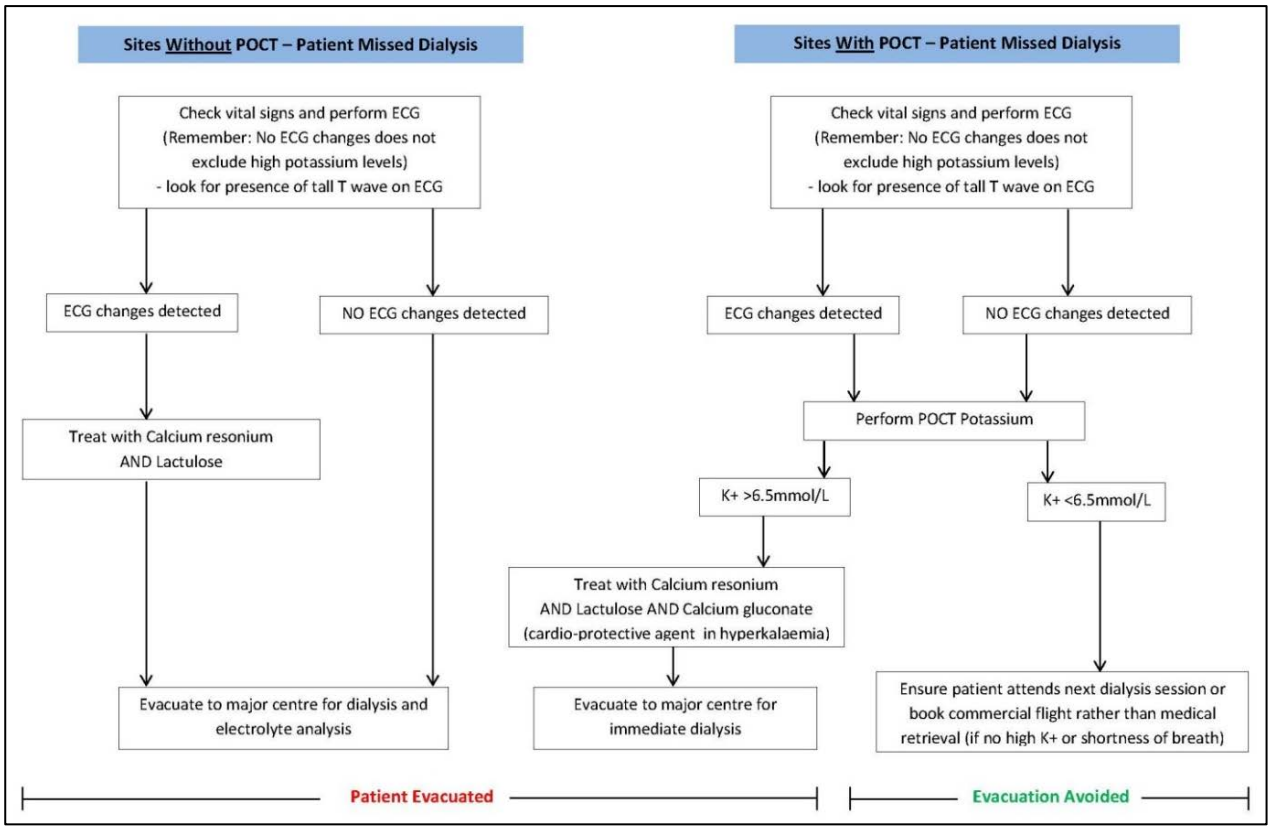
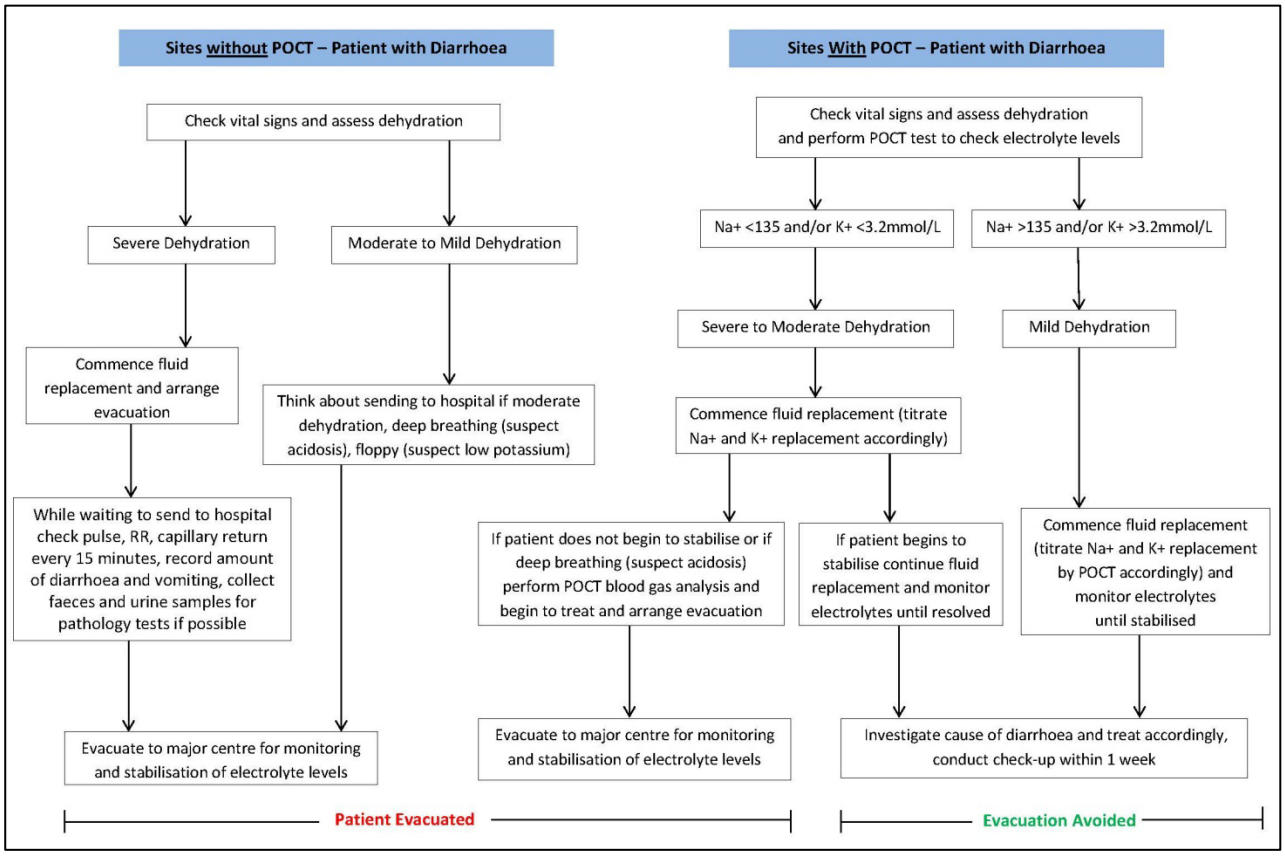


Figure 3 – Clinical pathway for patients with acute diarrhoea



POCT=point-of-care testing, non-STEMI=non ST elevation myocardial infarction, cTnI=cardiac troponin I, ECG=electrocardiogram, K+=potassium by POCT, Na+=sodium by POCT.

4.4 Assessment of POCT – Economic Impact

4.4.1 Study 1: Assessment of the economic impact of acute POCT in a remote setting

Spaeth, B, Kaambwa, B, Omond, R & Shephard, M 2018, 'Economic Evaluation of Point-of-Care Testing in the Remote Primary Health Care Setting of Australia's Northern Territory', *ClinicoEconomics* (Accepted 12 March 2018).

This study provides the results of an economic evaluation of acute POCT in the remote NT. This study used a decision analytic simulation model or 'decision tree' to assess whether POCT leads to costs savings compared to 'usual care' in the three separate acute medical presentations (outlined in the previous linking statement). This author conceived the study design, collected most data and contributed to the writing of the manuscript. The modelling and economic data analysis was conducted by a health economist (Kaambwa, B).

As mentioned, this economic analysis was based on the results from the previous clinical effectiveness study and determined from the number of unnecessary medical retrievals/evacuation prevented by POCT. This decision to evacuate or not evacuate the patient with the POC test results was based on a review of the patient's electronic record, results of basic medical equipment tests, clinical protocol and clinical interpretation by an experienced senior RMP. The decisions in 'usual care' were determined in the same way, with the exception of the availability of POC test results.

The costs associated with each acute presentation, both with and without POCT, were determined using time in motion studies and included costs of staff time, treatment, medication and consumables. The prevalence of each acute condition in the NT was then used to extrapolate the cost associated with both 'usual care' and POCT to provide an estimate of NT-wide costs.

The results indicated cost savings of $21.75 million dollars per annum to the NT health sector, which significantly outweighed the costs associated with implementing and maintaining POCT, including for chronic disease POC tests. Sensitivity analyses provided a breakdown of cost savings between the Top End ($16 million) and Central Australia ($5.8 million) regions of the NT due to the climatic differences in these locations.

The cost savings were greatest for patients with chest pain at $7,734 per patient, as the i-STAT troponin I test was able to provide a definitive diagnosis to rule out a significant number of patients not having an acute cardiac event. Cost savings were also substantial for patients who had missed a

dialysis session at $4,500 per patient, as i-STAT potassium results were used with well-defined cut-off ranges to inform decision making. A much lower cost saving was observed for patients with acute diarrhoea ($757 per patient); this was thought to be due the lack of any defined cut-off values for electrolyte levels (such as sodium and potassium) which inhibits clear decision making for patients with dehydration.

As highlighted in the literature review of this thesis and further discussed in the contextual statement, prior to this study there was a significant gap in the literature related to the cost of acute POCT outside of the hospital setting. As such, this study is the first to demonstrate the significant cost saving associated with using POCT in acute care in the primary health care sector.

The series of studies discussed up until now has proven the NT POCT Program to be clinically and operationally effective, and analytically sound, for both acute and chronic disease POC tests as well providing a significant economic benefit to the NT health care sector.

A further four studies focus on the long-term sustainability of POCT in remote primary health care settings.

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Economic Evaluation of Point-of-Care Testing in the Remote Primary Health Care Setting of Australia's Northern Territory

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Key Words:

acute, remote health, primary care, retrieval, acute care, myocardial infarction, dialysis, dehydration, indigenous health, pathology testing, medical retrieval, cost-effectiveness.

ABSTRACT

Aim: To determine the cost-effectiveness of utilising point-of-care testing (POCT) on the Abbott i-STAT device as a support tool to aid decisions regarding the emergency medical retrievals of patients at remote health centres in the Northern Territory (NT) of Australia.

Materials and Methods: A decision analytic simulation model-based economic evaluation was conducted using data from patients presenting with three common acute conditions (chest pain, chronic renal failure due to missed dialysis session(s) and acute diarrhoea) at six remote NT health centres from July to December 2015.

The specific outcomes measured in this study were the number of unnecessary emergency medical retrieval prevented through POCT. Cost savings through prevented unnecessary medical retrievals for each presentation type were then determined and extrapolated to give per annual NT-wide estimates.

Results: POCT prevented 60 unnecessary medical evacuations from a total of 200 patient cases meeting the selection criteria (48/147 for chest pain, 10/28 for missed dialysis and 2/25 for acute diarrhoea). The associated cost savings were AUD $4,674, $8,034 and $786 per patient translating to NT-wide savings of AUD $13.72 million, $6.45 million and $1.57 million per annum (AUD $21.75 million in total) for chest pain, missed dialysis and acute diarrhoea presentations, respectively.

Conclusion: This study demonstrated that POCT when used to aid decision making for acutely ill patients delivered significant cost savings for the NT healthcare system by preventing unnecessary emergency medical retrievals.

INTRODUCTION

The health status of Australians living in rural and remote communities is generally poorer than that of matched populations living in urban Australia. This trend is consistent across both chronic and acute disease presentations.[1] Remotely located patients requiring urgent medical care are most often transferred via aerial medical retrieval services to the nearest metropolitan hospital emergency department. The decision to evacuate a patient from a remote health facility is made based on the best available evidence at the time using clinical interpretation, basic medical equipment and discussion with an on-call medical practitioner often based at a tertiary hospital. The lack of medical staff and equipment often necessitates the patient is evacuated so as to err on the side of caution. This is because in the remote NT, if patients are not able remain in community due to clinical requirements, they must be evacuated as no overnight clinical services are available within these remote health facilities. This may lead to unnecessary hospitalisations. The Australian Institute of Health and Welfare (AIHW) reported that across 2008-09, approximately 8.5% of all hospitalisations (30.6/1000 persons) in Australia could have been avoided if managed effectively out of hospital.[2] This trend is amplified with increasing remoteness for most acute and chronic conditions with the NT having the highest rate of avoidable hospitalisations in Australia (47.8/1000 persons).[2]

In the NT, the cost of aero-medical evacuations is borne by the NT Department of Health, which quotes a cost of $141.59 per minute flight time in its Fees and Charges Manual.[3] For a one-hour return medical retrieval this equates to a total cost of $8,495 per evacuation. This figure is consistent with published data from rural and remote Queensland aero-medical evacuations of $8,520 per one-hour inter-hospital transfer.[4] The cost of medical evacuations via helicopter is substantially higher at $16,171 per one-hour return flight.[3] The CareFlight 2014/15 Annual Report documented a total of 2789 emergency evacuations for the Top End of the NT (111 [4%] of which were via

helicopter),[5] based on an average two-hour return flight; this equates to an annual cost estimate of $47 million dollars per annum for the Top End jurisdiction alone. Rural and remote disadvantage is also reflected in poorer standards of general services and health infrastructure including pathology services. POCT allows pathology testing to be conducted during a patient visit with results immediately available for patient care.[6] POCT has a particular niche in rural and remote communities where access to mainstream laboratory services is generally poor, there are long delays in transporting pathology samples to laboratories, turnaround time for delivery of test results back to the local health service may be slow, and patient loss to follow-up is high.[7,8] For medical emergencies in these sectors, the speed of POCT provides critical practical and operational benefits by providing another tool to assist in the triage of acutely ill patients. The additional clinical information provided by POCT adds valuable data within the patient assessment. This extra data reduces the intrinsic risk implied by deciding to leave a patient in a community, with its lower level of available clinical care. POCT also identifies patients with high risk but an absence of clinical signs (eg a patient clinically stable post infarct).

POCT is considered to be generally more expensive than traditional laboratory pathology testing as it is not able to achieve the same economy of scale.[9-11] However, a limited number of studies have examined the cost effectiveness of POCT in a rural or remote context. One previous study based on data from a hospital in rural New Zealand demonstrated that POCT improved diagnostic certainty and thereby reduced the number of transfers to the major base hospital by 62% and increased weekly discharges from 7 pre-POCT to 34 post-POCT, with associated cost savings of NZ$362,138 per annum.[12]

Previous studies from our research group have evaluated the analytical safety, operational efficiency and clinical effectiveness of the i-STAT (Abbott Point of Care, Princeton, USA) POCT device in the primary care setting in remote NT.[13-16] The use of the i-STAT device in the remote NT includes

tests for cardiac troponin I, electrolytes, blood gases, urea, creatinine, glucose, ionised calcium and international normalised ratio (INR) with results for each test available in 10 minutes or less. The present study from our group is the first to provide an economic evaluation of POCT on the i-STAT for acute presentations in this setting. Our hypothesis is that POCT will prevent unnecessary medical evacuation and thereby lead to cost savings. Unnecessary evacuations were defined as the number of evacuations that would have taken place in the absence of POCT results ie based solely on clinical interpretation, basic medical equipment and discussion with an on-call off-site medical practitioner. This analysis took the form of a model-based probabilistic economic evaluation assessing whether POCT leads to costs savings through preventing unnecessary medical retrievals when compared to usual care.

METHODS

Site Selection

In Australia's Northern Territory, remote health care is provided through primary health care facilities that have limited infrastructure, resources and staffing levels, with high rates of staff turnover. These remote health facilities are generally located many hundreds of kilometres from the nearest major tertiary hospital, necessitating air transport as the best (and often only) option for acutely ill patients.

Six remote health services in the NT that have access to on-site POCT (and were current participants in the NT i-STAT POCT Program) were selected to evaluate the clinical and cost effectiveness of the management of acute patient presentations. The six remote health centres comprised two large centres (servicing an Aboriginal population base of between 2000-3000 clients), two medium-sized centres (approximately 1000 clients) and two small centres (<500 clients). Two of the health centres were located in the Central Australian region (which covers the southern half of the NT which

comprises a mainly desert environment) and four were from the Top End of the NT (which comprised the tropical northern half of the Territory).

Acute Presentations

The economic evaluation in this study focussed on three common acute presentations observed in the NT: chest pain or other symptoms suggestive of acute coronary syndrome (ACS) with no obvious ST-elevation on electrocardiogram (ECG); symptoms resulting from missed dialysis session(s) in the setting of chronic renal failure (CRF); and symptoms suggestive of acute dehydration due to diarrhoea and/or vomiting. A detailed description of the normal pathways for each acute condition and how POCT changes these pathways was provided in separate paper by our research group, which outlined the clinical effectiveness of POCT.[15] The i-STAT tests investigated in this study were: Troponin I for ruling out ACS; potassium and creatinine to detect CRF; and sodium, potassium and chloride for assessing possible acute dehydration.

Adverse Events

To determine if patients who remained in the remote communities experienced any adverse events, the electronic case notes within the PCIS were examined for each patient ten days post their initial presentation. Adverse events included any secondary acute presentation, a medical evacuation or death.

Ethics Registration

Data on the prevalence of the three presentation types in patients serviced by the remote health centre network of the NT Department of Health was sourced from the NT Health Data Warehouse (NTHDW), requiring the investigators to gain ethics approval for this project from the Menzies School of Health Research Ethics Committee (Application Number 2015-2469, approved September 2015). A data release application form for NTHDW was also lodged in November 2015 and approved

on 20 May 2016. A condition of Ethics Approval was that all remote community and individual patient identities must be kept anonymous.

Development of the economic evaluation model

A decision analytic simulation model (DASM), or 'Decision Tree'[17,18] was used to assess whether POCT leads to costs savings compared to usual care in the three separate acute medical presentations outlined above. A modelling framework is ideally suited to demonstrate and explore the importance of the inherent uncertainty in the cost-effectiveness question.[19] In the POCT arm, the decision to medically evacuate a patient was made on the basis of on-site i-STAT results from the participating remote health centres. In the usual care arm, the project's Chief Clinical Investigator (Senior Rural Medical Practitioner in the NT) provided an independent clinical judgement on whether each patient would or would not have been evacuated to hospital should the results from the i-STAT device not have been available at the time of the presentation. This decision was based on clinical interpretation, results of basic medical equipment tests and review of the patient's electronic record. This process is exactly the way clinical decisions about evacuations were made routinely prior to POCT being available at all sites, with the Clinical Advisor having considerable experience in these decision-making processes, both pre- and post the introduction of POCT in the NT.

Model structures and inputs

The structures of the DASM for each condition are shown in Figure 1. The pathways for the modelled acute presentations within the POCT and usual care arms were designed to mirror those observed in the general population during the course of this study. The pathways were also informed by a review of the literature and advice from clinical experts on the research team. The model combined estimates of probabilities relating to transitions between the models' health states, resource use/cost and the number of evacuations avoided in each arm.

Probabilities providing a quantitative estimate of the likelihood that a given event within the clinical pathways would occur were obtained from the NT Department of Health Patient Care Information System (PCIS) and are presented for both POCT and usual care arms (data supplied in supplementary Table 1).

Resource use and subsequent costs associated with both the POCT and usual care arms were estimated to calculate mean costs per patient for both arms (supplementary Table 2). Total costs per patient were estimated by combining resource use data and unit costs for these resources (derived from published data sets including those from the NTHDW). Total costs per patient were calculated as the sum of staff costs (incurred when carrying out assessments and tests and undergoing training), equipment costs (including costs of the i-STAT device) and costs of supplies (eg consumables such as i-STAT cartridges, syringes for blood sampling, gloves and protective equipment). Drug costs (eg morphine, clopidogrel, enoxaparin, calcium resonium and lactulose) and treatment costs (eg oxygen, saline and oral hydration solutions), other on-going operational costs of conducting i-STAT testing and other clinical assessments and costs of medical evacuations also formed part of total costs. Equipment and training costs were annuitized at 5% and based on a conservative lifetime of 5 years.[20] An annual maintenance cost for equipment of $1,039 was also included in the costing. All resource costs used in the model are reported in Australian dollars at 2017/18 unit prices. Appendix I provides a description of the resource use and data estimates split into pre-evacuation, evacuation and prevalence estimates.

Economic evaluation

A patient level analysis was undertaken from a health sector (Medicare) cost perspective and the results reported in terms of cost savings due to prevention of unnecessary medical evacuation. Probabilistic analyses were used in the base case and sensitivity analyses based on 100,000 Monte

Carlo simulations. To facilitate the probabilistic analyses, beta distributions were used to model the probability of transitions between health states while gamma distributions were fitted to all costs.

The availability of estimates on the cost of a medical evacuation for a single patient (supplementary Table 3) enabled incremental cost savings due to medical evacuations avoided to be calculated. These savings were calculated as the average weighted round-trip cost of a medical evacuation times the number of unnecessary medical evacuations avoided less the incremental cost (supplementary Table 3). Per patient incremental cost savings for each medical presentation were then extrapolated to the general NT population through multiplying them by the prevalence estimates for each respective medical presentation.

Sensitivity analysis for the economic evaluation was undertaken to assess uncertainty in the cost savings due to avoided medical evacuations by splitting the sample into Top End services (n=40 services) cost of per medical evacuation or Central Australian services (n=32 services) and applying the respective costs of medical evacuations for these services (supplementary Table 3).

RESULTS

A summary of the economic evaluation results provided in Table 1 shows that the mean ± standard error (SE) costs per patient (presented for the usual care and POCT arms, respectively) were $257 ± 1 and $341 ± 1 (Acute Chest Pain), $274 ± 1 and $308 ± 1 (Missed Dialysis) and $204 ± 1 and $306 ± 1 (Acute Diarrhoea). The total cost of a round trip medical evacuation was estimated as $22,560 per patient (data supplied in supplementary Table 3).

Patients Presenting with Chest Pain (without ST elevation on ECG)

Compared to usual care, POCT for patients with acute chest pain (POCT – Chest Pain) was more expensive (by $84 per patient; 95% CI: $81 to $86) but also more effective (prevented 0.2109

unnecessary medical evacuations per patient; 95 % CI: 0.2106 to 0.2112, Table 1). Adopting the 'POCT – Chest Pain' strategy and then spending $34,097 per 100 patients, as opposed to $25,720 per 100 patients under the 'Usual Care – Chest Pain' strategy, would lead to 21 unnecessary medical evacuations being avoided (Table 1). Adopting the 'POCT – Chest Pain' strategy in place of usual care would lead to cost savings (due to unnecessary medical evacuations avoided) of $4,674 per patient, translating to cost savings of $13.72 million per annum for the entire NT population (Table 2) based on an acute chest pain prevalence figure estimate of 2,936 for the NT in 2015.

Patients Presenting with Chronic Renal Failure/Missed Dialysis Session(s)

POCT for patients with CRF who missed one or more dialysis sessions (POCT – Missed Dialysis) was more expensive (by $34 per patient; 95% CI: $32 to $36) than usual care for these patients (Usual Care – Missed Dialysis) but also more effective (prevented 0.3577 unnecessary medical evacuations per patient; 95% CI: 0.3572 to 0.3582). Adopting the 'POCT – Missed Dialysis' strategy and then spending $30,808 per 100 patients, as opposed to $27,370 per 100 patients under the 'Usual Care – Missed Dialysis' strategy, would lead to 36 unnecessary medical evacuations being avoided (Table 1). A decision to adopt POCT instead of usual care for patients who missed dialysis would lead to cost savings of $8,035 per patient, translating to cost savings of $6.45 million per annum for the entire NT population (Table 2) based on a 2015 prevalence figure estimate of 803 people that missed dialysis in the NT in 2015.

Patients Presenting with Acute Diarrhoea

POCT for patients with acute diarrhoea (POCT – Diarrhoea) was more expensive than usual care for these patients (Usual Care – Diarrhoea) by $102 per patient (95% CI: $100 to $103) but also more effective (ie this strategy prevented 0.04 unnecessary medical evacuations per patient; 95% CI: 0.0384 to 0.0403). Adopting the 'POCT – Diarrhoea' strategy and then spending $30,596 per 100 patients, as opposed to $20,438 per 100 patients under the 'Usual Care – Diarrhoea' strategy, would

lead to 4 unnecessary medical evacuations being prevented (Table 1). Adopting the 'POCT – Diarrhoea' strategy in place of usual care would lead to cost savings of $786 per patient, translating to cost savings of $1.57 million per annum for the entire NT population (Table 2) based on an acute diarrhoea prevalence figure estimate of 2,001 for the NT in 2015.

Sensitivity Analysis

In the sensitivity analyses, restricting the analysis to just the Top End services (n=40; cost per medical evacuation per patient = $25,491 as per supplementary Table 3) resulted in cost savings of $5,292 per patient for acute chest pain, $9,084 per patient for missed dialysis and $901 per patient for acute diarrhoea. The corresponding overall savings for these Top End services were $11.50 million, $3.24 million and $1.23 million per annum (Table 2). When the analysis focussed on Central Australian services (n=32; cost per medical evacuation per patient = $17,610 – as per supplementary Table 3), cost savings per patient were $3,630 (acute chest pain), $6,264 (missed dialysis) and $591 (acute diarrhoea) leading to corresponding overall savings for these services of $2.77 million, $2.79 million and $0.37 million per annum respectively.

No adverse events were recorded within ten days of the initial presentation for patients who remained in the community.

DISCUSSION

A recent international study highlighted the importance of conducting setting-specific cost-effectiveness studies for POCT and the need for clinicians, policymakers and industry to address the gaps in knowledge base in this area.[22] This study is the first in Australia to provide a detailed economic evaluation of acute POCT in the remote primary care setting.

Within this setting, POCT was shown to deliver an estimated cost saving of $21.75 million due to prevention of unnecessary medical retrievals for the whole NT. In terms of clinical presentation, savings were greatest in the 'chest pain' patient group ($13.72 million) compared to the savings in the 'missed dialysis' ($6.45 million) and the 'acute diarrhoea' groups ($1.57 million). The differences in costs savings for Central Australia ($5.94 million) and Top End ($15.98 million) were due to differences in prevalence and total numbers of evacuations in these jurisdictions. Although the cost of delivering the POCT pathway per patient was slightly higher (by $84, $34 and $102 respectively) for the three clinical presentations than the usual care pathway, the cost savings in prevented evacuations far outweighed this small cost impost.

This research highlights that POCT can produce substantial cost savings, which significantly outweigh operational costs, through preventing unnecessary medical evacuations when used in the rural and remote health care setting, where access to timely pathology results is not available. These cost savings could be realised by other rural and remote jurisdictions nationally and internationally through adoption of quality-assured POCT networks to aid decision making for acute presentations with the additional benefit of increasing patient safety.

This study has some limitations. First, this research project did not investigate the additional in-hospital costs saved through preventing admission to a tertiary hospital. The effects of unnecessary medical evacuations on patient/community (eg loss of productivity or social or emotional wellbeing of Indigenous patients) were also not included in this study. However, an Australian report on the economic value of pathology found that troponin testing alone reduced the number of admissions to metropolitan emergency departments resulting in cost savings of approximately $166.5 million per annum.[23] The same report also estimated that troponin testing enabled an early discharge strategy to be safely pursued for approximately 40% of patients with suspected ACS.[23] Including data on admissions prevented as well as broader costs and outcomes would most likely have made

POCT even more cost-effective. This finding is similar to the present study in which 38% of patients presenting with chest pain (and no ST-elevation) did not require an evacuation as a result of on-site troponin I testing on the i-STAT device. Costs associated with keeping the patient in a remote health facility for monitoring were also not included in this study. These costs are however estimated to be minimal as no overnight stay beds are available in remote health clinics due to NT government policy.

Second, the clinical and cost effectiveness of POCT in this study was only examined for three common acute presentation types. A survey of clinical staff indicated that the i-STAT was also being used for additional acute presentations such respiratory disorders and sepsis, as well as for the management of patients on anticoagulation therapy. The use of the i-STAT for these presentations is likely to provide additional clinical and cost benefits which have not been part of this study. It is also noteworthy that the cost of administering the entire NT POCT Program, operational costs and the cost of the i-STAT device (including servicing and maintenance) were calculated for all POC testing conducted on the i-STAT device during the study period (including for example INR, blood gas and lactate testing). A small percentage of evacuations in the NT are provided by helicopter (<5%); this mode of evacuation is extremely costly (approximately $16,167 per hour compared to $8,495 per hour for a fixed-wing air evacuation) but was not factored into the economic evaluation because data on the number of helicopter evacuations was not able to be sourced from the Central Australian region; as a result, the total cost savings documented in this study may be slightly underestimated. The average per patient cost of using the i-STAT was calculated to be $58; however, the costs per patient varies depending on the number of patient tests performed on the i-STAT (for example, for one of the health centres servicing a smaller population in our study, the per patient cost of using the i-STAT test was $76.35, whereas for the one of the larger centres the per patient cost was $31.58).

Lastly, some of the sample sizes used in estimating the probabilities for the models were small and could therefore reduce the power of our analyses. Future research should consider replicating this analysis in bigger samples.

While the focus of this study was to examine the clinical and cost effectiveness of POCT for acute presentations, it also highlighted a major cultural benefit of POCT. The prevention of unnecessary medical retrievals enabled many patients to remain in their community, rather than having to suffer the social and emotional trauma associated with dislocation from their families by having to undergo an evacuation for further investigation to a tertiary institution.

CONCLUSION

Until now, the current literature from metropolitan tertiary settings indicated that, while POCT can generate improved clinical outcomes, it is generally more expensive than traditional laboratory pathology testing. However, little information is available on the economic effectiveness of POCT in remote settings, where POCT has a particular niche in providing access to critical pathology results in a timely manner. This study demonstrates POCT can deliver significant cost savings (of the order of nearly AUD$22 million per annum) for the health care system through ruling out unnecessary and expensive emergency medical retrievals in remote Australia.

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AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analysed during the current study available from the corresponding author on a reasonable request.

AUTHORS' CONTRIBUTIONS

BS initiated and led the design of the study with input from MS, BK and RO. BK performed the economic analysis. MS provided oversight for the study. RO provided expert clinical advice. BS and BK took primary responsibility for writing the manuscript. MS and RO contributed to editing the manuscript. All the authors approved the final manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interests.

CONSENT FOR PUBLICATION

Not applicable.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was given by the Menzies School of Health Research Ethics Committee. Reference Number 2015-2469.

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Table 1 Costs, effectiveness and cost savings based on the number of unnecessary medical evacuations avoided

Strategy	Mean (SE) cost per patient (AU $)	Difference (95% CI) in costs (AU $)	Mean (SE) Effectiveness[a] per patient	Difference (95% CI) in Effectiveness[a]	Cost savings per patient[c]– NT (AU $)	Cost savings per patient[c] – TE (AU $)	Cost savings per patient[c] – CA (AU $)
Acute Chest Pain							
Usual Care	257.20 (0.85)	83.76 (81.41, 86.12)	0.64613 (0.0012)	0.21090 (0.21063, 0.21117)	4,674.11	5,292.36	3,630.18
POCT	340.97 (0.85)		0.85703 (0.00010)				
Missed Dialysis							
Usual Care	273.70 (0.77)	34.38 (32.21, 36.45)	0.03557 (0.00012)	0.35769 (0.35721, 0.35817)	8,034.96	9,083.52	6,264.46
POCT	308.08 (0.61)		0.39326 (0.00031)				
Acute Diarrhoea							
Usual Care	204.38 (0.53)	101.58 (99.91, 103.25)	0.56059 (0.00034)	0.03934 (0.03835, 0.04033)	785.93	901.26	591.20
POCT	305.96 (0.59)		0.59993 (0.00030)				

[a] Effectiveness was measured in terms of the number of unnecessary medical evacuations avoided per patient, [b] ICER = Incremental cost-effectiveness ratio, [c] Incremental cost savings per patient associated with POCT due to medical evacuations avoided were calculated as the average weighted round-trip cost of a medical evacuation [$21,717 (base case – NT as a whole), $24,539 (Top End) and $16,952 (Central Australia)] times the difference in the number of medical evacuations avoided (ie incremental effectiveness) less the incremental cost, SE = standard error, TE = Top End, CA = Central Australia.

Table 2 Total cost savings estimates for the Northern Territory, Top End and Central Australia

Acute Presentation Type	POCT Cost savings per patient (AU $)	PCIS Prevalence (%)[a]	Estimated Remaining Prevalence[b]	NT TOTAL estimated Prevalence[c]	Average Cost of Evacuation (AU $)	Total Cost Savings (AU $ millions)
Chest Pain without ST-elevation on ECG	$4,674	1621 (6.98%)	1315	2936	$22,560	$13.72
Top End	$5,292	#1239 (7.55%)	†934	2173	$25,491*	$11.50
Central Australia	$3,630	^382 (5.62%)	ºº381	763	$17,610	$2.77
Chronic Renal Failure with Missed Dialysis session	$8,035	427 (1.84%)	352 (1.84%)	803	$22,560	$6.45
Top End	$9,084	#204 (1.24%)	†154 (1.24%)	358	$25,491*	$3.24
Central Australia	$6,264	^223 (3.38%)	ºº222 (3.38%)	445	$17,610	$2.79
Acute Diarrhoea with symptoms of dehydration	$786	1097 (4.73%)	906 (4.73%)	2001	$22,560	$1.57
Top End	$901	#781 (4.76%)	†589(4.76%)	1370	$25,491*	$1.23
Central Australia	$591	^316 (4.65%)	ºº315 (4.65%)	631	$17,610	$0.37
					Top End Total Savings	$15.98
					Central Australia Total Savings	$5.84
					Northern Territory Total Savings	**$21.75**

[a] PCIS prevalence = direct prevalence of each condition obtained from 2015 NT Data Warehouse figures (ie number of patients with the condition/total number of people living in remote communities serviced by DoH remote health centres in the NT) [21]

[b] Estimated Remaining Prevalence = % prevalence from Data Warehouse figures multiplied by the total number of people living in remote communities serviced by the Aboriginal community controlled health sector in the NT)[21]; assumes % prevalence from Data Warehouse figures is the same for remote communities serviced by the Aboriginal community controlled health sector.

[C] NT Total estimated prevalence = sum of a+b

*More weight was given to three large sites/centres in the Top End as determined by the number of evacuations in this calculation

#TE PCIS Population = 16402; ^CA PCIS Population = 6794; Total PCIS Population = 23196

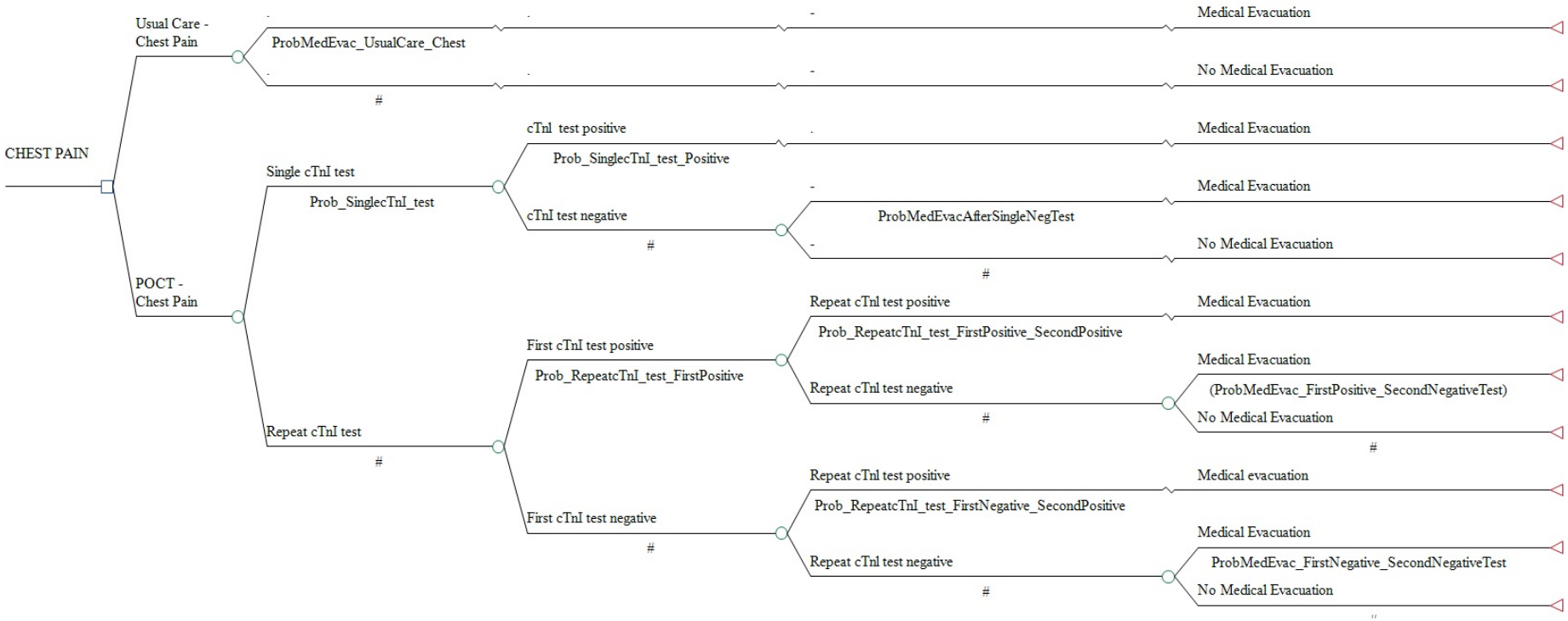
†TE NGO Population = 12372; ººCA NGO Population = 6782; Total NGO Population = 19154

NT total remote population = 42,350

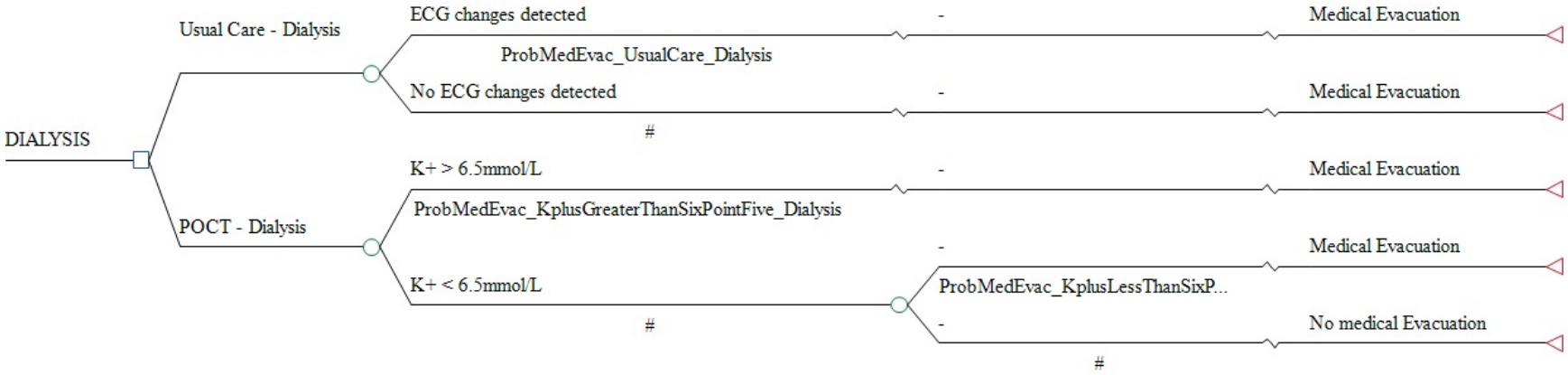
AU = Australian Dollars

Figure 1 A-C: Decision analytic simulation model for each condition

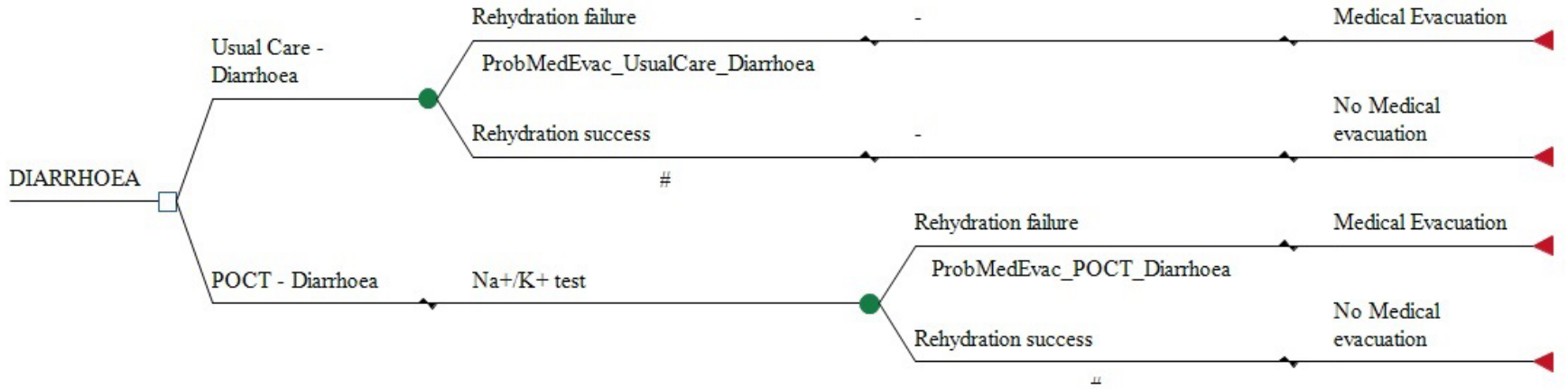
A. Patients with Acute Chest Pain without ST elevation on ECG



B. Patients with Chronic Renal Failure who have missed a dialysis session(s)



C. Patients with Acute Diarrhoea



Supplementary Table 1 Estimates of transition probabilities & distributions used in analysis[a]

Disease presentation, model arm and description of probability	Prob. [r, n][b]
ACUTE CHEST PAIN[c]	
Point-of-care testing Arm	
Probability of having a single cTnI test *(Prob_SinglecTnI_test)*	0.755 [r=111, n =147]
Probability of having a positive result from a single cTnI test *(Prob_SinglecTnI_test_Positive)*	0.027 [r=3, n =111]
Probability of having a negative result from a single cTnI test *(1 - Prob_SinglecTnI_test_Positive)*	0.973 [r=108, n =111]
Probability of being evacuated following a negative result from a single cTnI test *(ProbMedEvacAfterSingleNegTest)*	0.102 [r=11, n =108]
Probability of not being evacuated following a negative result from a single cTnI test *(1 - ProbMedEvacAfterSingleNegTest)*	0.898 [r=97, n =108]
Probability of having a repeat cTnI test *(1 - Prob_SinglecTnI_test)*	0.245 [r=36, n =147]
Probability of having a positive result from the first of repeat cTnI tests *(Prob_RepeatcTnI_test_FirstPositive)*	0.028 [r=1, n =36]
Probability of having a negative result from the first of repeat cTnI tests *(1 - Prob_RepeatcTnI_test_FirstPositive)*	0.972 [r=35, n =36]
Probability of having a two positive results from the repeat cTnI tests *(Prob_RepeatcTnI_test_FirstPositive_SecondPositive)*	1.000 [r=1, n =1]
Probability of having a positive and then a negative result from repeat cTnI tests *(1 - Prob_RepeatcTnI_test_FirstPositive_SecondPositive)*	0.000 [r=0, n =1]
Probability of having a negative and then a positive result from repeat cTnI tests *(Prob_RepeatcTnI_test_FirstNegative_SecondPositive)*	0.086 [r=3, n =35]
Probability of having a two negative results from the repeat cTnI tests (1 - Prob_RepeatcTnI_test_FirstNegative_SecondPositive)	0.914 [r=32, n =35]
Probability of being evacuated following a positive and then a negative result from repeat cTnI tests *(ProbMedEvac_FirstPositive_SecondNegativeTest)*	0.000 [r=0, n =0]
Probability of not being evacuated following a positive and then a negative result from repeat cTnI tests *(1 - ProbMedEvac_FirstPositive_SecondNegativeTest)*	0.000 [r=0, n =0]
Probability of being evacuated following two negative results from repeat cTnI tests *(ProbMedEvac_FirstNegative_SecondNegativeTest)*	0.094 [r=3, n =32]
Probability of NOT being evacuated following two negative results from repeat cTnI tests *(1 - ProbMedEvac_FirstNegative_SecondNegativeTest)*	0.906 [r=29, n =32]
Usual Care Arm	
Probability of being evacuated in the usual care arm *(ProbMedEvac_UsualCare_Chest)*	0.354 [r=52, n =147]
Probability of not being evacuated in the usual care arm *(1 - ProbMedEvac_UsualCare_Chest)*	0.646 [r=95, n =147]
ACUTE DIARRHOEA	
Point-of-care testing Arm	

Disease presentation, model arm and description of probability	Prob. [r, n][b]
Probability of having rehydration failure *(ProbMedEvac_POCT_Diarrhoea)*	0.400 [r=10, n =25]
Probability of having rehydration success *(1 - ProbMedEvac_POCT_Diarrhoea)*	0.600 [r=15, n =25]
Usual Care Arm	
Probability of being evacuated in the usual care arm *(ProbMedEvac_UsualCare_Diarrhoea)*	0.440 [r=11, n =25]
Probability of not being evacuated in the usual care arm *(1 - ProbMedEvac_UsualCare_Diarrhoea)*	0.560 [r=14, n =25]
MISSED DIALYSIS	
Point-of-care testing Arm	
Probability of being evacuated following a positive Potassium assay test result *(ProbMedEvac_KplusGreaterThanSixPointFive_Dialysis)*	0.143 [r=4, n =28]
Probability of having a negative Potassium assay test result *(1 - ProbMedEvac_KplusGreaterThanSixPointFive_Dialysis)*	0.857 [r=24, n =28]
Probability of being evacuated following a negative Potassium assay test result *(ProbMedEvac_KplusLessThanSixPointFive_Dialysis)*	0.542 [r=13, n =24]
Probability of not being evacuated following a negative Potassium assay test result *(1 - ProbMedEvac_KplusLessThanSixPointFive_Dialysis)*	0.458 [r=11, n =24]
Usual Care Arm	
Probability of being evacuated in the usual care arm *(ProbMedEvac_UsualCare_Dialysis)*	0.964 [r=27, n =28]
Probability of not being evacuated in the usual care arm *(1 - ProbMedEvac_UsualCare_Dialysis)*	0.036 [r=1, n =28]

[a] The source of all data on probabilities was the Northern Territory Data Warehouse. The Beta distribution was used to model all probabilities in the probabilistic sensitivity analysis (PSA)

[b] Figures are Probability [occurrences(r), population size (n)]. These figures were actual occurrences and population sizes observed in each of the pathways for the three acute presentations and as recorded in the Northern Territory Data Warehouse. Variable names used in the model for the probabilities and shown in the model structures (Figure 1) are presented in italics besides respective descriptions of these probabilities. Note that '1 – probability' in the model structures is represented by '#' within the model structures.

[c] cTnI = Troponin I test

Supplementary Table 2 Estimates costs & distributions used in the base case

Description	Estimate (AU $)	Distribution[b]	Source
ACUTE CHEST PAIN			
Point-of-care testing Arm			
cTnI test[a] Negative			
Nurses - general care	$76.22	Gamma	Time and Motion study
District Medical Officer	$26.79	Gamma	Time and Motion study
Supplies and consumables[c]	$76.00	Gamma	Time and Motion study
Drugs and other treatment[d]	$1.13	Gamma	Time and Motion study
Cost of i-STAT[e] and training[f]	$57.57	Gamma	Time and Motion study
Total	$237.71	Gamma	Time and Motion study
cTnI test[a] Positive			
Nurses - general care	$39.42	Gamma	Time and Motion study
Nurses - Evacuation monitoring	$26.28	Gamma	Time and Motion study
District Medical Officer	$32.15	Gamma	Time and Motion study
Supplies and consumables[c]	$98.34	Gamma	Time and Motion study
Drugs and other treatment[d]	$10.48	Gamma	Time and Motion study
Cost of i-STAT[e] and training[f]	$57.57	Gamma	Time and Motion study
Total	$264.25	Gamma	Time and Motion study
Usual care arm			
Nurses - general care	$39.42	Gamma	Time and Motion study
Nurses - Evacuation monitoring	$26.28	Gamma	Time and Motion study
District Medical Officer	$32.15	Gamma	Time and Motion study
Supplies and consumables[c]	$174.17	Gamma	Time and Motion study
Drugs and other treatment[d]	$1.54	Gamma	Time and Motion study
Total	$273.56	Gamma	Time and Motion study
MISSED DIALYSIS			
Point-of-care testing Arm			
K+ test[a] normal (not evacuated)			
Nurses - general care	$96.19	Gamma	Time and Motion study
District Medical Officer	$35.37	Gamma	Time and Motion study
Supplies and consumables[c]	$49.79	Gamma	Time and Motion study
Drugs and other treatment[d]	$2.86	Gamma	Time and Motion study
Cost of i-STAT[e] and training[f]	$57.57	Gamma	Time and Motion study
Total	$241.78	Gamma	Time and Motion study
K+ test[a] high (evacuated)			
Nurses - general care	$131.41	Gamma	Time and Motion study
Nurses - Evacuation monitoring	$26.28	Gamma	Time and Motion study
District Medical Officer	$26.79	Gamma	Time and Motion study
Supplies and consumables[c]	$49.79	Gamma	Time and Motion study
Drugs and other treatment[d]	$11.15	Gamma	Time and Motion study
Cost of i-STAT[e] and training[f]	$57.57	Gamma	Time and Motion study
Total	$131.41	Gamma	Time and Motion study
Usual Care arm			
Nurses - general care	$131.94	Gamma	Time and Motion study

Nurses - Evacuation monitoring	$26.28	Gamma	Time and Motion study	[a] cTnI =
District Medical Officer	$43.94	Gamma	Time and Motion study	
Supplies and consumables[c]	$68.75	Gamma	Time and Motion study	
Drugs and other treatment[d]	$3.67	Gamma	Time and Motion study	
Total	$274.58	Gamma	Time and Motion study	
ACUTE DIARRHOEA				
Point-of-care testing Arm				
Na+/K+ test[a] negative				
Nurses - general care	$139.82	Gamma	Time and Motion study	
District Medical Officer	$26.79	Gamma	Time and Motion study	
Supplies and consumables[c]	$17.87	Gamma	Time and Motion study	
Drugs and other treatment[d]	$4.19	Gamma	Time and Motion study	
Cost of i-STAT[e] and training[f]	$57.57	Gamma	Time and Motion study	
Total	$246.24	Gamma	Time and Motion study	
Na+/K+ test[a] positive				
Nurses - general care	$139.82	Gamma	Time and Motion study	
Nurses - Evacuation monitoring	$26.28	Gamma	Time and Motion study	
District Medical Officer	$26.79	Gamma	Time and Motion study	
Supplies and consumables[c]	$17.87	Gamma	Time and Motion study	
Drugs and other treatment[d]	$4.19	Gamma	Time and Motion study	
Cost of i-STAT[e] and training[f]	$57.57	Gamma	Time and Motion study	
Total	$272.52	Gamma	Time and Motion study	
Usual care arm				
Nurses - general care	$144.55	Gamma	Time and Motion study	
Nurses - Evacuation monitoring	$26.28	Gamma	Time and Motion study	
District Medical Officer	$35.37	Gamma	Time and Motion study	
Supplies and consumables[c]	$4.36	Gamma	Time and Motion study	
Drugs and other treatment[d]	$5.02	Gamma	Time and Motion study	
Total	$215.58	Gamma	Time and Motion study	

Troponin test; Na+/K+ test = Sodium/Potassium test; K+ test = Potassium test; [b] Distributions used in probabilistic sensitivity analysis; [c] Costs of supplies and consumables include those associated with conducting an electrocardiography (ECG), oxygen, syringes for blood sampling, gloves and protective equipment; [e] Costs of drugs or other treatment included expenditure on morphine, aspirin, glyceryl trinitrate spray, oral rehydration solution, saline;
[e] Costs of i-STAT included costs of i-STAT cartridges, gloves, syringes for blood sampling
[f] Cost associated with i-STAT training, quality testing processes and program management

Supplementary Table 3 Costs of Medical Evacuation per patient

Description	Estimates	Source
Evacuation by air		
Number of services covered (out of 72)	66	CA LAPT; TE LAPT
Weight contribution to total evacuation cost	0.92	Calculated
Total for the Northern Territory		
Average duration of evacuation in minutes (round trip)	164	CA LAPT; TE LAPT
Cost per minute	$136	NT F&C Manual
Round trip total evacuation cost	$23,220	Calculated
Weighted Round trip total evacuation cost	$21,285	Calculated
Top End (n=40)[a]		

Average duration of evacuation in minutes (round trip)	186	TE LAPT
Cost per minute	$136	NT F&C Manual
Round trip total evacuation cost	$28,318	Calculated
Weighted Round trip total evacuation cost	$25,958	Calculated
Central Australian services (n=32)		
Average duration of evacuation in minutes (round trip)	126	CA LAPT
Cost per minute	$136	NT F&C Manual
Round trip total evacuation cost	$17,840	Calculated
Weighted Round trip total evacuation cost	$16,354	Calculated
Evacuation by road[b]		
Number of services covered (out of 72)	6	CA LAPT; TE LAPT
Weight contribution to total evacuation cost	0.08	Calculated
Total for the Northern Territory		
Average kilometres (round trip)	180	CA LAPT; TE LAPT
Cost first 10 kilometres	$727	NT F&C Manual
Cost for subsequent kilometres	5	NT F&C Manual
Round trip total evacuation cost	$15,291	Calculated
Weighted Round trip total evacuation cost	$1,275	Calculated
Top End		
Average kilometres (round trip)	226	TE LAPT
Cost first 10 kilometres	700	NT F&C Manual
Cost for subsequent kilometres	5	NT F&C Manual
Round trip total evacuation cost	$15,506	Calculated
Weighted Round trip total evacuation cost	$1,292	Calculated
Central Australian services		
Average kilometres (round trip)	134	CA LAPT
Cost first 10 kilometres	700	NT F&C Manual
Cost for subsequent kilometres	5	NT F&C Manual
Round trip total evacuation cost	$15,076	Calculated
Weighted Round trip total evacuation cost	$1,256	Calculated
Evacuation by air and/or road		
Total for the Northern Territory	$22,560	Calculated
Weighted Round trip total evacuation cost		
Top End	$25,491	Calculated
Weighted Round trip total evacuation cost		
Central Australian services	$17,610	Calculated
Weighted Round trip total evacuation cost		

[a] More weight was given to three large health centres as determined by the number of evacuations in this calculation (which were 175, 250 and 250).
[b] An assumption was made that the same cost/kilometre for the road ambulance applies to St John Ambulance in cases where the road ambulance was met half way by St John Ambulance during evacuations.
CA LAPT= Central Australian Low Acuity Patient Transfer Logistics Coordinators
TE LAPT=Top End Low Acuity Patient Transfer Logistics Coordinators
NT F&C Manual = Northern Territory Department of Health Fees and Charges Manual

4.5 Sustainability of a POCT program

4.5.1 Study 1: Methods and results on sustainability or remote POCT program

Shephard, M, **Spaeth, B**, Mazzachi, B, Auld, M, Schatz, S, Lingwood, A, Loudon, J, Rigby, J & Daniel, V 2014, 'Toward Sustainable Point-of-Care Testing in Remote Australia - the Northern Territory i-STAT Point-of-Care Testing Program', *Point of Care*, vol. 13, no. 1, pp. 6-11. DOI 10.1097/POC.0000000000000009

This study demonstrates the sustainability of the NT POCT Program across the first four years of the Program. This author contributed to the study design, collected most of the data and assisted in the writing and editing of the manuscript.

As outlined, this study provides the governance structure to support the NT POCT Program and the sustainable methods for delivering POCT training and assessing POCT operator competency. Also provided are results to support the operational, analytical, clinical and cultural effectiveness of the NT POCT Program across the first four years of the Program.

Operational effectiveness is demonstrated through the number of remotely located health professionals accessing POCT training, and the increased usage of all i-STAT cartridge types across years one to four. The positive acceptance of POCT in this setting is also demonstrated through increased satisfaction with the pathology service after the introduction of POCT.

Long-term analytical performance is demonstrated through comparing the median between-device imprecision achieved by remote health services to the median within-device imprecision achieved by Australian laboratories measuring the same analytes. As discussed in the study, a limitation of this analysis is that POCT between-device imprecision was compared to within-device imprecision obtained by laboratories (with between-device variability expected to be greater than within-device imprecision). Despite this limitation, the imprecision for the remote i-STAT devices remained comparable to, and in some cases better than, the median imprecision achieved by laboratories. Due to the inability to access laboratory imprecision data for INR, the between-device imprecision for INR was compared to the analytical goal for INR recommended by the Australian Government.

Clinical and cultural effectiveness was demonstrated through two clinical case studies which highlighted the clinical benefits of POCT to patients in remote locations as well as how POCT enabled an Indigenous woman to remain in her community and have her INR closely monitored. Also

demonstrated by these cases is how POCT can increase patient safety in remote locations through the rapid identification of acute illness (in this case non-STEMI ACS) and close monitoring of chronic disease (in this case assisting to keep INR level within a tight therapeutic range), thus minimising the chance of adverse events.

The significance of this study is that it establishes the sustainability of the NT POCT Program in this remote and challenging environment, and demonstrates how this has led to the effectiveness of POCT in this setting for both acute and chronic care. The challenges for POCT were also highlighted which included maintaining high standards of training in the face of high staff turnover.

This next study provides a more detailed description of the effective and sustainable methods developed to manage the high workload experienced by POC Coordinators in training remotely located POCT operators.

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In accordance with Clause 20.5 and Clause 8 of Appendix F of the RHD Policies and Procedures, a candidate must sign a declaration that the thesis does not contain any material previously published or written by another person except where due reference is made in the text or footnotes. There can be no exception to this rule. Material produced jointly by a candidate and their supervisors or others can be included in the narrative of the thesis only if it is the original work of the candidate. To ensure compliance with the Australian Code for the Responsible Conduct of Research (2007), if the thesis involves the original work of the joint authors other than the candidate, this work must be fully acknowledged in exactly the same way as the work of other authors. A candidate is required to obtain permission from any co-authors to include their work in the thesis.

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   Writing and editing: **80%**

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   Brooke and Prof Mark Shephard worked collaboratively on the development of the research design.
   Brooke was supervised by Prof Mark Shephard in the data collection and analysis process.
   Brooke completed the initial draft of the manuscript. Prof Mark Shephard provided major editing of the manuscript. Co-authors Beryl Mazzachi, Malcolm Auld and Steven Schatz provided minor edits to the draft manuscript and approved the final version.

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Towards Sustainable Point-of-Care Testing in Remote Australia -

The Northern Territory i-STAT Point-of-Care Testing Program

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ABSTRACT

Since 2008 in Australia, the Northern Territory Department of Health has partnered with the Community Point-of-Care Services unit (now the Flinders University International Centre for Point-of-Care Testing) to deliver quality-assured point-of-care testing on the i-STAT device (Abbott Point of Care, Doncaster, Australia) for the provision of selected pathology services in 33 of its remote health centres in the Territory. A set of agreed research outcomes were developed jointly to assess and validate the operational and clinical effectiveness, as well as the analytical safety of POC testing in remote Northern Territory health centres.

Across the first four year's of the program, over 500 health professional staff have been trained as qualified POC testing operators and more than 21,250 patient tests on the i-STAT have been performed. Analytical quality for POC testing has met profession based analytical goals and/or state of the art laboratory performance for most tests. Clinical case studies sourced from the i-STAT central data station (which electronically captured de-identified patient and quality data from all remote services) has confirmed the clinical effectiveness of POC testing for acute and chronic conditions. Community satisfaction with POC testing was validated using qualitative surveys of device operators. Greater than 80% of respondents believed POC testing was more convenient than the laboratory and assisted in the stabilisation of patients with acute illness. The Northern Territory i-STAT Point-of-Care Testing Program has therefore proven operationally effective, analytically sound, clinically and culturally effective, and has been well-received by health professional staff.

Key Words: point-of-care testing, i-STAT, remote, clinical effectiveness, safety, sustainability

INTRODUCTION

The Northern Territory (NT) in Australia is one of the most remote regions in one of the most geographically isolated countries of the world. The NT Government's Department of Health is responsible for the delivery of general health services through a network of remote health centres. These remote health centres are situated on average 275 kilometres (range 100 to 700 kilometres) from the nearest hospital and they service an average population of 523 people, most of whom are Indigenous. A remote health centre is typically staffed by three to four full-time Remote Area Nurses, one to two Aboriginal Health Workers, while almost no remote health centres have a resident medical practitioner and very few have regular specialist services.[1] In one year, remote health centres in the Northern Territory receive an average of more than 8500 patient visits but only 35 visits by a doctor. Emergency services are facilitated by on-call Medical Officers, who field around 1,800 phone calls every month with approximately 50% of these resulting in an emergency medical retrieval.[2] Retrievals generally involve the patient being transported via aeroplane or helicopter to the nearest hospital emergency department in the two main towns in the Territory – Darwin (in the Top End) or Alice Springs (in Central Australia).

Access to pathology services in the NT has generally been poor. In 2007, an internal NT Government report noted that, among remote health services in the Top End, only 10 of 28 remote health centres had daily access to pathology, eight had access twice a week, two had access once a month and the remaining had variable access depending on seasonal weather conditions which were particularly poor during the wet season. In Central Australia, almost no remote health services had daily access to pathology. These problems were exacerbated in 2007 by the collapse of regional air services, which were the primary means of transporting pathology samples.

As a result, the NT Government decided to use point-of-care pathology testing (POC testing) as an innovative and practical means of providing pathology services in its remote health centres. Since

2008, the Northern Territory Department of Health has partnered with the Community Point-of-Care Services unit at Flinders University to deliver quality-assured POC testing (POCT) on the i-STAT device (Abbott Point of Care, Doncaster, Australia) for the provision of selected pathology services in many of its remote health centres in the Territory.[3] The Flinders' Community Point-of-Care Services unit (which is now incorporated under the Flinders University International Centre for Point-of-Care Testing) has had wide experience in the delivery of community-based POC testing models in Aboriginal and Torres Strait Islander medical services and general practices across Australia for the past 15 years.[4-10] A set of agreed research outcomes were developed jointly by the NT Government and the Community Point-of-Care Services unit to assess and validate the operational and clinical effectiveness, as well as the analytical safety of POCT in remote NT health centres. This paper examines progress towards achieving these outcomes across the first four years of the program.

METHODS

Remote Health Services

Thirty three remote health centres from the NT Department of Health (11 from the Top End and 19 from Central Australia) have participated in the program, while 3 Aboriginal Community Controlled Health Services under the auspices of the Aboriginal Medical Services Alliance of the Northern Territory (AMSANT) have also joined the program. The general location of these health centres is shown in figure 1.

POC Device

The i-STAT 300 analyser (Abbott Point of Care, Doncaster, Australia) is a hand-held, light-weight (520g), portable, battery-powered POCT device which uses disposable testing cartridges of four

different types chosen by the NT Government for the measurement of selected test profiles and individual tests for the program (Table 1).

Governance

The Program is governed by a Management Committee which includes the Chairperson (MS) and the POC Coordinator (BS) from the Flinders' Community Point-of-Care Services unit, and a Clinical Advisor (VD), Professional Practice Co-ordinators (JL, JR) and Professional Practice Nurses (MA, SS, AL) who act as Regional POC Supervisors from the Northern Territory Remote Health Branch.

The Flinders' Community Point-of-Care Services unit is responsible for tasks including the production of training resources, conducting primary training workshops, maintaining a competency register of trained operators and a device asset register of all POCT devices in field use, managing the central data station for the i-STAT through which de-identified patient results and quality testing data are captured electronically from the field devices, preparing monthly summary reports for the Management Committee, and implementing a quality management framework to monitor analytical performance of the i-STAT devices. The NT Remote Health Branch team orders and dispatches i-STAT reagents and consumables to each health centre, co-ordinates the delivery of mobile field training, and prepares and updates Government policy documents on the use and conduct of POC testing in remote NT health centres.

Training and Competency Assessment

The program's training resource package comprises a comprehensive 38-page training manual, a set of A3 laminated posters which provide a simple visual step-by-step guides on how to conduct patient and quality testing, and electronic resources such as a power-point presentation, DVD and web-streamed video presentations which take the trainee through the theory and practice of POC testing on the i-STAT.

Training for remote health centre staff is available through several flexible modes of delivery:

- attendance at a primary training workshop, delivered in Darwin or Alice Springs by the Flinders' Community Point-of-Care Services unit
- attendance at an on-site training visit, delivered at the remote health centre by a Regional POC Training Supervisor (the Professional Practice Nurse from the Top End or Central Australia). In addition, a mobile network of 15 District Trainers (Area Service Managers) have also been trained specifically to assist with mobile on-site training
- access to a program of self-directed study for trainee Remote Area Nurses, using the program's training resource package
- access to web-based (on-line) training via the Northern Territory Government's intranet web-site, and,
- via videoconference.

A training checklist details every aspect of training (including theory and practice) that the trainee must complete during the training session. At the completion of the theoretical training, all candidates are required to correctly answer a set of written competency questions and to perform a practical test on the i-STAT using quality control samples in the presence of a member of the program's primary or mobile training teams. Upon successful completion of this written and practical assessment, a competency certificate is issued by the Flinders' Community Point-of-Care Services unit. The certificate features the successful candidate's operator identification number and is valid for two years, after which time competency must be renewed.

Assessment of Effectiveness of POC testing

Operational effectiveness is monitored by the Flinders' Community Point-of-Care Services unit, who provide monthly summaries for the NT POC Testing Management Committee on items including (but not limited to):

- Number of patient tests performed (by location, operator and cartridge type)
- Number of test errors (by location, type of error and operator)
- Number of electronic simulator tests on the i-STAT
- Summary of participation in quality management processes (by location).

Since October 2010, a monthly feedback report on operational performance has also been sent to the Health Centre Manager responsible for each remote health centre in the program. The feedback report provides a 'snapshot' of the workflow statistics for their health centre during the past month and features, in simple coloured graphical form, statistics on the number of each cartridge type used (which can be a guide for ordering of further stock), a list of the operators who performed tests during that month and the most common errors that occurred across the month (both of which can be used for educational purposes and for identifying which operators had a high error rate and why), and a summary of quality testing that has been completed for that month.

A quarterly newsletter is also produced by the Management Committee which is distributed to all participating remote health centres. The newsletter includes a technical bulletin to provide POC testing operators with information about common errors and how to take action to rectify them. It also features a POC 'Operator of the Month', interesting clinical cases and other updates.

Monthly quality control (QC) testing has been the mainstay of the quality framework used for the surveillance of analytical quality. A QC result sheet has been designed to provide the POCT operator

with a simple, practical guide to assess, interpret and act on the analytical performance of the POC testing device.

The between-site imprecision achieved in the NT POCT Program has been calculated for each test and QC level at the completion of each year of the program's operation.

To monitor clinical effectiveness, the program's central data station has been used to search for interesting clinical cases where POC testing (across different test profiles) has resulted in an improved clinical outcome for patients with both acute and chronic clinical presentations.

A questionnaire was distributed to all remote health centre staff in the second year of the program to determine levels of satisfaction among health professional staff trained as POC device operators in the NT POCT Program. The questionnaire was implemented using an online survey provider and results were analysed using the Stata 9.0 software program (StataCorp, College Station, Texas, USA).

RESULTS

Training of i-STAT Device Operators

Over the first four years of the program a total of 506 remote health centre staff have been trained as i-STAT operators (164 in year 1, 73 in year 2, 131 in year 3 and 138 in year 4); this represents the building of a significant workforce capacity. However, staff turnover has been a significant issue with 131 operators (36%) either leaving the Territory or moving internally within the Territory to a site without access to POC testing.

Operational Effectiveness

The total volume of i-STAT patient testing has continued to rise steadily across each year of the program, reaching 6,837 patient tests in year 4 and totalling 21,251 since the program started (figure 2). This increasing volume of testing reflects the generally high level of acceptance of POC

testing by health professional staff in the Territory. A breakdown of testing by cartridge type shows a similar trend, with INR being the test most commonly performed (representing over 40% of the total testing conducted and averaging 226 tests per month), followed by Chem8+ (30%; 172 tests per month), troponin (22%; 123 tests per month) and CG4+ (8%; 48 tests per month). The high rate of INR testing is due to the high prevalence of rheumatic fever (and resultant atrial fibrillation) in remote NT communities.

There was unanimous agreement from Health Centre Managers that monthly feedback reports assisted in monitoring the use of the i-STAT device in their health centre.

Analytical Quality

Table 2 documents the between-site imprecision observed for quality control testing across each year of the NT POCT Program for selected analytes and lot numbers of control material which had the highest number of repeated analyses performed. Observed performance is compared to the median imprecision achieved for the same analytes by Australasian laboratories participating in the most recent testing cycle of the RCPA Quality Assurance Programs Blood Gas and Co-oximetry program. For INR, the analytical goal recommended by the Australian Government in the recent Point-of-Care Testing in General Practice Trial was used as the benchmark for analytical performance for this test.[7] The observed performance on the i-STAT remained very consistent across each year of the program and met the analytical goals for imprecision against which they were compared.

Clinical Effectiveness

The following two cases, one relating to an acute presentation and the other to a chronic episode of care, are used as illustrative examples of the clinical effectiveness of POC testing in the Northern Territory.

Case 1: This case involved a 73 year-old male tourist in 2009. He had suffered a myocardial infarction in 2008 and previously undergone angioplasty surgery in 1997 and coronary artery bypass surgery in 1993.

The patient, who had a history of intermittent claudication, developed pain in a lower limb after bushwalking. This was relieved with his prescribed nitroglycerine spray. Later in the evening he developed strong chest pain, which resolved 20 minutes after self-administration of nitroglycerine spray. Chest pain recurred 2 hours later prompting presentation to the health centre at 01:30 am. He was treated with nitroglycerine spray and aspirin which relieved the chest pain. There were no major changes on ECG and his observations were stable. However, as the patient had a previous cardiac history including myocardial infarction in 2008, blood was taken and staff at the clinic performed a cardiac troponin I POC test on the i-STAT at 02:10 am.

The troponin I result was 0.12 ng/mL (<0.08ng/mL being negative). The troponin I result was raised slightly, indicating that a cardiac event may have occurred and it was too early after the event to see a significant rise in this cardiac marker. The District Medical Officer from the Top End was contacted immediately and a medical evacuation to the Royal Darwin Hospital was decided upon at 03:20am. The troponin I was measured by the laboratory at Royal Darwin Hospital later that day and had increased to 0.44 ng/mL. The patient was diagnosed with non-ST elevation myocardial infarction.

In summary, POCT on the i-STAT was able to detect an increase in troponin I levels early after a cardiac event, leading to an early evacuation and a positive outcome for the patient. The Top End District Medical Officer stated: “The clinical outcome was good and may have been missed if the troponin I test was not done. This highlights the importance of having an i-STAT at all remote health centres. A big win for the patient and the i-STAT”.

Case 2: This case involved a 53 year-old female patient on warfarin therapy over a 6-month period from January to July 2009. The patient was obese (BMI>30) with a history of type 2 diabetes and was diagnosed with rheumatic heart disease in 2007. She had been on warfarin therapy for atrial fibrillation to reduce the risk of stroke. Her target range for INR was between 2.5 and 3.5.

Prior to the i-STAT device being available at the remote health centre responsible for this patient, she was required to travel over 200 kilometers and back to Alice Springs on a regular basis to have her INR measured by the local laboratory there and have her warfarin therapy adjusted. After the introduction of the i-STAT, this patient was able to have her INR measured on-site in her remote health centre 21 times over the 6-month period between January and July 2009 with 76% of results within the recommended therapeutic range (figure 3).

In summary, POCT for INR allowed this patient's warfarin therapy to be closely and effectively managed within the community over a 6-month period, minimising her risk of stroke and allowing her to remain in the community with her family. Her daily life was not socially disrupted. The nurse at her remote health centre stated that INR testing was not performed as often as necessary for good management prior to the i-STAT device becoming available. The nurse commented further that she was very satisfied with the i-STAT device as the health centre was now able to manage all their warfarin patients on-site.

Satisfaction with POC Testing

Thirty nine respondents completed the i-STAT questionnaire. The percentage of respondents who were satisfied with their pathology service increased from between 29% and 54% when the laboratory was used to between 84% and 100% after POC testing was introduced for the different i-STAT tests ($p < 0.001$, Fishers exact chi-squared test). When asked in what ways POC testing had improved pathology service delivery at their remote health centre, 95% of respondents stated that

it was more convenient than the laboratory service, 84% believed it had assisted in the stabilisation of acutely ill patients and 42% indicated that it had assisted in reducing the need for medical retrievals (figure 4).

CONCLUSION

Most communities in Australia's remote Northern Territory are located hundreds or even thousands of kilometres from the nearest central laboratory service. Pathology samples may take from several days to several weeks to reach laboratories, with similar times reported for results to be returned to health services. There are also many significant health issues which affect the Territory's large Indigenous population in particular, including very high rates of chronic and acute diseases and the high incidence of preventable hospitalisations.

In 2008, the Northern Territory Government's Department of Health contracted the Community Point-of-Care Service unit from Flinders University to establish a collaborative framework by which POC testing for acute and chronic care tests could be conducted safely on the i-STAT analyser and coordinate the delivery of the Northern Territory Point-of-Care Testing Program in the field.

Across the first four year's of the program, over 500 health professional staff have been trained as qualified POC testing operators and more than 6800 patient tests on the i-STAT have been performed. Analytical quality for POC testing has met profession based analytical goals and/or state of the art laboratory performance for most tests. Clinical case studies sourced from the i-STAT central data station (which electronically captured de-identified patient and quality data from all remote services) has confirmed the clinical effectiveness of POC testing for acute and chronic conditions. Community satisfaction with POC testing was validated using qualitative surveys of device operators. Greater than 80% of respondents believed POC testing was more convenient than the laboratory and assisted in the stabilisation of acutely ill patients. The Northern Territory Point-

of-Care Testing Program has therefore proven operationally effective, analytically sound, clinically and culturally effective, and has been well-received by health professional staff.

The main challenges for the program's sustainability continue to be maintaining standards of training and analytical quality in the face of high staff turnover[11,12], logistic issues and maintenance of cold chain procedures during transport of selected quality control materials to remote health centres (notably the frozen control provided for troponin I), the generally short shelf-life to expiry of quality control materials available from Abbott for the i-STAT, and the current lack of Medicare reimbursement from the Australian Government for the i-STAT POC tests. During the next five years, it is the Management Committee's intention to expand the program to all health centres in the Territory, including those Aboriginal Community Controlled Health Services in the Territory under the jurisdiction of AMSANT, funds permitting.

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Figure 1 - General location of remote health centres participating in the Northern Territory Point-of-Care Testing Program. As shown by the map, the majority of health centres are geographically isolated from the three main towns in the Territory, namely Darwin, Katherine and Alice Springs.

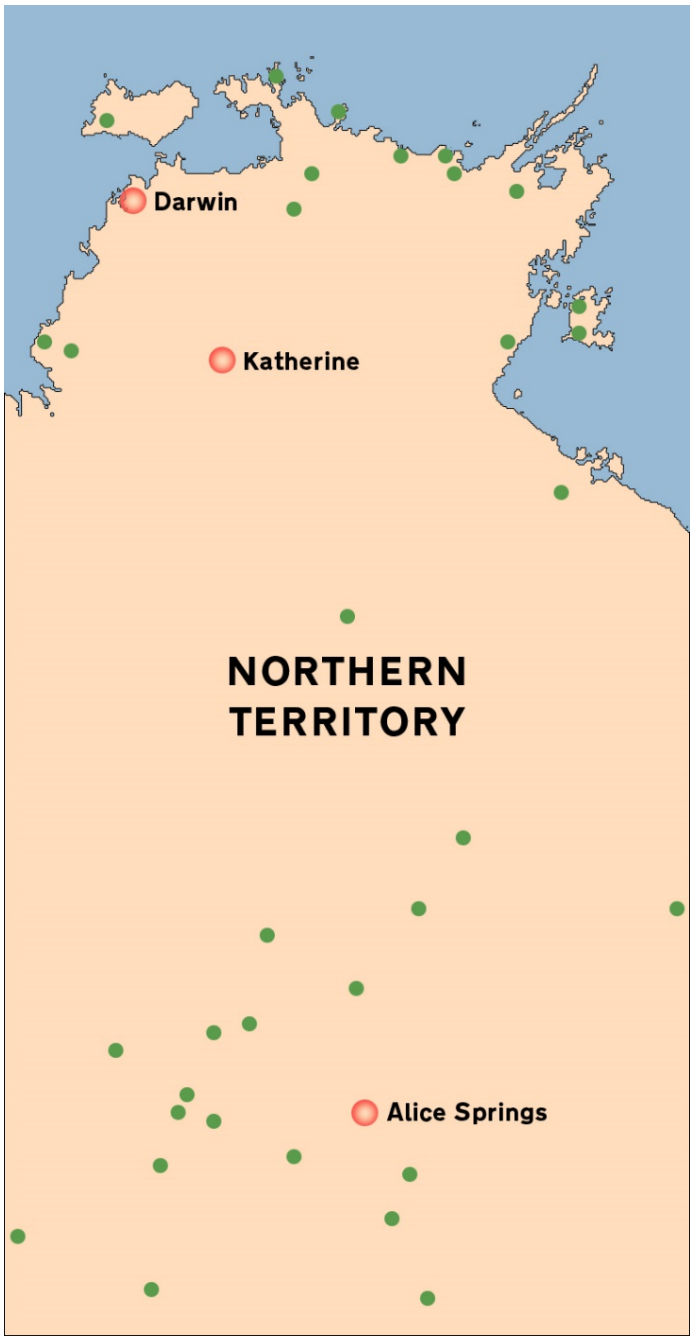


Figure 2 - Total number of i-STAT patient tests conducted across the first four years of operation of the program, split by cartridge type.

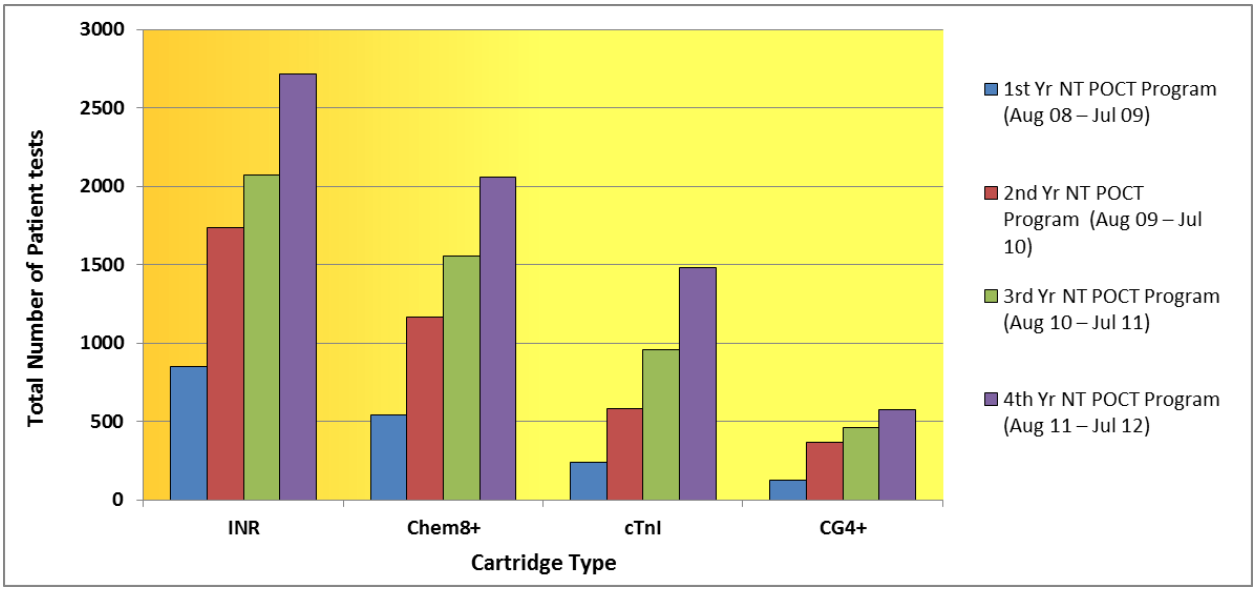


Figure 3 - Results of INR POC testing conducted on a 53 year-old female in a remote Northern Territory community.

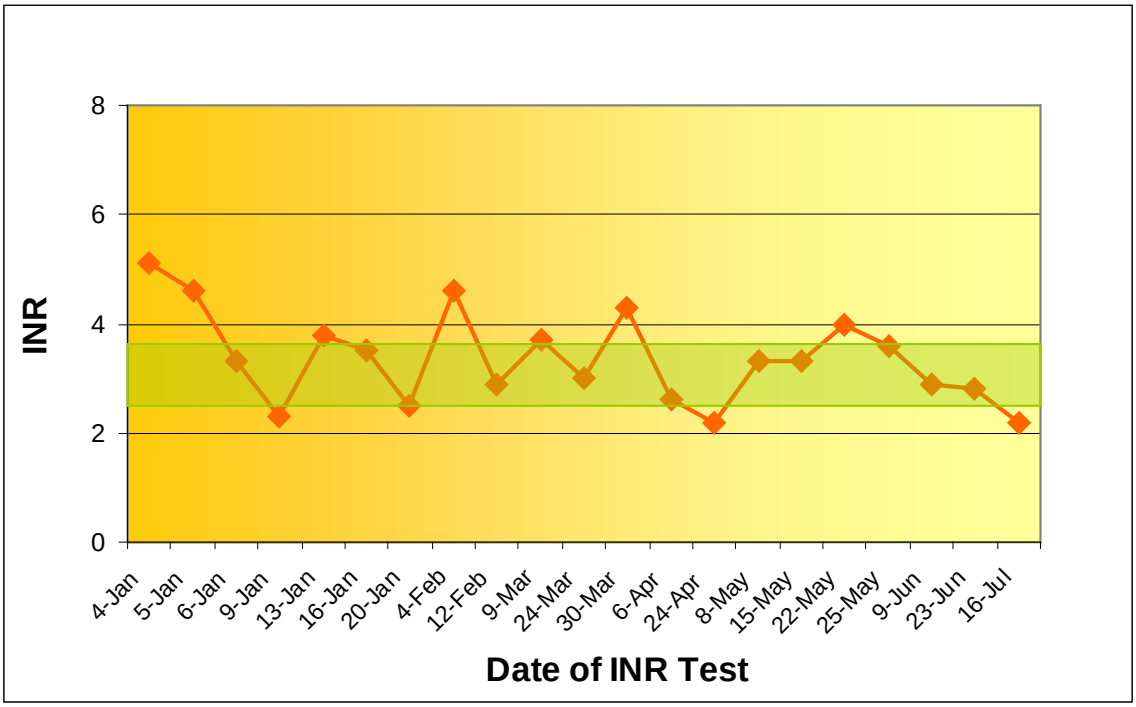
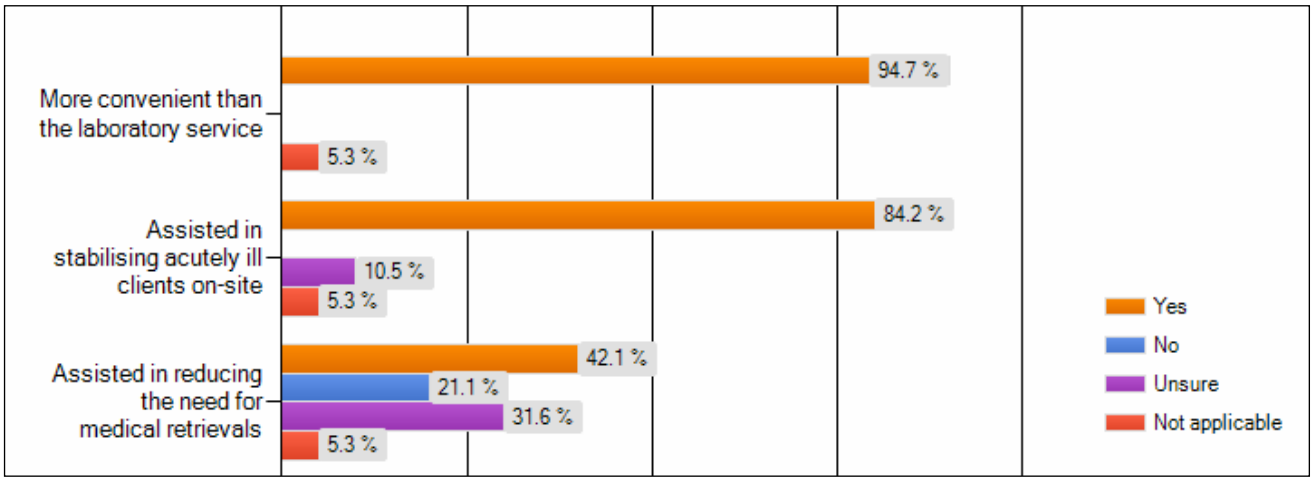


Figure 4 - Responses to questions relating to satisfaction with pathology services after introduction of the i-STAT device in the Northern Territory Point-of-Care Testing Program.



TABLES

TABLE 1. POC tests conducted on the i-STAT in the Northern Territory Point-of-Care Testing Program.

Cartridge name	POC Tests	Sample type and volume	Sample volume	Time for result
Chem8+	Electrolytes, total CO2, urea, creatinine, glucose, ionised calcium, haemoglobin	Venous whole blood	95 µL	2 mins
CG4+	Blood gases and lactate	Venous whole blood	95 µL	2 mins
PT/INR	International Normalised Ratio	Capillary whole blood	20-45 µL	5 mins
CTnI	Troponin I	Venous whole blood	17 µL	10 mins

TABLE 2. Comparison of analytical quality observed with quality control testing for selected analytes in the Northern Territory Point-of-Care Testing Program and analytical goals.

Analyte	Units	Quality Control Level	Year 1 n	Year 1 CV%	Year 2 n	Year 2 CV%	Year 3 n	Year 3 CV%	Year 4 n	Year 4 CV%	Goal# CV%
Sodium	mmol/L	3	118	0.5	141	0.7	171	0.5	128	0.4	0.8
Potassium	mmol/L	3	118	0.7	141	0.8	171	0.8	128	0.7	1.7
Chloride	mmol/L	3	118	1.0	141	0.7	171	1.1	128	1.0	0.9
Glucose	mmol/L	3	118	1.3	141	1.3	171	0.9	128	0.8	2.5
INR	n/a	2	125	7.0	223	6.0	147	5.7	75	6.6	7.0*
pH	n/a	1	96	0.2	147	0.2	65	0.1	126	0.7	1.7
Lactate	mmol/L	1	96	1.9	147	2.8	65	1.8	126	2.6	4.3

Median imprecision achieved by laboratories in the Royal College of Pathologists of Australasia's (RCPA) Blood Gas and Co-oximetry Quality Assurance Program, Cycle 48, 2012; *Analytical Goal for INR recommended by the Australian Government in the PoCT in General Practice Trial; n = number of QC replicates for that level and lot number of QC material; CV% = between-site imprecision.

4.5.2 Study 2: Challenges and methods for POC Coordinators in providing training to remotely located POCT operators

Shephard, M, Halls, H, McAteer, B, Mazzachi, B, Motta, L, **Spaeth, B** & Shephard, A 2013, 'Management challenges for point-of-care coordinators in delivering training and competency programs', *Point of Care*, vol. 12, no. 2, pp. 84-5.
DOI 10.1097/POC.0b013e318265e1c8.

This study highlights the challenges to POC Coordinators in providing POCT training to remotely located health professionals, and provides solutions to these challenges. The challenges described in this study were identified by this author (and colleagues) through their roles as POC Coordinators. This author also contributed to the development of the solutions to overcome these challenges, and the writing and editing of this editorial.

As outlined in the editorial, the challenges experienced by POC Coordinators in managing isolated POCT networks included staff shortages, high workloads and high rates of staff turnover experienced in these locations. The geographic location of the health services participating in the NT POCT Program and QAAMS Program also made it difficult for the POC Coordinator to conduct on-site training and for the remotely located staff to travel to a central location to receive training.

The solutions developed by this author (and colleagues) included the development of training modules to enable POCT training to be delivered by teleconference or through self-directed learning via a website with 24/7 access, and the automation of the POCT competency assessment process. These methods have significantly improved access to POCT training for remotely located health professional staff and increased the efficiency of these processes for the POC Coordinator.

The next study describes how the development of sustainable and effective POCT models in Australia have contributed to increasing the resilience of rural and remote communities.

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1. **Publication Details: Shephard MDS, Halls H, McAteer B, Mazzachi B, Motta, L, Spaeth B, Shephard A,** Management Challenges for Point-of-Care Coordinators in Delivering Training and Competency Programs, Published in *Point of Care*, 2013;12(2):84-85.

   Section of the thesis where the publication is referred to: Throughout the entire thesis.

   Candidate's (Brooke Spaeth) Contribution to the publication:

   Research Design: **30%**

   Data Collection and analysis: **70%**

   Writing and editing: **30%**

   Outline your (the candidate's) contribution to the publication:

Prof Mark Shephard provided the analysis of information, contributed to the first draft and approved the final version of the manuscript.
Heather Halls, Bridgit McAteer, Beryl Mazzachi, Lara Motta, Brooke Spaeth and Anne Shephard contributed to data collection and provided edits to the final version of the manuscript.
Brooke Spaeth also assisted the research design, data analysis and contributed to writing of the first draft.

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Invited EDITORIAL for Point of Care: The Journal of Near Patient Testing,

Submitted 31/05/2012

MANAGEMENT CHALLENGES FOR POINT-OF-CARE CO-ORDINATORS IN DELIVERING TRAINING AND COMPETENCY PROGRAMS

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Conflict of Interest: The authors' unit receives research support from Siemens Healthcare Diagnostics.

The roles and responsibilities of Point-of-Care (POC) Co-ordinators are numerous and ever-expanding. The ordering and despatch of reagents and consumables, confirming lot numbers and expiry dates, managing stock wastage, maintenance of quality testing result sheets, management and provision of feedback on quality testing data, verification of patient results, managing device errors, device maintenance and repair, and managing compliance and regulatory issues (to mention just a few tasks) places substantial demands on the POC Co-ordinator's time. With the support of industry, the ability to automate many of these manually intensive tasks should be a goal to which all managers of POC networks strive.

In practice, the nature and extent of the challenges faced by POC Co-ordinators often depend on the clinical, cultural and geographic setting in which the POC testing network operates. The two largest POC testing models which our unit co-ordinates are the QAAMS (Quality Assurance for Aboriginal and Torres Strait Islander Medical Services) Program and the Northern Territory POC Testing Program. The QAAMS Program is a national POC testing model for diabetes management operating in over 160 Indigenous medical services across mainly rural and remote Australia.[1-3] The Northern Territory Program provides POC testing for acute and chronic diseases in 41 remote Indigenous health centres in the Territory. [4]

Due to the extreme geographic isolation of many of these health services and given that the POC device operators who conduct patient testing in these programs may be one of several different health professional groups, the POC Co-ordinators and supporting scientific staff responsible for these programs face unique challenges with the management of operator training and competency assessment in particular. This aspect of delivering these models therefore forms the basis of this editorial.

Organisation of POC training sessions for health professional staff from remote communities can be very difficult. Due to the competing time demands on staff in remote health services, not all staff are able to attend on-site training sessions delivered by the POC Co-ordinator; conversely the cost of flying remote staff to a central location (capital city) for training are prohibitive and health centre managers are reluctant to allow staff the additional time away from the service. Staff turnover rates in remote health centres are also high[5] and it is often difficult to maintain continuity of patient and quality POC testing during periods when services are understaffed or when there are no trained operators available at remote services. Hard copies of manual training resources such as primary training manuals and posters summarising quick guides on how to perform patient and quality testing are often misplaced when staff turn over, leaving the next POC operator without key reference material. The ability of the POC Co-ordinator to deliver immediate on-site training sessions when new staff replacements arrive is compromised by the demands of distance and time.

For this reason, training for our large networks has evolved in recent years to include a range of flexible automated and electronic options, which aim to simplify the manual workload and the travel and time demands on the POC Co-ordinator and provide a more sustainable means for the delivery of training. In the QAAMS Program, web-streamed videos of training are now available through a password-protected 'Participant Only' section of the website. These videos systematically take the participant through the principles and practice of POC testing for this program and can be viewed at any time that is convenient for the trainee device operator. The full training manual, poster sets, training aids for the interpretation of patient results, quality control result sheets, reagent and consumable ordering sheets, quarterly newsletters, contact details for the POC Co-ordinator and scientific and technical support, are also all available for direct electronic downloading from the website. However, in Australia, some remote services experience difficulties with internet service provision and may be unable to effectively access the web resources. As a result, all participating

services are also provided with a DVD containing a complete electronic copy of all the information that is found on the website. As additional options, training is also now available through either videoconference or Skype. This latter low cost option is now also being used regularly for training with international communities participating in the ACE (Analytical and Clinical Excellence) POCT Program for diabetes management being delivered by our International Centre for Point-of-Care Testing. Opportunities for participants to attend an annual workshop or a regional workshop remain available and these create an environment where the often isolated POC device operator no longer feels 'alone' but rather can experience the co-operative and collaborative nature of the network.

Competency assessment and maintenance of competency registers is an important adjunct to training and another pivotal role of the POC Co-ordinator. For many years, these tasks were performed manually in our two remote networks. Our competency assessment processes have traditionally involved the completion of both written and practical components; the written assessment being administered manually by the POC Co-ordinator during on-site visits and the practical assessment involving the trainee performing testing of both quality control and quality assurance samples (and obtaining analytical sound results for these samples). However, the number of trained operators has now grown to more than a thousand in the QAAMS program and close to 400 in the Northern Territory POC Testing Program. This has meant that the manual marking of competency forms, checking of quality results, the preparation of competency certificates (including assignment of operator identification numbers), recording of details regarding expiration of competency and the date for completion of competency renewal has become too time consuming for the POC Co-ordinator. An electronic solution has also been developed to streamline these processes and reduce the manual time and labour burden on the POC Co-ordinator. Written competency assessment forms can now be downloaded direct from the website, completed by the candidate after viewing the videos and then emailed (or faxed) to the POC Co-ordinator.

Alternatively, through a new tailored connectivity package developed for QAAMS, competency forms can be completed and marked electronically, with a competency certificate automatically generated once the practical component has been completed by the candidate. While many electronically-based competency programs now require only a written assessment of competency, our philosophy remains steadfast in the belief that a practical component is essential to the competency process, as it provides evidence to confirm the new operator has the necessary practical skills to conduct the POC test with confidence and assurance. Our new system also alerts the POC Co-ordinator when competency renewal is due for current device operators.

In summary, as POC testing networks grow in size and complexity, there is an increasing need to reduce the time demands that manual processes impose on the POC Co-ordinator. The capacity to automate as many of these processes as possible clears the way for the more efficient and effective delivery of a POC testing service, particularly in geographically isolated regions. This brief editorial illustrates how the automation of tasks relating to just one aspect of a POC Co-ordinator's role – training and competency – can significantly improve the efficiency of such POCT networks.

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4.5.3 Study 3: Methods and results to increase community resiliency in Australia using POCT

Shephard, M, **Spaeth, B**, Motta, L & Shephard, A 2014, 'Point-of-care testing in Australia: Practical advantages and benefits of community resiliency for improving outcomes.', in G Kost & C Curtis (eds), *Global Point-of-Care - Strategies for Disasters, Complex Emergencies, and Public Health Resilience.*, American Association of Clinical Chemistry Press, Washington DC, pp. 527-35.

This peer-reviewed book chapter describes how several POCT models in Australia have contributed to improving community resilience in rural and remote locations. This author contributed to data collection, data analysis and the writing and editing of this book chapter. The particular sections provided by this author were outlined and discussed within the contextual statement.

The QAAMS Program and NT POCT Program are described with operational, analytical and clinical results provided to demonstrate how each model contributes to improving community resilience and building significant workforce capacity in rural and remote locations. As outlined in the chapter, these community-based POCT models provide advantages to the patient, POCT operator and treating practitioner through providing more timely pathology results and, thus, a more convenient and accessible pathology service.

For the patient, POCT provides more patient-centred care which can enhance the patient experience and contribute to improved motivation to improve their health. This chapter also provided examples of improvements in clinical outcomes for patients with both chronic and acute disease as well a quantitative data on improvements in glycaemic control of patients with diabetes.

For the operator, POCT can create a greater sense of ownership and empowerment within the community to provide a more patient-oriented and convenient pathology service. Also outlined is that AHWs and remote area nurses were able to achieve analytical performance equivalent to that of trained laboratory technicians and scientists.

For the treating practitioner, POCT can improve their relationship with the patient through enabling pathology results to be available in the same consultation and allowing more rapid changes to treatment or clinical management.

To the community, POCT can build a strong sense of engagement as the devices can be taken into the community for health promotion or awareness events. POCT may also prevent the unnecessary dislocation of patients from the community by allowing their chronic or acute condition to be closely monitored and stabilised safely in the community and, thus, contribute to community resilience.

This study is the first to specifically discuss how POCT contributes to increasing the resilience of rural and remote communities.

The next study demonstrates the long-term sustainability of the NT POCT Program through providing results on key effectiveness measures in year seven of the Program during which a significant expansion of POCT services occurred.

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All authors contributed to the analysis of clinical and operational data.
Mark Shephard provided the first draft of the chapter with all authors contributing to the editing and approving the final version.

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CHAPTER 48: POINT-OF-CARE TESTING IN AUSTRALIA:

PRACTICAL ADVANTAGES AND BENEFITS OF COMMUNITY RESILIENCY FOR IMPROVING OUTCOMES

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ABSTRACT

A Brief Overview of Point-of-Care Testing in Australia

Point-of-care (POC) testing in community settings has come of age in Australia, particularly over the past decade, due to significant technological and analytical advances in device and reagent manufacture, an increasing array of new tests and test profiles, and the development of large-scale national and state-wide community-based programs that have delivered evidence-based clinical, operational and strategic benefits to the community (1,2).

Australian Point-of-Care Testing Models

The national Quality Assurance for Aboriginal and Torres Strait Islander Medical Services Program (QAAMS) is the largest and longest-standing community-based POC testing program in Australia. QAAMS supports the quality-assured conduct of POC testing for hemoglobin A1c (HbA1c) and urine albumin:creatinine ratio (UACR) on the Siemens DCA Vantage® to assist diabetes management in over 175 Aboriginal and Torres Strait Islander medical services across Australia. QAAMS has been funded continuously by the Australian Government since its inception in 1999, and is managed by the Flinders University International Centre for Point-of-Care Testing (formerly known as Community Point-of-Care Services) in partnership with the Royal College of Pathologists of Australasia (RCPA) Quality Assurance Programs Pty Ltd (3-5). A government-commissioned independent review of QAAMS concluded that: "All sources of evidence suggest that the QAAMS Program is meeting best practice standards in the areas of Indigenous healthcare, diabetes management and Point-of-Care Testing [and] QAAMS is one of the few programs to successfully navigate the cultural complexities and potential pitfalls of chronic disease management in Indigenous communities (6)."

Separate state-wide i-STAT® networks now operate in Queensland and the Northern Territory. The Queensland network is managed by Pathology Queensland and has devices located in over 140 rural and remote locations in Queensland where there are no laboratories and a further 32 hospitals with on-site laboratories (7). The Northern Territory network is managed through a partnership between the Flinders University International Centre for Point-of-Care Testing and the Northern Territory Department of Health, and operates in 33 remote health centers in some of the most isolated areas of Australia (8-9).

In South Australia, the Integrated Cardiovascular Clinical Network SA (iCCnet SA) provides an integrated solution to ensure that patients presenting to rural and remote hospitals in South

Australia receive access to appropriate cardiac care. As part of this comprehensive service, troponin POC testing is embedded into an agreed clinical pathway for patients presenting with chest pain/acute coronary syndrome (10).

From 2005 to 2007, the Australian Government commissioned a comprehensive study of POC testing in general practices in Australia (the Point of Care Testing in General Practice Trial). The clustered randomized controlled trial involved 53 general practices and 4968 patients with chronic conditions including diabetes, hyperlipidemia or coagulation disorders (11-13). The lead organisations responsible for delivering the trial were The University of Adelaide Discipline of General Practice, the Community Point-of-Care Services unit at Flinders University and the RCPA Quality Assurance Programs Pty Ltd.

Each of these Australian POC testing models have been conducted under quality-assured frameworks that have delivered evidence-based outcomes highlighting the analytical quality, the clinical effectiveness and (where appropriate) the cultural effectiveness of POC testing (4,5,10,12).

EMERGING OPPORTUNITIES FOR POC TESTING IN AUSTRALIA

Several major opportunities and challenges for POC testing in Australia remain. POC testing for infectious diseases in community settings has only recently begun to gain momentum in Australia (14). The Australian Government approved the use of POC testing for HIV in community settings in December 2013 and several trials involving POC testing for HIV have been undertaken in urban sexual health clinics (15). A new randomized trial involving POC testing for chlamydia and gonorrhoea called TTANGO (Test, Treat And GO) has recently commenced in remote Indigenous communities (16). National standards for the conduct of POC testing in Australia are not currently available (at the time of writing). A set of interim standards was developed for use in the Point of Care Testing in General Practice Trial by a subcommittee of the Australian Government Department

of Health and Ageing Quality Use of Pathology Committee (17). A major issue for POC testing in Australia is that most POC tests, notably those in the general practice arena, are not currently eligible for the rebates under the Government's Medical Benefits Scheme (Medicare) and therefore the cost of POC testing must be borne by the practice or the patient.

Practical Advantages and Benefits of Point-of-Care Testing

The growth of community-based POC testing in Australia has undoubtedly benefited from several factors:

- The movement towards 'patient-centred' health care delivery
- The care of patients with chronic diseases has increasingly devolved from the hospital to the community
- The vastness of the Australian continent and the geographic isolation of many rural and remote communities have inhibited the ability of laboratory services to deliver pathology results in a timely manner and this has facilitated the need and requirement for POC testing (Figures 1 and 2).

The most remote health service in the QAAMS Program is approximately 1500 kilometers (930 miles) from the nearest capital city in one direction and 1000 kilometers (620 miles) from the nearest town in the opposite direction. Clearly the scale of distance in a country like Australia precludes laboratory testing from being effective in many instances.

The use of community-based POC testing, particularly in geographically isolated Australian communities, has practical advantages for the patient, the health professional performing POC testing, the treating practitioner and the community overall.

Patient

For the patient, the immediacy of the POC test result provides a convenient and timely service, negating the need for a return visit to obtain their pathology results. Only a small volume of blood or urine (generally less than 100 microliters) is required to perform most POC testing and therefore sample collection can be far less stressful if for example a fingerprick rather than a venipuncture can provide adequate sample volume. There is also a sense of ownership of the sample which, for Indigenous patients, is a culturally sensitive issue and a significant practical advantage of POC testing. The patient can observe his/her own sample being loaded onto the POC device and can see their result displayed on the screen of the device when the test is completed. In both the QAAMS and Point of Care Testing in General Practice Trial, patient surveys have concluded that patients view POC testing as motivational in terms of better managing their own condition and strengthening their relationship with the doctor (4,18).

Operational Efficiency: The operational efficiency of POC testing for the patient was recently demonstrated in a clinical audit of 40 diabetes patients (who had all shown a decrease in HbA1c of greater than 1.5% post the introduction of POCT) from remote Northern Territory communities in QAAMS. The audit compared the efficiency of POC testing versus laboratory testing over an equivalent time period (15 months) using a 'before and after' study design. Long turnaround times for receipt of laboratory results and follow-up consultation with patients were identified during the period prior to the introduction of POC testing, compared to immediate receipt and actioning of results using POC testing. Frequency of HbA1c testing was also higher with POC testing than the laboratory (Table 1).

The operational efficiency of POC testing has also resulted in a significant and sustained increase in the volume of patient POC testing for acute care (electrolytes, cardiac markers and blood gases) in the Northern Territory POC Testing Program. In the year prior to the introduction of POC testing,

422 tests for acute care markers were performed by regional laboratories in the Territory servicing the centers now participating in the Program. Following the introduction of POC testing in August 2008, the volume of acute care testing more than doubled in the first year to 901 patient tests. This uptake in POC testing has continued across each year of the Program with 5043 acute care tests being performed in year 5 of the Program (Figure 3).

POC Testing Operator

Health professionals conducting community-based POC testing in Australia are generally nurses or Indigenous Health Workers (Aboriginal or Torres Strait Islander Australians who live and work in their communities and who have a qualification in primary health care) but may also include diabetes educators, nutritionists, pharmacists, and other allied and administrative personnel. In the community models developed by the Flinders University International Centre for Point-of-Care Testing, POC testing device operators (whether Indigenous or non-Indigenous) have described their satisfaction in having the responsibility for performing POC testing in their communities. The success of the Indigenous POC testing programs that the International Centre manages has unquestionably resulted from ensuring the Indigenous Health Worker has a pivotal role as the POC testing operator; Indigenous Health Workers provide a crucial communication bridge between management staff, the community and the non-Indigenous health staff and are a committed, passionate and hard working group of health professionals. In the QAAMS Program, Indigenous Health Workers have become highly proficient at performing routine POC testing within their services and can achieve standards of analytical quality at least equivalent to the laboratory (5).

Analytical Performance: The long-term analytical performance for quality control (QC) and quality assurance (QA) testing for HbA1c by POC testing operators in the QAAMS Program is shown in Table 2 and Figure 4. Bi-level QC testing in QAAMS has continued to meet benchmarks for analytical quality recommended by the Australian Government and expected of Australian laboratories

(desirable and minimum analytical goals for imprecision of 3% and 4%) over the past 7.5 years. The average imprecision observed across this period is 2.6% ± 0.53 for QC 'Normal' and 3.1% ± 0.53 for QC 'Abnormal'. For QA testing, the quality of analytical performance observed in the QAAMS Program has continued to improve over the past decade (Figure 4) and is also meeting analytical benchmarks. It is possible to directly compare the performance of QAAMS participants with Australian laboratories for HbA1c testing because QAAMS and the laboratory-based RCPA Glycohaemoglobin QA Program use identical material. For the past 5 years, there has been no statistical difference between the imprecision achieved by QAAMS and Australian laboratories, with the median imprecision for HbA1c QA testing averaging 2.42% ± 0.15 for QAAMS sites and 2.52% ± 0.26 for Australian laboratories (p=0.08).

Sound analytical performance for POC testing for acute pathology markers has also been observed over the past 5 years in the Northern Territory POC Testing Program, with remote area nurses meeting laboratory benchmarks of quality (Table 3).

Collectively, this data shows unequivocally that, with sound continuing education, training, competency assessment and support programs in place, non-laboratory trained POC testing operators can achieve equivalent analytical performance to that of trained laboratory technicians and scientists.

Satisfaction with POC Testing: In terms of stakeholder satisfaction levels, both patients and device operators have reported statistically significant improvements in satisfaction levels with pathology service delivery following the introduction of POC testing for chronic and acute diseases (Table 4). In the Diabetes Management Along the Mallee Track Program (20) managed by the International Centre in the rural north west corner of the state of Victoria, POC services were optimized in 2011 through the introduction of a new and improved suite of POC devices for chronic disease management. Satisfaction levels with POC testing among diabetes patients accessing this service

was high following the initial introduction of the POC testing service in 2004 but increased even further (to 98%) in 2011 following this optimization process (unpublished observation).

Treating Practitioner

For the treating practitioner, POC testing provides rapid results that can be used to enhance clinical decision making at the time of consultation, for the management of both acute and chronic conditions. POC testing can maximize the health outcome benefit to the patients as a result of the treating practitioner being able to take immediate action on the POC test result. Examples of clinical outcome measures that have been used to assess the effectiveness of POC testing in community-based Australian settings are summarized in Table 5.

Evidence from QAAMS across three separate studies over 6 years (Table 6) has shown that the introduction of POC testing has resulted in improvements in glycemic control (as observed by statistically significant reductions in HbA1c) both within individual diabetes patients and between groups of diabetes patients who had three or more HbA1c POC tests performed during the study periods. Improvements in the percentage of patients achieving glycemic targets (HbA1c <7%) and a reduction of patients with poor control (HbA1c) has also been recorded in QAAMS and in the Diabetes Management along the Mallee Track Program (Table 7).

In remote Northern Territory communities, the ability to make an informed on-site clinical decision on acutely ill patients as to whether they could be stabilized *in situ* or required a medical evacuation to a tertiary hospital has been crucial in improving both clinical and operational outcomes. Preliminary data on the cost effectiveness of i-STAT® POC testing in the Territory has shown that medical retrievals prevented as a result of accessing pathology results by on-site POC testing has resulted in a cost saving of approximately US $4.5 Million per year (unpublished observation).

Community Engagement

POC testing fosters and builds a strong sense of community engagement by ensuring that the patient is the central focus of the pathology service being delivered and by empowering the community health service to have greater ownership and control of the way their pathology service and resultant health information is managed.

When POC testing is being established within a new community, it is imperative that the POC Coordinator takes time to engage and listen to the community, their thoughts and their aspirations. Time and patience is required to define and explain the clinical, operational and economic benefits (and limitations) of introducing POC testing into the community setting. For Indigenous POC testing models in particular, community engagement is crucial to the acceptance and ultimate success of the program.

Due to their portability, POC devices can be taken into the community and linked with community events such as health promotion activities, chronic, acute or infectious disease awareness and health screening days. Through access to on-site POC testing for chronic conditions such as diabetes and coagulation disorders, patients can remain in their communities for treatment and management and are not dislocated from their family members. For Indigenous patients, separation from family to attend treatment clinics in large cities or towns can create significant social and emotional problems and therefore having POC testing locally available helps build community resilience.

It is imperative to ensure there will be an element of progressive knowledge transfer and capacity building; so that, as a POC testing program is implemented, the community is empowered with the resources to manage and sustain the program long-term. With all of the models developed by the International Centre, this involves systematically embedding a functional clinical governance structure for the organization and accountability of POC testing, a tailored continuing program for

training and competency assessment of device operators, implementation of sustainable quality management practices fit for purpose and relevant and appropriate for the device(s) being used and documentation of policies and procedures in flexible formats depending on the clinical, cultural and geographic settings where community-based POC testing is practiced.

Towards Building a Sustainable and Resilient Workforce Capacity

The ultimate aim of progressive knowledge transfer is to build a sustainable and resilient community workforce that has the capacity to undertake routine quality-assured POC testing for its intended clinical purpose, whether it is for acute care, chronic or infectious disease care. In the QAAMS Program over the past four years, 939 POC testing operators have been trained, with the percentage of those undertaking online training increasing from 19% (in 2009-2010) to 48% (in 2011-2013). In the Northern Territory, training has been provided for 673 remote area nurses as POC testing operators for both acute and chronic clinical needs since mid 2008. However it should be noted that disproportionately high rates of health professional staff turnover remain the biggest single factor affecting efficient health service delivery (including POC testing) in remote Australian communities. In two separate studies, 53% of nurse POC testing operators who left their general practice during the Point of Care Testing in General Practice Trial were from remote locations, while 33% of nurse operators in the Northern Territory POC Testing Program left their remote health service during the first year of operation of this program (9,19). In addition, it is critical that only trained operators with a current certificate of competency perform POC testing to ensure valid pathology results are generated by POC testing and patient safety is not compromised.

In the Northern Territory POC Testing Program, a lock-out of unauthorised device operators was implemented in 2012 following a short period where untrained operators were using the i-STAT® without having completed the required training program. During this period, the cartridge error rate for unauthorized operators was double that of trained operators; these errors were pre-analytical

errors only, with patient or QC results being suppressed and not reported by the device and therefore patient safety was not compromised.

In the QAAMS Program an Indigenous Leaders Team, comprising an Indigenous Health Worker from each state and Territory of Australia who has demonstrated outstanding leadership and commitment to POC testing, has also been established to work at the national governance level of the program on cultural safety and advocacy for POC testing.

The building of a resilient POC testing workforce has additional advantages for the community during periods of escalated activity or need, such as the untimely impact of a natural or man-made disaster where major disruption to normal health care practices may occur and where it may be necessary to employ “crisis standards of care”. The ability to mobilize a local workforce that (i) is familiar with and trained in the principles and practice of POC testing, (ii) has the ability to adapt their skills and undertake “just in time” training for different POC testing applications needed in a disaster scenario and (iii) can show leadership in the time of crisis, is a major advantage in both the first-line response and recovery phase of a disaster event.

CONCLUSION

There is a sound evidence base that community-based POC testing in Australia has enhanced service delivery, assisted in improving patient outcomes (in both chronic and acute disease contexts) and facilitated community engagement (particularly in Indigenous communities). Across much of the vast Australian landmass, there are now many communities that are utilizing POC testing for specific clinical needs and have built significant workforce capacity for conducting POC testing. Nonetheless, it is acknowledged that in remote communities in particular, staff retention rates are a constant problem which can erode efforts to maintain POC testing workforce capability, while the current lack of Medicare rebates for most POC tests is likely to impede its uptake in some primary care

settings. Building community capacity to undertake quality-assured POC testing for routine patient care can have flow-on benefits in terms of preparedness and response in disaster scenarios.

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22. Shephard MD, Allen GG, Barratt LJ, Barbara JA, Paizis K, McLeod G, et al. Albuminuria in a remote South Australian Aboriginal community: results of a community-based screening program for renal disease. Rural Remote Health 2003;3:156.

Figure 1 - The general location of Aboriginal and Torres Strait Islander medical services in the QAAMS Program. Eighty percent of the Australian population live within 50 kilometers (approximately 30 miles) of the sea. More than 75% of the Australian landmass is classed as remote, including all of the interior of Australia, which is very isolated geographically.

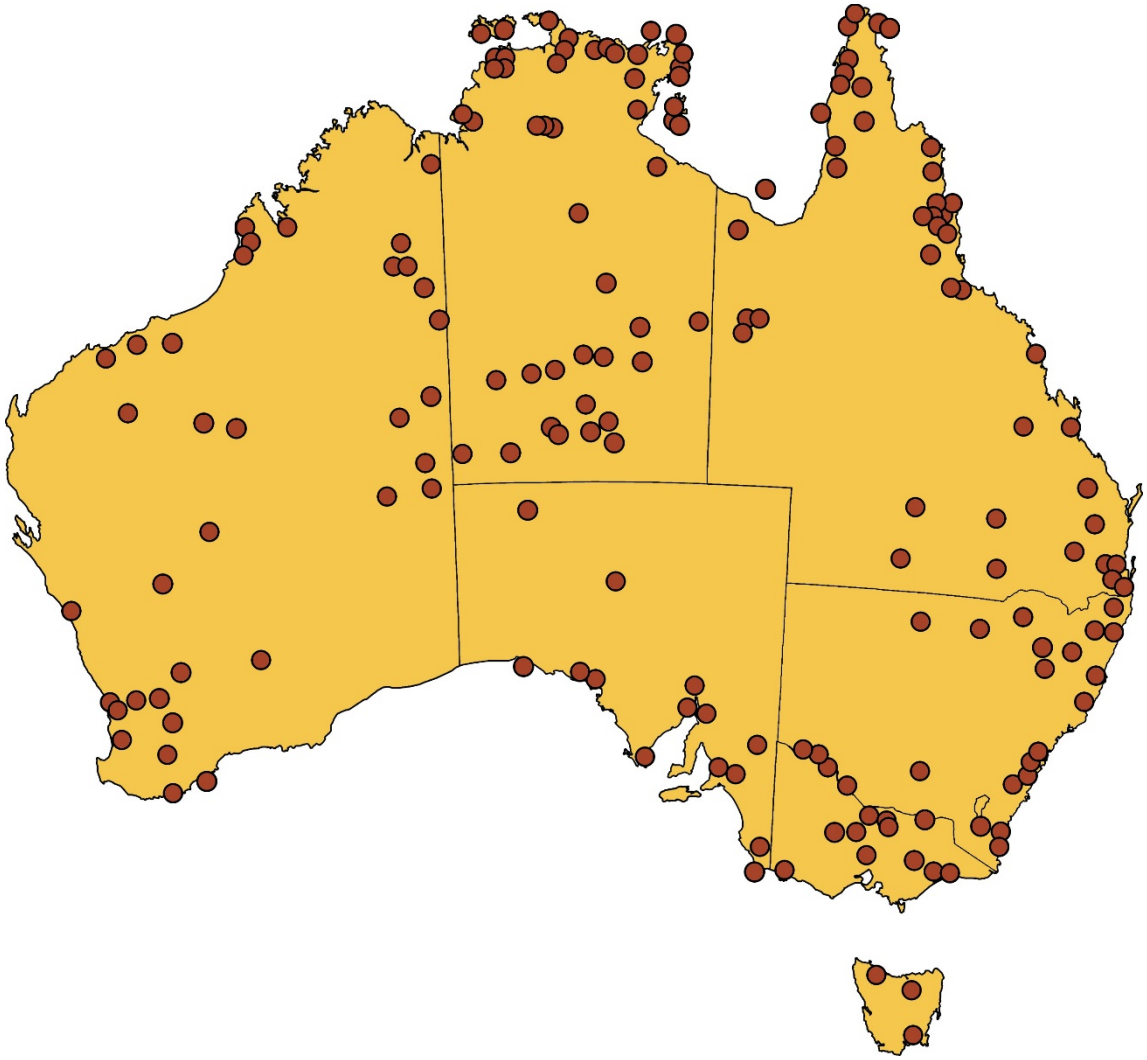


Figure 2 - The general location of remote health centers participating in the Northern Territory POC Testing Program. As shown by the map, the majority of health centers are geographically isolated from the three main towns in the Territory, Darwin, Katherine and Alice Springs.

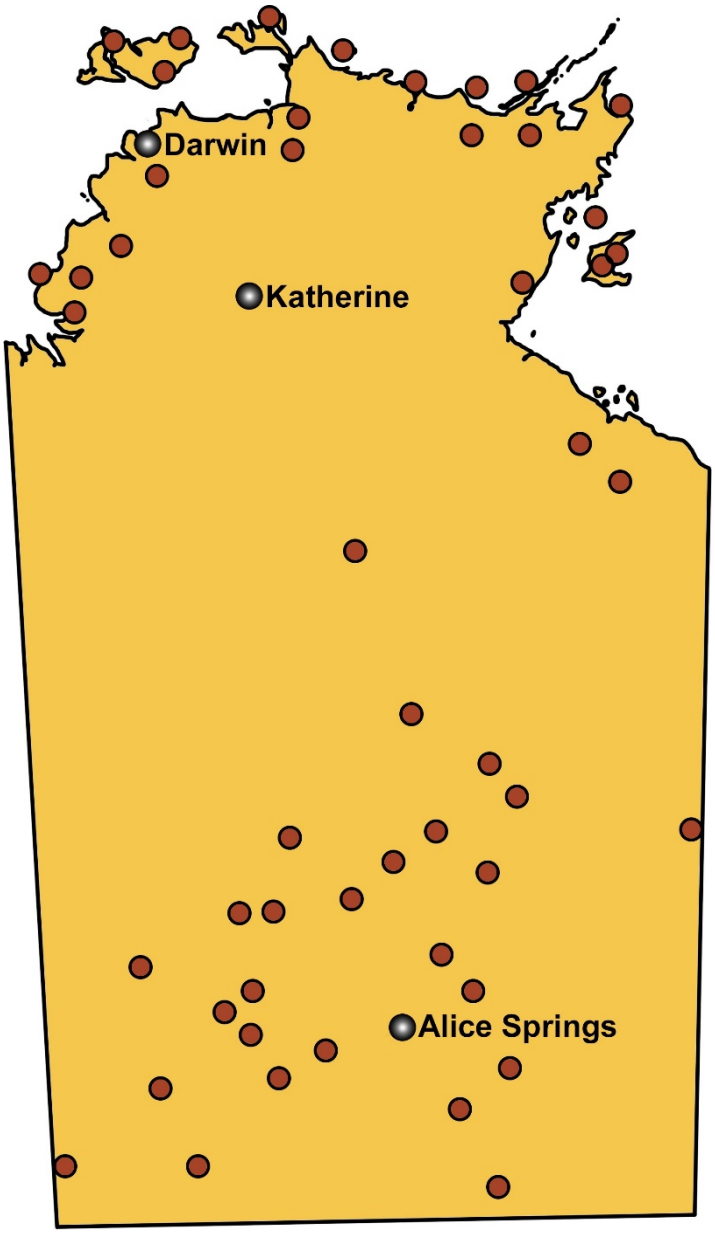
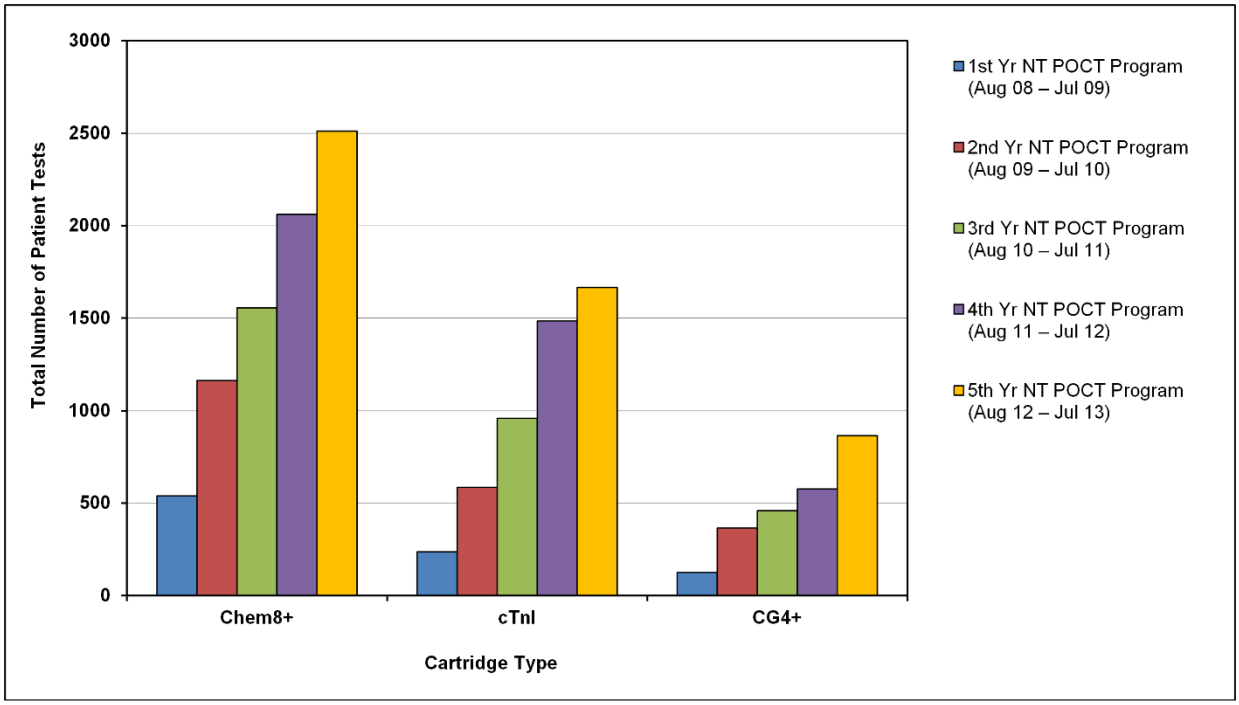


Figure 3 - Volume of patient POC testing for electrolytes (Chem8+), troponin I (cTnI) and blood gases (CG4+) performed on the Abbott i-STAT® POC device across all participating services in the first 5 years of the Northern Territory POC Testing Program



Footnote: The Chem8+ cartridge also performs urea, creatinine, ionised calcium, glucose and calculated hemoglobin in addition to electrolytes. The CG4+ cartridge also performs lactate in addition to blood gases.

Figure 4 - Comparative imprecision (median CV%) observed for HbA1c quality assurance testing in QAAMS (by POCT) and in Australian laboratories (all methods) over 10 years (2002-2012).

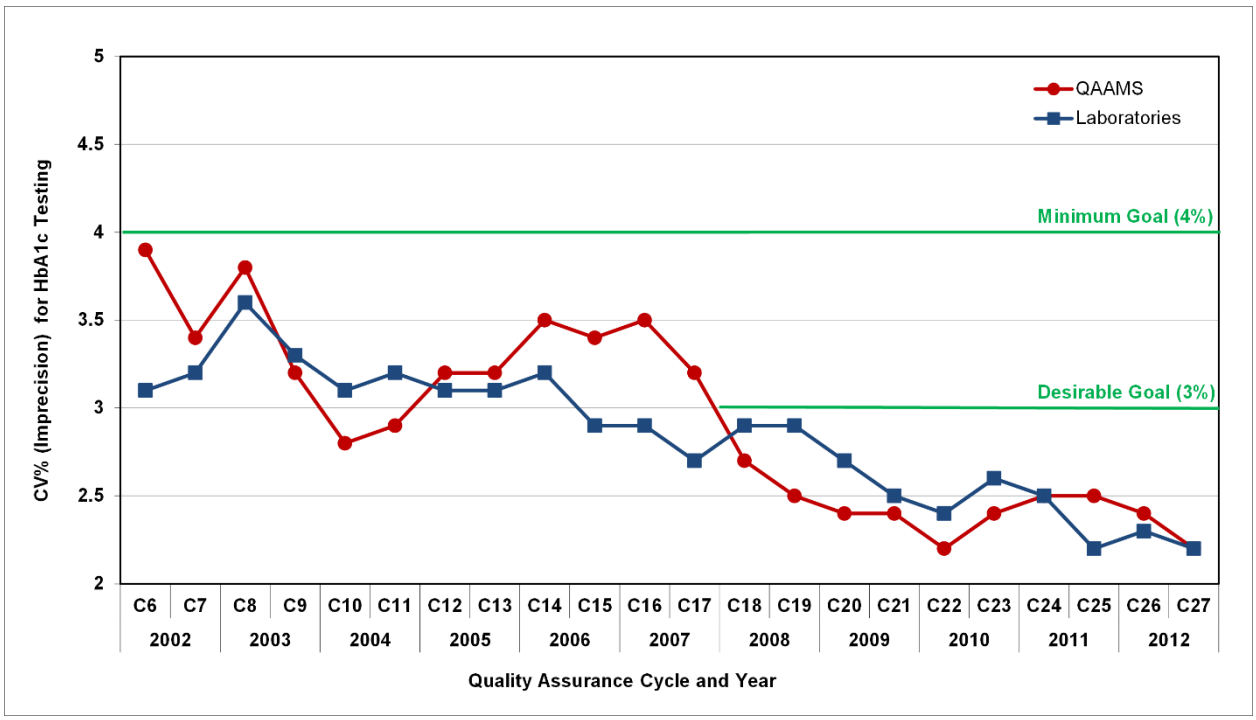


TABLE 1. Comparison of the clinical and operational efficiency of POC testing versus laboratory HbA1c testing for pathology service provision in a subset of 40 diabetes patients from remote Northern Territory health centers.

Parameter	15 months Before POC Testing	15 months After POC Testing
Mean (±SD) change in HbA1c % (mmol/mol); first to most recent result	9.5% (80 mmol/mol) ±1.6 to 9.8% (84 mmol/mol) ± 1.3	10.6% (92 mmol/mol) ±1.6 to 7.9% (63 mmol/mol) ± 1.3
Mean turn-around time for reporting of HbA1c result	42 (±30) hours	6 minutes
Mean turnaround time for patient follow-up and consultation	24 (±15) days	Less than 15 minutes
Mean (±SD) number of HbA1c tests per patient	2.7 tests (±1.7)	4.2 tests (±0.8)

TABLE 2. Imprecision (median CV%) for HbA1c quality control testing in QAAMS, 2006-2013.

	Median Within Site Imprecision (CV%)														
Year	**2006**		**2007**		**2008**		**2009**		**2010**		**2011**		**2012**		**2013**
Cycle	**C14**	**C15**	**C16**	**C17**	**C18**	**C19**	**C20**	**C21**	**C22**	**C23**	**C24**	**C25**	**C26**	**C27**	**C28**
QC Normal	3.1	2.3	3.2	2.7	2.2	2.4	2.2	1.8	2.5	2.6	4.0	2.3	2.9	2.8	2.4
QC Abnormal	3.3	3.1	4.1	3.5	3.9	3.9	2.6	2.6	2.9	3.0	3.5	2.3	2.7	3.0	2.3

TABLE 3. Imprecision (median CV%) for quality control testing on the i-STAT® in the Northern Territory POC Testing Program, 2008-2013.

		Median Between Site Imprecision (CV%)					
Analyte	**Units**	**2008-09**	**2009-10**	**2010-11**	**2011-12**	**2012-13**	**Goal CV%[#]**
Sodium	mmol/L	0.5	0.7	0.5	0.4	0.4	0.8
Potassium	mmol/L	0.7	0.8	0.8	0.7	0.8	1.7
Chloride	mmol/L	1.0	0.7	1.1	1.0	1.1	0.9
Glucose	mmol/L	1.3	1.3	0.9	0.8	2.2	2.5
INR	n/a	7.0	6.0	5.7	6.6	6.7	7.0*
pH	n/a	0.2	0.2	0.1	0.7	0.2	1.7
Lactate	mmol/L	1.9	2.8	1.8	2.6	1.8	4.3

[#]Median imprecision achieved by laboratories in RCPA Blood Gas and Co-oximetry QAP, Cycle 48, 2012; *Analytical Goal for INR recommended by the Australian Government

TABLE 4. Comparison of stakeholder satisfaction (POC testing device operators and patients) before and after the introduction of POC testing in the Northern Territory (NT) POC Testing Program (9), the QAAMS Program (4) and the Diabetes Management Along the Mallee Track Program (20).

Program	Stakeholder	Test	Satisfaction	% Unsatisfied	% Unsure	% Satisfied	n	p
NT POC Testing	Operators	Electrolytes	Before POC testing	34	13	54	39	<0.001
			After POC testing	0	4	96		
QAAMS	Operators	HbA1c, UACR	Before POC testing	30	28	42	57	0.271
			After POC testing	4	7	90		
	Patients	HbA1c, UACR	Before POC testing	11	28	61	159	0.007
			After POC testing	3	6	91		
Mallee Track	Patients	HbA1c, UACR, lipids	Before POC testing	29	19	51	36	0.001
			After POC testing	9	6	85		

TABLE 5. Examples of clinical outcome benefits from accessing POC testing in rural and remote Australian communities.

Clinical Outcome	Measure	POC Test	Example of Community Program Where Benefit Observed
Chronic disease	Improved glycemic control	HbA1c	QAAMS Mallee Track Point of Care Testing in General Practice Trial
	Improved operational efficiency for patients	HbA1c	QAAMS
	Stabilization of renal function Early identification of renal disease risk	Creatinine and eGRF Urine ACR	NT POC Testing Umoona Kidney Project (21,22)

	Stabilization of patients on warfarin therapy	INR	NT POC Testing
Acute disease	Early risk stratification for acute coronary syndrome	Troponin I	NT POC Testing
	Rapid stabilization of septic shock	Potassium	NT POC Testing

TABLE 6. Observed improvements in glycemic control of diabetes patients who had three or more HbA1c POC tests performed during the study periods.

Program	Baseline HbA1c (Mean ± SD)	After POC Testing (Mean ± SD)	Time After POC Testing	No. of Patients
QAAMS Study 1 (2006)	9.3% ± 2.0	8.6% ± 2.0*	12 months	74
QAAMS Study 2 (2010)	8.8% ± 2.2	8.2% ± 2.2*	29 months	272
QAAMS Study 3 (2012)	9.2% ± 2.1	8.8% ± 2.2*	15 months	181

*Change in glycemic control was statistically significant ($p < 0.05$, paired t-test)

TABLE 7. Observed improvements in glycemic control among diabetes patients accessing POC testing in an Indigenous and a non-Indigenous POC testing program.

Program		HbA1c (Mean ± SD)	Achieving Optimal Glycemic Control HbA1c <7%	Achieving Controlled Glycemia HbA1c <8%	Exhibiting Poor Glycemic Control HbA1c >10%	No. of Patients
QAAMS Study 1 (2006)	Before POC testing	9.3% ± 2.0	15%	28%	35%	74
	After POC testing (12 months)	8.6% ± 2.0*	27%	47%	23%	
Mallee Track (2005)	Before POC testing	7.6% ± 1.6	33%	59%	13%	54
	After POC testing (10 months)	7.1% ± 1.4*	63%	91%	6%	

*Change in glycemic control was statistically significant ($p < 0.05$, paired t-test)

4.5.4 Study 4: Methods for sustainable expansion of a POCT program

Spaeth, B, Shephard, M, Auld, M & Omond, R 2017, 'Immediate pathology results now available for all remote Northern Territorians', in L Coleman (ed.), *14th National Rural Health Conference*, Cairns, Queensland. Available at: <http://www.ruralhealth.org.au/14nrhc/sites/default/files/Spaeth%2C%20Brooke_A4.pdf>.

This study describes how the NT POCT Program remained sustainable through a significant expansion of POCT to all remote health services in the NT of Australia. This author designed this study, performed a majority of the data collection and analysis, and provided the first draft of the manuscript with co-authors contributing to the editing process.

Described is the significant expansion of the NT POCT Program to provide an i-STAT device to all remote primary health care services (from 36 having an i-STAT device to 72) in the NT. This expansion was a direct result of the evidence-base for POCT in the NT provided by this author's previous studies. The strategies developed and employed by this author (and colleagues) to ensure the successful and sustainable expansion of POCT services to the remote health facilities are described in this study. In particular, two initiatives conceived and implemented by this author are outlined which has been discussed in the contextual statement; these are the POCT Feedback Report and the POCT consumable ordering process.

Results for operational, analytical, clinical and cost effectiveness were also provided to demonstrate the sustainability of the NT POCT Program across the expansion period. As outlined in the study, the average number of operators trained each month more than doubled, with trainees indicating high levels of satisfaction with the quality of the POCT training provided. Also, the number of POC tests conducted increased by approximately one-third with the analytical performance of the i-STAT devices was equivalent to laboratory testing and remaining stable across the expansion period. The reason the number of POC tests did not increase two-fold after the number of health services with an i-STAT device doubled, is that the health clinics servicing larger populations had access to POCT prior to the rollout.

A case study was also provided in this study for a paediatric patient with an acute illness to highlight the clinical and cultural effectiveness of POCT in this setting.

An audit of patient cases where an i-STAT troponin I test was performed was conducted by a medical registrar with the assistance of this author. This audit provided an initial estimate of cost saving through unnecessary medical evacuations prevented by POCT of between $640,000 and $3.8 million. As discussed in the contextual statement, this initial data was then used to perform a more in-depth economic assessment of POCT in the remote NT.

This study was the first to describe several novel strategies to ensure the sustainable large-scale expansion of POCT in a remote primary health care setting. As discussed in the contextual statement, this study was presented at a major national rural health conference in Australian. As such, evidence for the use of POCT in this setting was also provided to support the introduction or expansion or POCT services in other rural or remote jurisdictions.

The final study included in this thesis validates the methods developed by this author through describing how a POCT program using these methods was successfully implemented in a rural location outside of Australia.

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1. **Publication Details: Spaeth B, Shephard MDS, Auld M, Omond R,** Immediate pathology results now available for all remote Northern Territorians, Published in *Proceedings of the 14th National Rural Health Conference, editor Leanne Coleman, Cairns, Queensland, 26-29 March 2017. Canberra: National Rural Health Alliance, 2017.*

Section of the thesis where the publication is referred to: Throughout the entire thesis.

Candidate's (Brooke Spaeth) Contribution to the publication:

Research Design: **90%**

Data Collection and analysis: **90%**

Writing and editing: **90%**

Outline your (the candidate's) contribution to the publication:

Brooke Spaeth designed the research project, provided the collection of data and analysis of data with supervision from Mark Shephard. Brooke provided the first draft of the manuscript and approved the final version.
Mark Shephard supervised research design, assisted with data analysis and provided edits to the final version of the manuscript.
Dr Rodney Omond assisted with data analysis and provided edits to the final version of the manuscript.
Malcolm Auld assisted with data collection and provided edits to the final version of the manuscript.

☑ I confirm that the details above are an accurate record of the candidate's contribution to the work

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☒ I confirm that the details above are an accurate record of the candidate's contribution to the work

Name of Co-Author 4: **Dr Rodney Omond** Signed: Rodney J Omond Date: 28/03/2018

Immediate pathology results now available for all remote Northern Territorians

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ABSTRACT

Introduction: The Northern Territory (NT) Point-of-Care Testing Program commenced in 2008 in 36 remote health centres in the NT. Using the Abbott i-STAT point-of-care testing (POCT) device, this program provides immediate pathology results to participating health centres enabling rapid diagnosis and treatment or monitoring of a range of acute and chronic conditions.

In 2015, under the direction of the NT Department of Health, the program was expanded to every remote health service in the Territory. The large-scale rollout, doubling the program's size to 72 remote health services, required careful planning and innovation.

Methods: A team of scientists, professional practice nurses and rural medical practitioners who make up the NT POCT Program Management Committee coordinated the expansion. Strategies to rollout the program included: accessible training options including weekly teleconference training sessions; development of a website providing 24/7 Territory-wide access to training materials including web-streamed videos; on-site visits to provide initial device set-up, training and coordination; and the introduction of an innovative method to assist with consumable ordering (a primary obstacle for remote health services).

A survey was implemented during the rollout to determine the satisfaction of new staff completing POCT training. The analytical quality of POCT was monitored throughout the rollout period and results were compared to key performance indicators achieved by laboratories. A series of patient cases were reviewed and documented to demonstrate the cost effectiveness of POCT and provide examples where POCT had produced a defined clinical benefit.

Results: In the initial 6 months of the rollout, 158 new remote staff were trained as device operators with survey respondents expressing high satisfaction with the quality of training. The analytical

quality of POCT results remained stable during the rollout period and of equivalent standard to Australian laboratories.

Improvements in outcomes for acutely ill remote patients were identified through POCT enabling more rapid diagnosis and treatment. Cost savings through preventing unnecessary medical evacuations using POCT were substantial.

Conclusion: The NT POCT Program now provides equity of access to POCT for all remote Territorians, reducing the health care disadvantage for Australians living in remote locations compared to urban areas. The strategies employed can be used to implement similar POCT networks in other areas of remote Australia and internationally.

What is known about the topic?

- Point-of-care pathology testing provides an effective means of obtaining immediate pathology testing for patients in remote locations.

What does this paper add?

- Provides insight into the successful strategies and challenges of coordinating a major rollout of a point-of-care testing network.
- Provides new information on the benefits of using point-of-care testing in remote locations.

INTRODUCTION:

Australians living in remote areas experience a significantly higher burden of disease and avoidable hospitalisations compared to those living in urban areas.[1] Geographical isolation and its impact on access to health services and infrastructure are major factors contributing to the health disadvantage experienced by Australians living remotely.[2,3] The limited access to basic pathology testing for the prevention and management of chronic conditions and the triage of acute illness is a significant deficiency in health service delivery in remote locations. The nearest pathology laboratory is often located hundreds of kilometres from the remote community, with patients waiting several days and sometimes weeks for pathology results to be reported to their treating doctor.[2,4,5]

Point-of-care testing (POCT) allows pathology testing to be conducted during a patient visit with results immediately available for patient care.[6] POCT has a particular niche in rural and remote communities where access to mainstream laboratory services is generally poor and patient loss to follow-up is high.[5,7] For medical emergencies in these sectors, the speed of POCT provides critical practical and operational benefits.

The Northern Territory (NT) POCT Program commenced in 2008 as a partnership between the Flinders University International Centre for Point-of-Care Testing (ICPOCT), then known as Community Point-of-Care Services, and the NT Department of Health (DoH). The Abbott i-STAT (Abbott Point of Care, USA) device was initially introduced to 36 services to alleviate the shortfall in essential pathology tests due to a collapse in air services providing transport of pathology samples to laboratories.

The i-STAT device measures a range of pathology tests for emergency medical situations including electrolytes, urea, creatinine, cardiac troponin I, glucose, lactate, haemoglobin and blood gases. The

i-STAT also tests for International Normalised Ratio (INR) for the management of patients on warfarin therapy. Warfarin is a common anticoagulation medication used in remote NT to treat the symptoms of Rheumatic Heart Disease, such as atrial fibrillation, which is highly prevalent in remote Indigenous communities.[8] The i-STAT device requires a small venous or capillary sample of less than 100 µL with all results available in 10 minutes or less.

Previous evidence from the NT POCT Program indicates the i-STAT is (i) analytically sound and equivalent to laboratory standards and (ii) has been well accepted by trained remote area nurses who conduct POCT at participating sites, with the volume of tests conducted increasing significantly each year since inception.[9,10]

In 2015, the NT Government made the decision to undertake a major rollout of the i-STAT device to the remaining 36 remote health centres (22 DoH remote health centres and 14 Aboriginal Community Controlled Health Centres [ACCHS]), more than doubling the Program's size to 72 remote health services. The decision to expand the NT POCT Program was due, in part, to the findings of a coroner's inquest into the death of a young man due to a cardiac event, in which the coroner argued the life of a young man may have been saved if POCT for troponin had been available.[11]

METHODS:

The NT POCT Program Management Committee comprises a team of scientists, Professional Practice Nurses and Rural Medical Practitioners (RMP) with the governance structure of the Program outlined in Figure 1. The ICPOCT co-ordinates the management of the following services for the i-STAT: ongoing training and competency assessment of health professional staff; management of a quality testing program; technical support; surveillance of de-identified patient results; coordination

of monthly meetings and production of reports for the NT POCT Program Management Committee; and assessment and documentation of agreed research outcomes. To assist the rapid and effective rollout of new i-STAT devices to the 36 new health services, an i-STAT Rollout Project Manager was appointed to support the implementation.

A primary logistic obstacle for existing remote health services has been i-STAT consumable ordering and delivery, due mainly to the short expiration of stock, remote location of the services, limited fridge storage space and high turnover of remote staff. To assist with consumable ordering for rollout sites, several centralised hubs were established to enable the distribution of smaller numbers of consumables to surrounding health services. Additionally, regular statistics were provided as monthly feedback reports to each Primary Health Centre Manager (PHCM) to highlight the following statistics across the previous month: cartridge usage, individual operator usage of the i-STAT, common errors and participation rates in quality testing. The feedback report was designed to assist the PHCM to order stock, identify additional staff training requirements and ensure quality testing was completed timely. A survey was sent to all PHCMs receiving the report to obtain their feedback on its content and design.

Due to the significant number of remote staff from the rollout sites requiring training a series of flexible training options were developed. Primarily, training was delivered via weekly teleconference training sessions, open to all remote staff and hosted via GoToMeeting (www.gotomeeting.com), a teleconference software program that allows the trainee to view and listen to an interactive training presentation and ask questions. Alternative training options included on-site, face-to-face training sessions with a member of the NT POCT Program Management Committee or self-directed training using the training resources provided on the newly developed i-STAT webpage, hosted by the ICPOCT and providing 24/7 access to training materials including videos, step-by-step posters, troubleshooting guides and clinical protocols. After attending a training session, each trainee was

required to undertake a competency assessment involving a theoretical and a practical component to test their key knowledge and ability to perform tests on the i-STAT device and obtain results of acceptable quality.

During the i-STAT rollout period, a questionnaire to gauge satisfaction with the quality of training and to evaluate trainee confidence with using the i-STAT device was sent electronically via SoGoSurvey (www.sogosurvey.com.au) to each trainee. The survey was not compulsory and respondents could remain anonymous. The survey contained a series of short questions with respondents rating their level of satisfaction with aspects of training according to a 10-point sliding scale. A 'yes/no' question was asked about whether the trainee felt confident in using the i-STAT device and three open questions were included to obtain comments on the effectiveness of training, suggested improvements and operator's experience with patient testing using the i-STAT. Results were analysed by the SoGoSurvey software.

Analytical quality of each i-STAT device was monitored during the rollout using quality control testing material provided by the manufacturer. Key performance indicators of quality were accuracy (measured by the closeness of agreement of the mean value obtained by participating services and the target value assigned by the manufacturer [Abbott] for each quality control test) and the observed between-service imprecision, expressed as a coefficient of variation (CV%), for each test. The resultant CV%s were compared to the imprecision achieved by Australian laboratories enrolled in the Royal College of Pathologists of Australasia (RCPA) Quality Assurance Programs.

An initial cost effectiveness study was commissioned by the NT POCT Management Committee and undertaken by a medical registrar, Ming Chen, across 27 remote health centres. The primary outcome measure was evacuations prevented by using the i-STAT either to stabilise a patient on-site or to rule out a cardiac event using the troponin I test. In addition, by auditing and reviewing

clinical presentations, patient cases were identified whereby the i-STAT produced an improvement in clinical outcome.

RESULTS:

The NT POCT Program model now operates in 72 remote health facilities in the Territory (51 DoH remote health centres and 21 ACCHS).

In the initial 6 months of the rollout, 337 remote staff completed i-STAT training; 158 from new services and 179 from existing services. A comparison of operators trained before and after the rollout period is illustrated in Figure 2.0. The number of remote staff completing i-STAT training each month averaged 14 per month before and 34 per month after the rollout commenced.

Responses to the monthly feedback report survey indicated 77% of responding PHCMs (n=22) felt the reports were informative and 86% indicated they were a useful tool in assessing the effectiveness of the i-STAT at their remote health service. Prior to accessing feedback reports, the level of PHCM satisfaction with their knowledge of on-site i-STAT use was rated as: satisfied 27%, unsure 36%, unsatisfied 23% (and 14% did not answer). Since the feedback reports have been available, the level of satisfaction improved to: satisfied 63%, unsure 23%, unsatisfied 0% and 14% did not answer.

The training satisfaction survey was completed by 50 Remote Area Nurses, 3 Aboriginal Health Practitioners and one RMP, a response rate of 34% (54/158). Of the 54 respondents, 44 completed training remotely via teleconference and GoToMeeting presentation software and ten attended a face-to-face training session either on-site or centrally in Alice Springs or Darwin. Approximately 50% of respondents indicated they also used website resources as a useful adjunct to complete

training. Fifty (93%) respondents indicated they had a better understanding of how to use the i-STAT post-training.

A summary of responses to the 10-point sliding scale questions is summarised in Table 1. The average weighted score was greater than eight out of ten for each question indicating high satisfaction with the training session, instructors and resources. Comments to open response questions were overwhelmingly positive including:

"I have used the i-STAT for 15 years, but still learnt new information (in the training session), very informative and interactive"

"I was very satisfied with training and would recommended for anyone wanting to use the i-STAT equipment, thank you very much for your tutorial"

"… the i-STAT is very accurate and such a great tool, especially when handing over to the doctor over the phone; great trainers, knowledgeable and put their audience at ease".

During the rollout, the total number of POC tests increased across time as seen in Figure 3, with the monthly average before and after the rollout period being 876 tests and 1141 tests respectively, an increase of approximately 130%. The profile of tests remained stable before and after the rollout period, with INR the most frequently performed test (43%), followed by electrolytes (27%), troponin I (20%) and blood gases (10%).

Results of analytical quality are summarised in Table 2. The quality of POCT remained stable during the rollout period and of equivalent standard to the laboratory. The accuracy of quality testing was excellent, with the mean value obtained by participants for all tests being very close to target set by the manufacturer. The imprecision (CV%) observed for sodium, potassium, chloride, glucose, urea, creatinine, pH, lactate and troponin was better than or close to the median imprecision achieved by

Australian laboratories. For the blood gas analytes, bicarbonate (TCO_2), pCO_2 and pO_2, the imprecision was slightly higher than the median imprecision but met the 90th percentile imprecision achieved by laboratories of 6.5%, 4.6% and 6.5% respectively.

Results of the initial cost effectiveness study found that the evacuation of 80 patients were prevented specifically due to the availability of the i-STAT results on-site (equating to an estimated cost saving of $640,000). A further 474 troponin I tests provided reassuring results that the patient was not undergoing a cardiac event and thus did not require evacuation, resulting in an estimated cost saving of up to $3.8 million.

The audit and review of clinical presentations identified a number of patient cases where access to on-site POCT using the i-STAT resulted in an improvement in clinical outcome. One such example, involving serial electrolyte measurements on a patient with vomiting and diarrhoea is described:

Presentation: A mother presented to a remote clinic with a 22-month-old female child who had a 24-hour history of vomiting and diarrhoea, and a fever of 38.5°C. The mother also reported a member of her household had recently been treated for rotavirus. The child was alert and interactive and had been eating and drinking that day. A stool sample was sent to the nearest microbiology laboratory (over 900 kms away) for investigation of rotavirus. Paracetamol was administered and a temperature of 37.3°C recorded. The treating clinician allowed the patient to go home advising them to return the next day for review or to present earlier if the patient's condition deteriorated.

Follow up: The child returned to the clinic several hours later as the child's temperature had increased to 40.1°C. The RMP recommended further paracetamol therapy and requested electrolytes be measured on the i-STAT: results showed a sodium of 140 mmol/L (reference interval 132-143) and a potassium of 2.7 mmol/L (reference interval 3.5-5.0).

The patient then experienced two episodes of diarrhoea. The RMP discussed the i-STAT results with an on-call paediatrician who prescribed 30 mls oral rehydration solution (ORS) at 15-minute intervals until the patient stabilised and requested her electrolytes be repeated the next day. After 3 hours of ORS, the patient's temperature had improved to 37.1°C and she began to stabilise. The patient presented the next morning with repeat i-STAT results of: sodium 141 mmol/L and potassium 2.4 mmol/L.

The patient's potassium level had further declined and her weight had slightly decreased; she was now afebrile with a temperature of 36.6°C. Based on the results, a paediatrician prescribed oral potassium (1ml/kg) and follow-up electrolytes the following day, with results being: sodium 144 mmol/L and potassium 2.8 mmol/L.

The patient regained muscle turgor and resumed eating and drinking well. Continued ORS treatment was prescribed. The following day the patient had improved significantly and her electrolyte results were: sodium 142 mmol/L and potassium 3.2 mmol/L.
The microbiology results were reported 2 days later and were negative for rotavirus.

DISCUSSION:

The use of the i-STAT device in a remote primary health care setting is an innovative use of POCT outside of the conventional tertiary hospital emergency department.

The challenges of managing this large remote POCT network have included: the inherent difficulties associated with the distribution of POCT consumables (testing cartridges and quality materials) with short expiration dates; delivering training to remotely located staff with a high rate of turnover; and lack of Medicare rebates available to offset costs of POCT.

The development of the monthly feedback report to PHCMs has assisted in optimising inventory control of consumables by minimising consumable wastage and improving the ordering process; the report represents a novel and effective means of assisting the management and monitoring of POCT on-site and is recommended for any location where POCT is monitored remotely by a POCT coordinator.

Having a wide range of accessible and flexible training options has also contributed to the success of this large-scale rollout. A future aim of the program is that all new health centre staff should be required to complete POCT training as part of their remote health orientation to ensure they are qualified to immediately conduct POCT when they commence work in a remote health centre.

As previously shown, the quality of POCT undertaken in remote primary care was sound for most analytes.[10] The increased imprecision of the blood gas analytes was due, in part, to new staff taking time to adapt to the strict timing requirements for performing the testing of blood gases; where the quality sample must be tested immediately once the vial is opened to prevent gaseous exchange that occurs with exposure to air and subsequent skewing of gas results. Staff obtaining these erroneous results during training received feedback on test technique and additional training.

There is significant real-time benefit for the immediate pathology results produced by POCT in reducing the number of medical retrievals and contributing to significant cost savings. The patient case described in this study emphasises the long turnaround time for laboratory results in remote locations and highlights the ability of the i-STAT to assist in the stabilisation of an acutely ill paediatric patient on-site. The case also provides an example of a cultural benefit of POCT as it demonstrates how an evacuation from a remote region was avoided, allowing a patient to be treated and remain in the community with their family.

The benefit to patient safety and quality of care when stabilising a patient, either prior to a delayed evacuation or allowing the patient to remain and be treated in the community, is an invaluable asset of POCT. A limitation of the cost effectiveness data provided in this study is that it was not a full economic evaluation as it did not take into account the cost of administering the POCT program and cost of POCT consumables. To address this limitation, a more detailed and comprehensive cost benefit analysis is now being undertaken through an Emergency Medicine Foundation (EMF) grant awarded to the Flinders ICPOCT.

This innovative POCT program now ensures that all remote Territorians have equity of access to immediate pathology test results for a range of acute and chronic medical presentations and adds value to the current knowledge on the topic of emergency medicine in remote health care in Australia. The strategies described here and lessons learnt can be translated by other health professionals wanting to establish similar POCT networks in other remote or low resource settings.

ACKNOWLEDGEMENTS

We acknowledge the significant contributions from all past and present members of the NT POCT Program Management Committee in ensuring the successful implementation of the NT POCT Program.

The NT POCT Program Management Committee sincerely thanks Ming Chen for her contribution in examining the cost effectiveness of the NT POCT Program.

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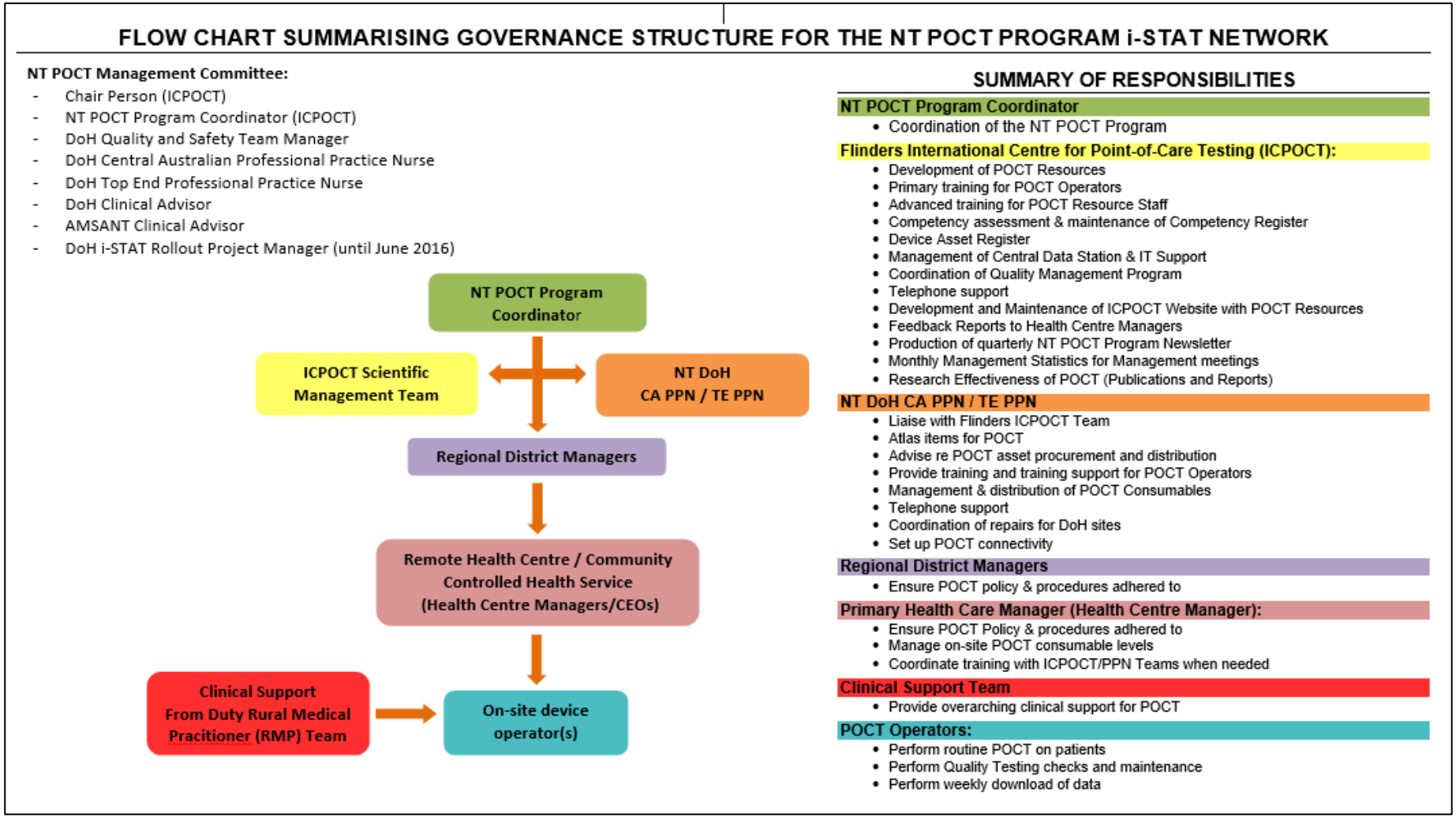
Figure 1 - Governance Structure of Northern Territory Point-of-Care Testing Program



ICPOCT= International Centre for Point-of-Care Testing, DoH= Department of Health, AMSANT= Aboriginal Medical Services Alliance Northern Territory, CA = Central Australia, TE= Top End, PPN= Professional Practice Nurse.

Figure 2 – Total remote staff completing i-STAT training before and during the rollout period

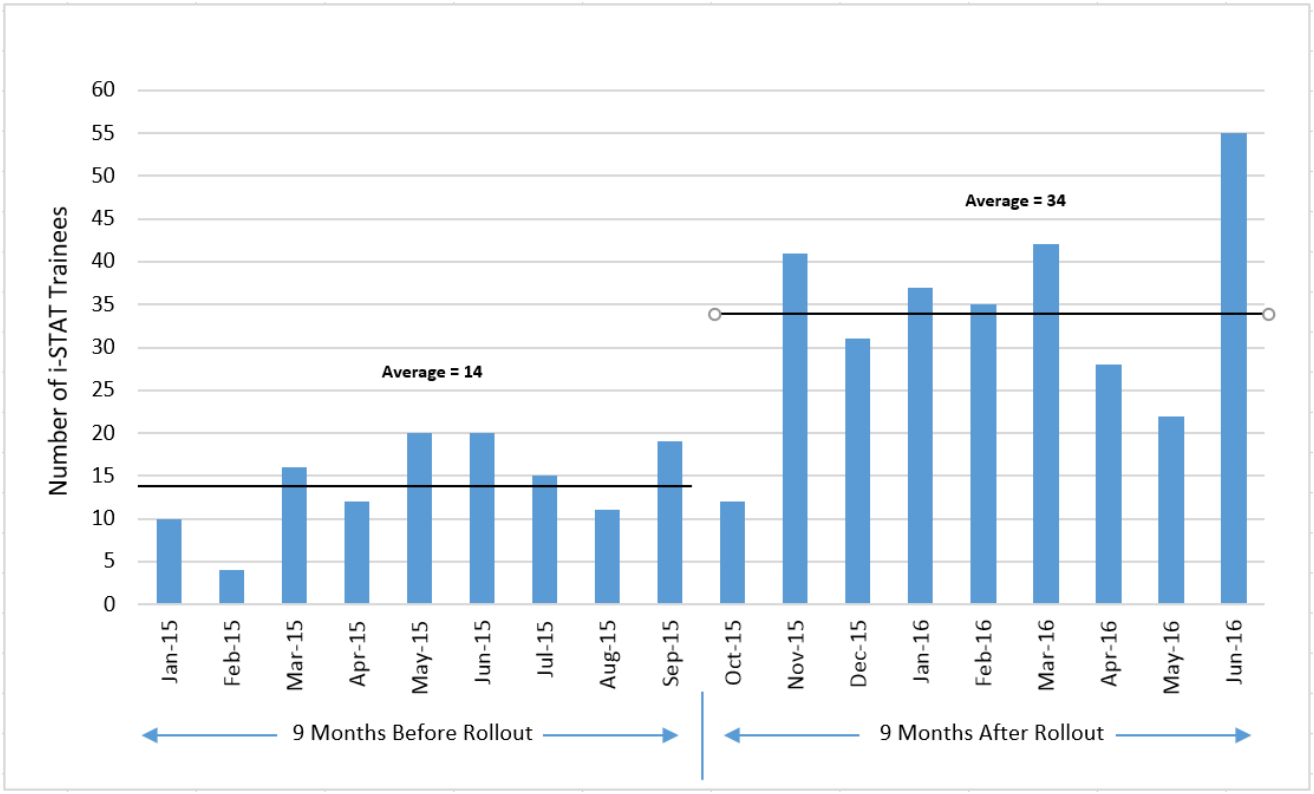


Figure 3 – Total monthly tests recorded 9 months before and 9 months during the rollout period

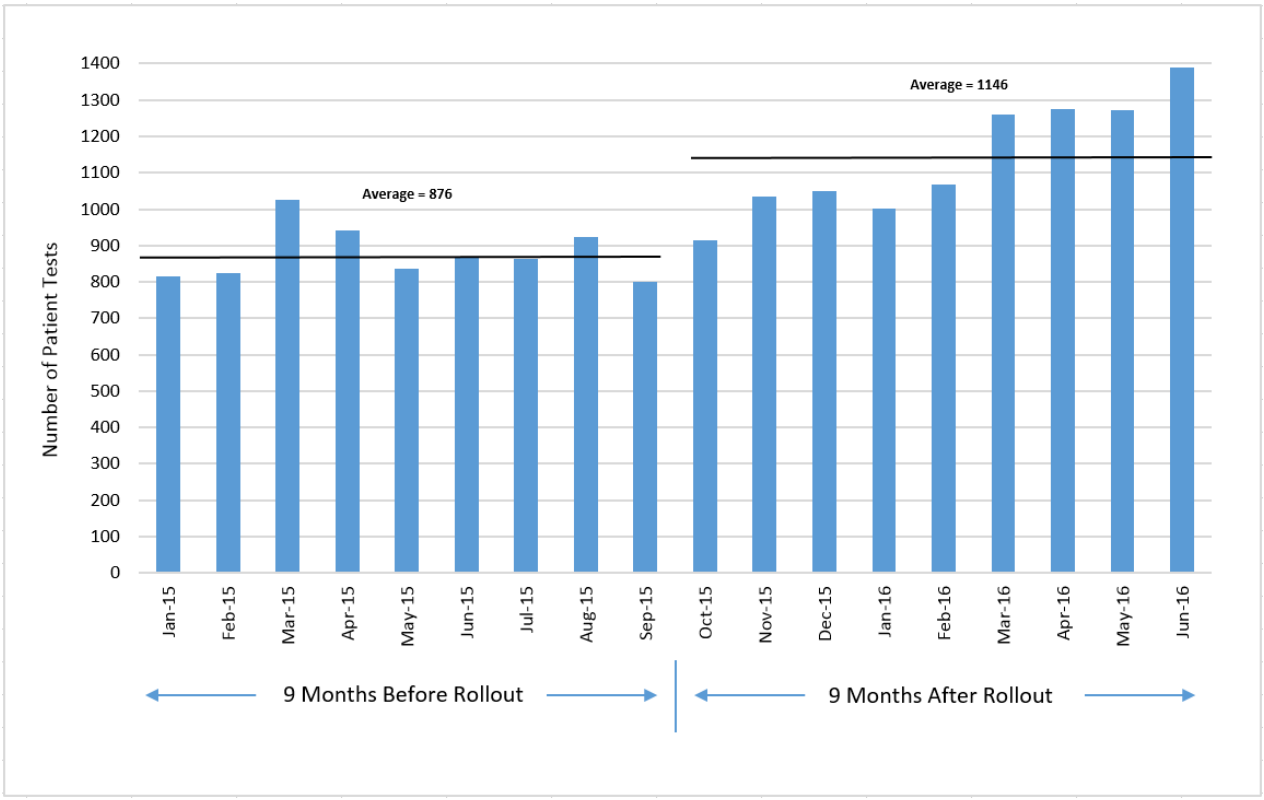


Table 1 – Summary of training satisfaction survey responses.

Question	No. Responses	Average Weighted Score (0- Very Poor, 10 – Excellent)
How would you rate the quality of the PowerPoint presentation provided during training?	46	8.7
How would you rate the quality of the Training Manual?	38	8.4
How would you rate the quality of the i-STAT “How To” Posters?	27	8.6
How would you rate the quality of the i-STAT “How To” website videos?	19	9.2
How would you rate the helpfulness of the trainer?	53	9.2
How would you rate the quality of instruction from the trainer?	53	9.2
How confident do you now feel about conducting patient testing on the i-STAT device?	54	8.9

Table 2 – Representative example from lot number with highest number of repeats during the i-STAT rollout period.

Analyte	Units	Lot Number	n	Target	Mean	CV%	Laboratory Median CV%
Sodium	mmol/L	301066	233	122.0	121.5	0.6%	0.9%^
Potassium	mmol/L	301066	233	2.9	2.9	0.8%	1.4%^
Chloride	mmol/L	301066	235	72	73	1.2%	1.2%^
Ionised calcium	mmol/L	301066	233	0.84	0.85	1.5%	1.3%^
Total CO_2	mmol/L	301066	235	17.0	16.2	5.9%	3.8%*
Glucose	mmol/L	301066	231	15.0	15.1	1.0%	2.1%^
Urea	mmol/L	301066	233	19.3	19.3	2.6%	2.5%^
Creatinine	µmol/L	301066	234	335.5	336.8	2.9%	2.7%^
HcT	%PCV	301066	234	17	16.6	3.5%	n/a
Haemoglobin	mmol/L	301066	234	58	56.3	4.6%	n/a
pH	n/a	301066	230	7.04	7.05	0.2%	1.4%*
pCO_2	mmHg	301066	226	61	59	3.9%	2.1%*
pO_2	mmHg	301066	223	83	86	6.5%	2.7%*
Lactate	mmol/L	301066	229	7.1	6.9	2.4%	4.6%*
Troponin I	ng/mL	011073	196	0.34	0.31	7.0%	7.7%^
INR	n/a	291067	274	2.2	2.2	7.1%	n/a

CV% = Coefficient of Variation percentage

^ Median imprecision achieved by laboratories in the Royal College of Pathologists of Australasia's (RCPA) General Chemistry and Therapeutic Drugs, Cycle 103, 2016.

* Median imprecision achieved by laboratories in the Royal College of Pathologists of Australasia's (RCPA) Blood Gas and Co-Oximetry, Cycle 57, 2016.

4.6 Transferability a POCT model

4.6.1 Study 1: Transfer of methods for a remote POCT program

McCormack, T, Ayub, R, Aziz, F, Motta, L, **Spaeth, B** & Shephard, M 2017, 'Point-of-care testing facilitates screening and treatment for anaemia in women and children in rural Pakistan', *Australian Journal of Rural Health*, Available online: DOI 10.1111/ajr.12395.

The primary aim of this study was to demonstrate the clinical effectiveness of POC Hb testing as a screening tool for detecting anaemia in women and children in rural Pakistan. However, this study also demonstrates the robustness of the methods developed by this author through translation to an international setting and using a different POCT device (HemoCue Hb 201+). This author played a large role in the study design and implementation of POCT, and also contributed to data collection, data analysis and editing of the manuscript.

As mentioned, the methods this author used to remotely train the POCT operators and monitor the analytical quality of POCT in this research study were based on those developed in for the NT POCT Program. As description of these methods, the POCT screening program, and the education provided to patients for the prevention and treatment of anaemia are also described in this study.

Anaemia was initially detected in approximately half of the women and children, as indicated by Hb levels of less than 120 g/L and 110 g/L respectively as measured by POCT. For these patients, immediate POCT results enabled treatment for anaemia to be initiated immediately and education provided. The effectiveness of this intervention was demonstrated by an increase in Hb levels (as measured by POCT).

Therefore, this study demonstrates how the methods developed by this author were successfully used to implement an analytically and clinically effective POCT model in an alternative rural setting.

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1. **Publication Details:** McCormack T, Ayub R, Aziz F, Motta L, Spaeth B, Shephard MDS. Point-of-care testing facilitates screening and treatment for anaemia in women and children in rural Pakistan, *Aust J Rural Health*, 2017.

Section of the thesis where the publication is referred to: Throughout the entire thesis

Candidate's (Brooke Spaeth) Contribution to the publication:

Research Design: **50%**
Data Collection and analysis: **30%**
Writing and editing: **20%**

Outline your (the candidate's) contribution to the publication:
Brooke contributed significantly to the research design and collected a majority of the analytical data. Brooke also provided analysis of analytical data. All authors contributed to the writing and editing of the final publication.

☑ I confirm that the details above are an accurate record of the candidate's contribution to the work

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Name of Co-Author 5: **Mark Shephard** _____ Signed: _____ Date: 17/12/17

Australian Journal of Rural Health – Original research paper

Point-of-care testing facilitates screening of and treatment for anaemia in women and children in rural Pakistan.

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ABSTRACT

Objective: To use point-of-care testing to screen and facilitate treatment for anaemia and to establish an estimate of the prevalence of anaemia in the local population.

Design: An uncontrolled before-and-after study design was used to evaluate the effectiveness of the intervention on the anaemia status of participants.

Setting: This study took place in a rural mountain community (population approx.1000) in the Haripur district in northern Pakistan.

Participants: Women of childbearing age (15 – 49 years) and children (12 - 14 years) were included in this study.

Interventions: The intervention included point-of-care testing for haemoglobin, treatment with mebendazole and oral iron supplementation, and an education campaign about anaemia delivered by community health workers and medical students.

Main outcome measures: The main outcome measure was an increase in blood haemoglobin over the study period. A secondary outcome measure was a positive change in anaemia status or classification post-intervention.

Results: Anaemia was initially detected in 64 (53%) women and 15 (47%) children. The mean Hb concentration increased significantly ($p<0.001$) from 118g/L to 130g/L (women) and 120g/L to 130g/L (children) post-intervention. Overall prevalence of anaemia in women ($p<0.001$) and children ($p<0.001$) decreased significantly (by 30% and 34% respectively) post-intervention.

Conclusions: Point-of-care testing used for the detection of anaemia in this rural community helped to identify the burden of disease and to reduce this significantly by way of rapid diagnosis, education and immediate medical intervention.

KEY WORDS: anaemia, rural, south-Asia, point-of-care, haemoglobin

What is already known on this subject?

- Anaemia is persistent health problem in South Asian countries, however estimates of the prevalence in rural Pakistan are varied
- School attendance is associated with improved knowledge about health and anaemia status, indicating that education is important for reducing anaemia
- Access to pathology services is limited in rural areas

What this paper adds:

- Shows that access to POCT can facilitate diagnosis and monitor treatment of anaemia in rural areas
- POC removes barriers to accessing pathology testing and improves patient follow-up
- A multifaceted approach (improving access to pathology services through POCT, treatment with medicine and delivering health education) can reduce prevalence of anaemia.

INTRODUCTION

Anaemia is a major public health problem affecting approximately 1.62 billion people globally, with a particularly high prevalence in developing countries [1-3]. Iron deficiency is the most common cause of anaemia on a global scale [4]. Anaemia can be the result of inadequate dietary iron or a parasitic infection [2]. Anaemia is persistent in South Asia, where the diet is scarce in meat and there is a cultural tendency for women to sacrifice nutrient-rich foods for male family members [5]. Parasitic infestations are common and can cause anaemia, resulting in long-term morbidity [5]. In the limited literature on anaemia in rural Pakistan, estimates of prevalence vary [1]. The WHO global database on anaemia (last updated in 2007) estimates that 30% of women and 53% of children in rural Pakistan suffer from anaemia [6].

Point-of-care testing (POCT) is pathology testing performed in a primary care setting during the patient encounter, with results immediately available for timely clinical action. POCT provides

patients in rural areas with access to health services which otherwise may not be available. This study aimed to develop and implement a community-based POCT program to detect and manage anaemia in women and children in rural Pakistan, and in doing so, gain an estimate of the prevalence of anaemia in this population.

METHODS

Study Population

This quasi-experimental uncontrolled before and after study took place from January to June 2014 in a rural mountain community (population approx. 1000) in the Haripur district of north Pakistan, 80 kilometres from Islamabad. Convenience sampling was used to select the participants, as a sampling frame was not available. A meeting was held to gain community support with elders from the community and stakeholders of Begum Mehmooda Welfare Trust, under whose auspices a basic health unit had been functioning for the past year. It was the wish of these stakeholders that women of childbearing age (15-49 years) and children (12-14 years) be targeted for this intervention. Permission for the participation of children was obtained from their parents.

POCT device and operators

The HemoCue Hb301 (HemoCue, Sweden) is a small (14x7x16cm), lightweight (500g), battery powered point-of-care (POC) device which measures haemoglobin (Hb) by absorbance spectrophotometry on 10µL of capillary (fingerprick) whole blood with results available in <10 seconds (measuring range 0-256g/L). The analytical performance of the four HemoCue devices used in this study was monitored with fortnightly bi-level quality control (QC) testing (low and normal controls with Hb concentrations of 70g/L and 131g/L respectively).

Twenty-two medical students at the Al Nafees Medical College and four community health workers were trained to conduct quality-assured POCT using the HemoCue by staff from the Flinders University International Centre for Point-of-Care Testing. During a 3-hour videoconference, students were taught the principles and practice of POCT, the WHO classification criteria for anaemia, how to conduct patient and QC testing, and maintenance and troubleshooting. Each student undertook a written and practical assessment to gain competency certification. A competency register was held electronically by the principal researchers.

Intervention

The qualified students and community workers visited the community and conducted door-to-door POC Hb testing on participants. Participants diagnosed with mild anaemia or moderate anaemia (according to the WHO guidelines in table 1) by POCT were given immediate treatment for eight weeks in the form of ferrous sulphate and folic acid tablets (60mg elemental iron, 0.5mg folic acid) [4]. Based on observations of the existing hygiene and sanitation conditions, all participants, regardless of their anaemia status, were dewormed with tablets or oral suspension mebendazole (single dose, 100mg). Participants diagnosed with severe anaemia (<80g/L) were dewormed and referred to the local health unit for a full blood count and iron supplementation. The students developed and delivered a health education campaign on anaemia comprising pictorial pamphlets, interactive posters, role-plays and question answer sessions at the local school.

Over 8 weeks, the community workers visited each participant at least 3 times (459 visits in total) to reinforce educational messages, counsel the participants about possible side effects of iron supplementation, and provide additional iron/folic acid treatment as required. A post-intervention POC haemoglobin test was conducted on all participants after the 8 week period.

Mean Hb concentration and prevalence (%) before and after intervention were assessed using the paired t-test and McNemar chi-square test respectively. Independent t-tests and chi-square tests

were applied to compare mean Hb and prevalence of anaemia by gender. For all statistical procedures, probability value (p) <0.05 was considered to be statistically significant.

Ethics approval

Obtained from the ethics committee of Isra University – Islamabad campus, Pakistan (Reference #ANMC/EC-15/02-14).

RESULTS

A total of 121 women and 32 children participated in the study and the average age of the subjects was 30.0 ± 9.6 years (women) and 13.8 ± 1.2 years (children). Of the children, 18 (56%) were female and 14 (44%) were male.

Capillary Hb was measured pre-intervention and eight weeks post-intervention. Anaemia was initially detected in 64 (53%) women and 15 (47%) children. The mean (SD) Hb concentration increased significantly from 118g/L (18) to 130g/L (15) in women (p<0.001) and 120g/L (18) to 130g/L (15) in children (p<0.001) over the study period (Table 2). Post-intervention haemoglobin testing was conducted on all study participants and there was no loss to follow-up.

The prevalence of anaemia in women decreased significantly (by 30%) post-intervention (P<0.001). At the commencement of the study, a quarter of the women had mild (24%) or moderate (26%) anaemia with 3% exhibiting severe anaemia. Post intervention, the prevalence of anaemia in each category decreased by 8% (mild), 18% (moderate) and to zero (severe) (Figure 1).

Only one pregnant woman participated in the study. Her first Hb test identified her as moderately anaemic (Hb 90g/L) and she was started on oral iron tablets, folic acid and calcium tablets, and referred to the basic health unit for further evaluation and management. A follow up Hb test eight

weeks later showed her Hb had risen to 114g/L and she was no longer anaemic. She went on to deliver a healthy baby.

The prevalence of anaemia in children decreased significantly (by 34%) post-intervention (P<0.001), while the prevalence of anaemia in each category declined by 28% (mild), 3% (moderate) and to zero (severe) (although numbers in each of the latter two categories were very low) (Figure 1). Male children were not significantly different from their female counterparts in either their mean (SD) Hb concentrations 122g/L (23) compared to 119g/L (13) (P=0.64), or their prevalence of anaemia, 43.8% in males and 45% in females (p=1). Mean Hb concentration increased significantly post-intervention both in women (by an average of 12g/L) and in children (by an average of 10g/L).

Monitoring of analytical quality

The four HemoCue devices exhibited sound analytical performance across the study period, with observed between-device imprecision (n=24) for the two levels of quality control (QC) material (target values 70g/L and 131g/L) of 1.7% and 1.3% respectively. All the field QC results were within the acceptable ranges of ±5g/L at <100g/L and ±5% at >100g/L; these ranges are identical to the allowable limits of performance used by the RCPA Quality Assurance Programs Pty Ltd for laboratory haemoglobin testing.

DISCUSSION

This study shows that anaemia continues to burden women and children in rural Pakistan. The most recent WHO data estimated the prevalence of anaemia in rural Pakistan to be 30% in women and 53% in children [6]. Comparatively, the results of this study, albeit a single rural community, showed a higher prevalence in women (53%) and a slightly lower prevalence in children (47%).

The basic health unit located in the community has a small laboratory, but despite 800 visits by members of the community over the last year, only 50 tests for haemoglobin had been conducted by the laboratory. Reasons for this low rate of testing are thought to include lack of awareness about anaemia due to limited education, and the cost of the test being prohibitively expensive for the community on a user-pays system. Throughout this study, over 300 Hb tests were conducted by POCT. Use of the HemoCue at the point-of-care facilitated diagnosis of anaemia by improving access to pathology and ensuring that there was no loss to follow up. The tests were provided free of charge to study participants. The point-of-care test enabled people to be screened and monitored for anaemia in their home, removing barriers which may prevent people from leaving their homes to attend the clinic. This finding was consistent with the evidence base that POCT can improve access to pathology testing for a wide range of chronic, acute and infectious clinical conditions in remote areas, which has been thoroughly documented in the literature [7-11]. The results of the quality control testing proved that the analytical performance of the HemoCue device was sound, providing confidence that the results generated were appropriate for patient care.

This study was conducted on a small sample size in one community, so rates of anaemia may not be generalisable to the wider population. The observed increase in Hb was not solely attributable to one intervention. Results were achieved via a combination of access to POCT (which was used to diagnose anaemia and establish an estimated prevalence), education about iron deficiency, and treatment with medication. The large study team and small size of the community meant that following up patients in their own homes was feasible, which may be difficult to replicate outside of a research setting. A control group was not incorporated into the study design, due to the isolation and poor health status of the study population.

CONCLUSION

This study contributes findings to a limited pool of knowledge about anaemia in rural Pakistan. More widely, it demonstrates the challenges faced by geographically isolated, resource-limited primary health care services, and how POCT can be an innovative solution to address these challenges. These findings illustrate the impact that POCT has on the capacity of a community to identify the burden of disease and to reduce this significantly by way of rapid diagnosis, education and immediate medical intervention.

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TABLES AND FIGURES

Table 1. Haemoglobin levels to diagnose anaemia at sea level (g/L) [6].

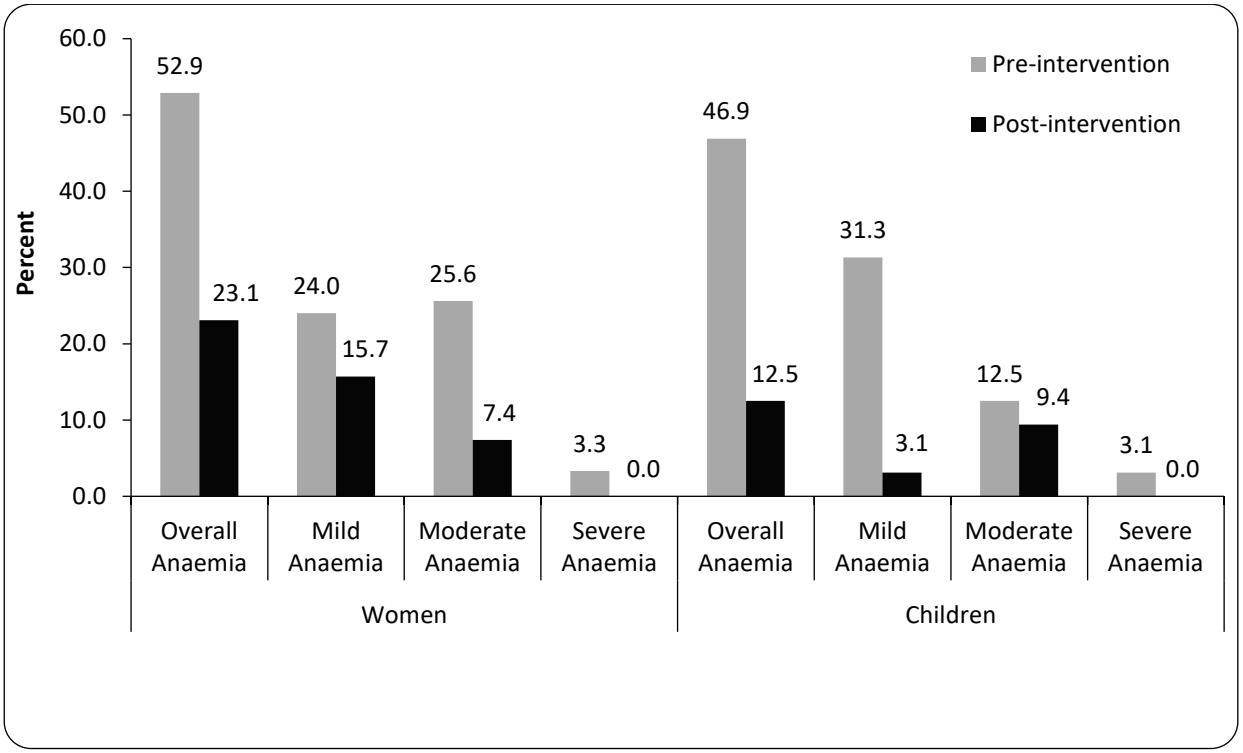
	Non-anaemia	**Anaemia**		
		Mild	*Moderate*	*Severe*
Children (12-14 yrs) and non-pregnant women	≥120	110-119	80-109	<80
Pregnant women	>110	100-109	70-99	<70

Table 2. Pre- and post-intervention comparison of haemoglobin concentration and prevalence of anaemia in women and children.

Variable	**Women (n=121)**		**Children (n=32)**	
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Haemoglobin (g/L)				
Mean (SD)	118 (18)	130* (15)	120 (18)	130* (15)
Prevalence of Anaemia[‡]				
n (%)	64 (53%)	28* (23%)	15 (47%)	4* (12%)

*p<0.001, [‡]Anaemia: Haemoglobin <120 g/L

Figure 1. Pre- and Post-intervention prevalence of anaemia by classification in women and children.



CHAPTER 5 DISCUSSION

As highlighted in the introduction to this thesis, POCT is now used in a variety of health care settings. The literature review initially found over two thousand studies which included the term POCT (or one of its synonyms) in its title or abstract. Many studies have provided evidence for or against the use of POCT within various levels of health care provision. However, the vast majority of these studies have been conducted in metropolitan tertiary hospital settings or large centralised GP settings. While the authors of these studies have suggested the benefits of POCT are likely to be amplified if used in more isolated locations, this may not necessarily be the case due to the many challenges faced by POCT in rural and remote locations which make POCT programs difficult to sustain. Furthermore, limited studies have been conducted in rural and remote locations or specifically focus on the use of POCT in these settings, as evidenced by the literature review in this thesis which identified significantly fewer studies (n=109) when the search was limited to those that focussed on rural, remote or isolated settings. Moreover, a significant number of the studies identified were either initial POCT device evaluations or studies which discussed the potential use of POCT in rural or remote settings but gave no quantitative or qualitative data to support its use. Only 68 studies remained after eliminating these two groups.

As highlighted in the contextual statement, 12 of the 13 peer-reviewed studies conducted by this author were conducted in a rural or remote location. The remaining study provided the initial evaluation of the analytical quality of a new POCT device to determine its potential acceptability for use in rural or remote settings. Therefore, collectively, the studies described in this thesis have provided a significant contribution to the literature on the use of POCT in rural and remote settings. In addition, each study has also provided new knowledge in the field of POCT. Five of the 13 studies were published in journals with a rural and/or remote health or primary care focus due to the applicability of POCT to these settings.

The studies conducted by this author provide tailored methods for the implementation of POCT in rural and remote locations. Also provided are the novel methods developed by this author to ensure the sustainability of POCT in isolated settings. In addition, these studies establish a significant evidence-base to support the use of POCT through demonstrating the analytical, operational, clinical and economic effectiveness of POCT in rural and remote locations. Finally, a translation of the systems developed by this author to an international setting verified the robustness of these methods.

The most notable contribution to new knowledge provided by this author is in implementation and outcomes assessment of POCT for acute care in remote primary health care settings. This is supported by the literature review, which identified no studies on the use of acute POCT in rural or remote primary health care. A summary of the additional contributions to knowledge in the field of POCT are provided here:

- The first study to provide an analytical evaluation of a new POCT device measuring creatinine in Australia.
- Two studies evaluated the analytical quality of POCT devices in settings not previously examined; one in a rural community screening program and the other in a remote Indigenous primary health care setting.
- Four studies on the NT POCT Program demonstrated the model to be analytically sound and operationally, clinically and culturally effective over a sustained period.
- Three studies also included descriptions of the initiatives conceived, designed and implemented by this author to ensure the sustainability of POCT in rural and remote locations.
- The first evidence provided for the timeliness and clinical effectiveness of POC HbA1c testing specifically in remote locations.
- The first study to highlight the clinical and operational benefits of POC INR testing for remotely located patients on anticoagulation therapy.
- The first in-depth analysis of the clinical effectiveness of POCT for the triage and stabilisation of acute presentations in remote primary health care settings.
- The first evidence on the economic benefits of acute POCT in the remote primary health care sector in Australia.

Furthermore, these research studies have provided this author with experience and knowledge on a range of research methods. The early studies provide the evidence of this author's ability to perform the accuracy and imprecision analyses required to conduct POCT device evaluations. Several studies also demonstrate this author's ability to conduct qualitative surveys using a variety of methods to measure responses. Several further studies demonstrate this author's ability to provide descriptive results on clinical effectiveness through providing a variety of case studies where POCT resulted in a defined clinical benefit to the patient. A further two studies used a 'before and after' cohort study design to investigate the clinical effectiveness of POCT in rural and remote

locations. Finally, one study demonstrated this author's experience in using economic modelling techniques to conduct cost-benefit analyses of POCT.

In addition to demonstrating the suitability and effectiveness of acute POCT beyond the tertiary hospital emergency department, the studies in this thesis demonstrate that POCT can influence tangible and 'real-world' outcomes in remote locations. These include improving patient safety, enhancing clinical decision making, improving the timeliness of diagnostic test results and preventing the unnecessary dislocation of Indigenous people from their traditional homelands. This research also demonstrates the wider benefits of POCT, including greater operational efficiency and significant cost savings to the health care sector.

Despite the contribution made to the POCT field, it is important to recognise, as with all research, that there are certain limitations. The limitations for each study were discussed within the individual manuscripts. In terms of the limitations related to this body of work, perhaps the most obvious limitation is that none of the studies used a RCT study design. RCTs are considered a superior form of research design as they aim to reduce possible bias and false causality. Therefore, a RCT is the ideal method to evaluate a new intervention, such as POCT, as it provides the most reliable scientific evidence either for or against the intervention (Spieth et al. 2016). However, a RCT did not fit with the context of the work conducted by this author as the ICPOCT provides POCT solutions in response to needs of a population or organisation. As such, many of the research studies conducted by this author were opportunistic with the aim of filling a gap in knowledge or delivering POCT as an innovative solution to a local or regional clinical problem at the time they were conducted. For example, a RCT study design was the original intention of the research study funded by the Emergency Medicine Foundation to investigate the clinical and cost effectiveness of POCT in remote NT. However, just prior to the submitting the research proposal, the NT DoH provided funding for the immediate rollout of POCT to all remote health services in the NT, meaning there was no opportunity to have a control group in this region. As outlined in the introduction of this thesis, this rollout of POCT came as a result of the recommendation by the coroner after the death of a man could have been avoided if POCT was available in his remote community health service. For this reason, it was deemed unethical to delay the implementation of POCT into the remaining remote health services to allow a RCT to be conducted. Furthermore, in 'real-life' field research, genuine randomised allocation to intervention or control is extremely difficult, if not impossible, to achieve (Rothwell 2006). This is particularly the case with remote Indigenous communities in Australia, as the communities differ substantially in population, disease incidence, physical location and facilities.

In addition, RCTs are generally short in duration, as evidenced by the two RCTs identified in the literature review, each of which were conducted over a period of less than two years. Undoubtedly, interventions that are shown to have only an immediate effect are inferior to those that show gains that are maintained over time. As such, several of the studies within this thesis provide strong evidence for the long-term effectiveness and sustainability of POCT in remote settings, despite not randomly allocating participants.

A limitation of NT POCT Program is that EQA testing did not form part of the surveillance of POCT analytical performance. As outlined in the introduction to this thesis, only QC testing was initially implemented as the core element of quality surveillance due to the expense of EQA testing material and the lack of resources in remote NT. Since the expansion of POCT to all NT remote health services, extra funding has been sourced and EQA testing is now being performed by several remote hub-sites in the NT.

Another possible limitation of this body of work is that several of the studies highlighted the clinical benefits of POCT through the use of individual patient case studies. Qualitative case studies of individual patients or scenarios have been suggested to potentially involve bias, as the researcher may only select cases which verify their hypothesis (Flyvbjerg 2006). However, it has been suggested that qualitative case studies have particular value in providing context within specific settings (Malterud 2001). Thus, while the case studies included this thesis do not provide quantitative or statistical assessment, they do nonetheless provide a powerful example of patient outcome benefits in real-life, real-time clinical situations. In the specific setting of the remote NT, these case studies provide valuable context for the difficulties experienced by remotely located patients and how POCT provides more patient-centred care to these individuals. This is particularly important for policy makers who may not comprehend or appreciate the challenges experienced by those living in remote and isolated locations. In addition, as outlined be the literature review, few studies have focussed on the use of POCT in rural and remote primary health locations, and therefore, these studies provide initial evidence and the foundation for future research in this area.

In terms of future directions, as the studies in this thesis have generally focussed on POCT for acute and chronic disease, future research is needed in the effectiveness of POCT for infectious diseases in remote settings. This is supported by the literature review, which identified very few studies which investigated the use of POCT for infectious or STIs in rural or remote locations. Also, several of these studies indicated that future research should investigate test performance, cost,

acceptability and outcomes of POCT for infectious disease (Natoli, L. et al. 2015; Natoli, L, Guy, RJ, Shephard, MDS, Donovan, B, et al. 2015). Many remote Indigenous communities of Australia experience high rates of infection and STIs (Davis et al. 2011; Gibney et al. 2017). This is also the case internationally, with high rates of infectious disease reported in many other Indigenous or isolated communities (Aledort et al. 2006; World Health Organization 2016).

The body of evidence presented in this thesis has contributed to reshaping policy direction for the provision of pathology service delivery in rural and remote Australia. The study on the timeliness of POC HbA1c testing provided valuable support toward securing ongoing funding from the Australian Government for the national QAAMS Program. The studies on NT POCT Program effectiveness influenced the NT Government's direction and commitment to purchasing i-STAT devices for all remaining remote health services in the NT and renewing the contract with Flinders University ICPOCT to provide the support services required for the expansion of the Program in 2015. Furthermore, these studies have directly influenced the decision of the NT Government to investigate adding further POC test suites into NT health services. As such, this author is now involved with two new research projects in the remote NT investigating the utility of POCT devices for other disease states. The first research project is an extension of the HemoCue WBC DIFF evaluation conducted in 2015 to implement the device into selected remote health services in the NT to determine the operational, clinical and cost effectiveness of this POCT device. This author was approached to be the co-supervisor of the honours student conducting the research study due to her expertise in implementing and managing POCT in remote locations and her experience with the HemoCue WBC DIFF device. More recently, this author has recently been invited as a chief investigator for a multi-country validation study administered by the WHO using POCT to detect STIs in low-resource settings, again due to this author's expertise in evaluating and managing POCT in remote locations.

The assessment of patient satisfaction with POCT in remote NT has only been cited in the form of patient case studies and a survey of health professionals indicating they believed patients were satisfied with the POCT service. As this author is passionate about improving health services available to patients in rural and isolated locations, she wishes to provide an in-depth investigation into the patient experience in accessing pathology services in rural and remote locations and, in doing so, determine the patient's perspective on the impact of POCT in these settings. In particular, this author wishes to measure the stress and anxiety experienced by patients waiting extended periods for pathology results and, therefore, also determine the mental health impact of POCT.

5.1 Conclusion

This ten year body of work critically describes the effective and sustainable methods for POCT evaluation, implementation and assessment in remote locations in Australia. Through addressing the challenges that generally prohibit the effective use of POCT in remote locations, this author has provided a significant evidence-base for the analytical, operational, clinical and economic effectiveness of POCT in remote and challenging environments. These benefits have also been translated internationally through the implementation of a POCT model in rural Pakistan.

Collectively, this body of work of provides a solid and significant evidence base for the use of POCT in rural and remote primary health care settings. This research has also shaped government policy on pathology service provision in the NT of Australia as POCT is now embedded in mainstream service delivery in every remote health facility. Several of the initiatives developed by this author are also now being used in other POCT models in Australia due to their proven efficacy. Through the dissemination of this research, the aim is to provide health service providers with the methods and evidence-base for implementing POCT to improve health service delivery to others living in remote and isolated locations.

CHAPTER 6 APPENDICES

Appendix A – Use of Connectivity for Managing Point-of-Care Testing

McAteer, B, Spaeth, B, Harms, V & Shephard, A 2016, 'Use of connectivity for managing point-of-care testing', in M Shephard (ed.), *A practical guide to global Point-of-Care Testing*, CSIRO Publishing, Clayton, VIC, Australia, pp. 66-75.

Appendix B – Point-of Care Testing for Drugs of Abuse

Vazquez, S & Spaeth, B 2016, 'Point-of-care testing for drugs of abuse', in M Shephard (ed.), A practical guide to global Point-of-care testing, CSIRO Publishing, Clayton, VIC, Australia, pp. 316-30.

Appendix C – Stakeholder Perspectives of Point-of-Care Testing

Braund, W, Spaeth, B, Auld, M, Busbridge, J, Foohey, L & Mardis, C 2016, 'Stakeholder perspectives of point-of-care testing', in M Shephard (ed.), *A practical guide to global Point-of-care testing*, CSIRO Publishing, Clayton, VIC, Australia, pp. 438-42.

Appendix D – 'Simply' Better Access to Pathology Diagnostics is Not so Simple

Spaeth, B 2017, *'Simply' better access to pathology diagnostics is not so simple*, ed. S Magnay, National Rural Health Alliance, Deakin West, ACT, viewed 12 December 2017, <https://ruralhealth.org.au/partyline/issue/59>.

Appendix A:

Use of Connectivity for Managing Point-of-Care Testing

Bridgit McAteer, **Brooke Spaeth**, Volker Harms and Anne Shephard

Summary

Connectivity encompasses the electronic capture of test results from a POCT device and the transfer of those results to a local computer, systems databases, or electronic medical records. The introduction of an international connectivity standard in 2002 helped provide the framework for engineers to design devices and work station interfaces that allowed multiple types of POCT devices to communicate bi-directionally with data management systems or laboratory information systems. For connectivity to be successful, the set-up process must be seamless, reliable and involve both clinical and technical professional staff. Attributes of a connectivity solution should allow control and management of all aspects of remote POCT, from quality control, calibration and maintenance protocols through to result validation, and include training records for all certified operators, POCT site accounts and workload statistics, a complete audit trail and traceability of testing pathways for individual POCT sites.

Introduction

In general terms, connectivity refers to the ability of electronic devices to link to and communicate with other computer systems, electronic devices, software or the internet. In the point-of-care testing (POCT) environment, connectivity 'encompasses the electronic capture of test results within a POCT device and transfer of those results to other computer systems, databases, or electronic medical records' (College of American Pathologists 2015).

Most POCT devices now have connectivity, enabling immediate availability of test results for viewing by clinicians and facilitating prompt clinical management (DuBois 2013). Connectivity has many

benefits and, with innovative technological advancements being developed at an extraordinary rate, there seems to be limitless boundaries for the future of POCT with connectivity.

The first near patient testing devices began to emerge in the 1980s and were designed for clinicians to use in general practices or, as they were known in the US, physician office laboratories (POLs). These devices were stand-alone, had manual data recording procedures and had little or no data output capability (DuBois 2013). The first POCT device to feature connectivity in the mid-1980s was a small, desktop chemistry instrument, the Kodak DT60, which was interfaced to a microcomputer at a POL. This device formed the foundation for understanding the operational and technical requirements for POCT connectivity (Jones 2010).

Initial attempts at connectivity were predominantly undertaken through proprietary firmware and software with scripted interfaces (DuBois 2010). Auto-scripting (automatically running a script) for POCT connectivity was established in 1991 for the then new i-STAT POCT device (Abbott Laboratories, Abbott Park, Illinois PA, USA) which was developed for testing basic blood chemistry. Connectivity trials of this device began at the Geisinger Medical Centre in Pennsylvania, where as part of their trauma protocol, they serially connected i-STAT devices to their laboratory information system (LIS). Connectivity proved beneficial as it reduced both administration time and turnaround time (TAT) for results (Jones 2008). As the benefits of connectivity became clearer, additional POCT devices were connected. It was not until the late 1990s that POCT connectivity became established in the market place. However, by the year 2000, there were still only around 20% of POCT devices connected (Jones 2010).

Early POCT devices were developed with manufacturer-specific data management interfaces, meaning there was little or no standardisation of these interfaces. Health organisations, information technology (IT) departments and data management system vendors were consequently left to deal with the challenges of different communication systems (wiring, computer, software) for each device.

Standardisation

With so many different manufacturer-specific interfaces on the market and with each requiring different communication systems, it was evident there was a need for standardisation. In 1999, the Clinical and Laboratory Standards Institute Area Committee on Automation received a proposal for POCT Connectivity Standardisation. The Point of Care Industry Connectivity Consortium was

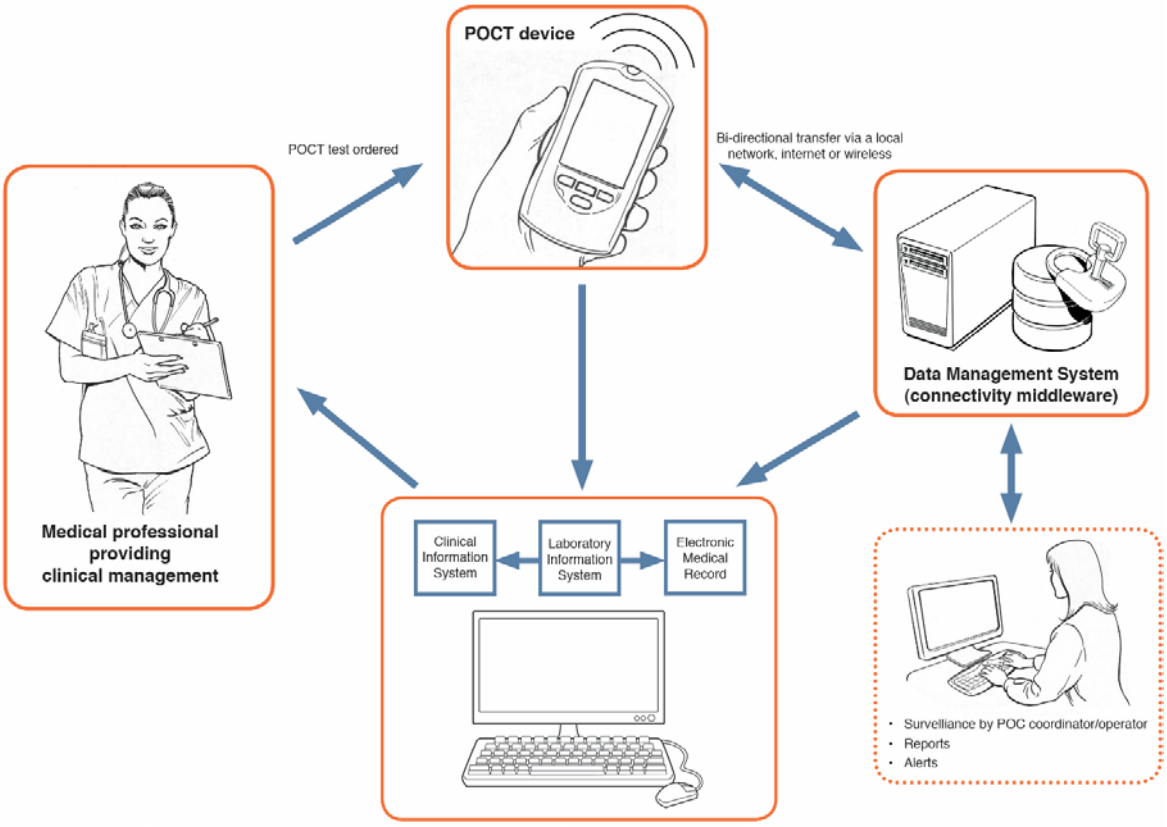
established at the same time and the two groups collaborated to develop the first POCT Connectivity Standard: POCT1-A which was published in 2002 by the National Committee for Clinical Laboratory Standards (NCCLS), now known as the Clinical and Laboratory Standards Institute (CLSI). The introduction of standardisation helped provide the framework for engineers to design devices and work station interfaces that allowed multiple types of POCT devices to communicate bi-directionally with access points and data management system (middleware) databases (POCT Consultative Group 2007). A newer, modified standard, POCT1-A2 (CLSI 2006), has since been released which has further improved connectivity by reducing the complexity of technical terms and incorporating a simpler, universal language, thereby making the guideline more user friendly and communication simpler (Bogner 2010). POCT1-A2 has also evolved to incorporate guidelines on wireless communication (DuBois 2010).

In principle, standardisation has benefitted both manufacturers and users by reducing the cost of product manufacture and decreasing the complexity of installation. Data management systems have become streamlined and more cost effective and network infrastructure and hardware (access points) are now re-usable. Standardisation has meant the selection of POCT devices can now be focussed on the functionality and effectiveness of the device rather than the constraints of connectivity.

Connectivity of POCT devices

Connected POCT devices can send results to an intermediate data management system or a laboratory information system; from there results may be sent to an electronic medical record, or clinical information system. Many POCT devices are ‘intelligent’ and have bi-directional interfaces which can send to and receive information from the POCT data management system (Figure 6.1). Other devices are uni-directional and can only send results to a data management system.

Figure 6.1: Schematic diagram of POCT connectivity.



Connectivity between the analyser and POCT data management system should be 'plug and play'. Access to the device settings required to set up the POCT device for connectivity may vary from manufacturer to manufacturer. Some device manufacturers will have a menu item on the device providing access to the parameter fields, while others supply software which needs to be installed on a computer before connecting to the analyser via a USB cable to configure the connectivity parameters. Manufacturers can also use a pre-configured USB stick to allow upload of connectivity parameters to the analyser. These connectivity parameters are supplied by the IT department that controls the network where the analysers are installed. Once an analyser has been configured on the network, via the parameter set up on the analyser, the analyser should connect to the POCT data management system seamlessly.

Data management system (middleware or connectivity) software can be provided by a specialised vendor or the device manufacturer. Some current suppliers (vendor and non-vendor specific) of data management software include:

- Integrated Software Solutions Ltd, (Winchester, Hampshire, UK) **v-Lab**
- Medical Communications Associates (Adelaide, SA, Australia) **ONDAS and POC2Doc**

- Abbott Laboratories, (Abbott Park, Illinois PA, USA) **Central Data Station System; Info HQ**
- Alere™ (Waltham, MA, USA) **RALS® systems**
- Radiometer (Copenhagen, Denmark) **Aqure**
- Conworx Technology GmbH(Berlin, Germany) **POCcelerator™**
- Roche (Basel, Switzerland) **IT 1000**
- TELCOR (Lincoln, NE, USA) **QML®**

POCT data management systems must be able to interface to analysers using the following message protocols HL7, ASTM, POCT1-a2, proprietary messages and ODBC type connections. A new protocol, Audio16, is being finalised by the Clinical and Laboratory Standards Institute and will be available in the near future enabling a much more standardised approach to the interfacing of instruments.

Table 6.1: Examples of devices that offer connectivity.

Point of Care Device	Manufacturer
ACCU-CHEK® Inform and Inform II via Cobas® IT 1000	Roche Diagnostics
Afinion™ AS100 Analyser System	Alere™
CLINITEK 500® Urine Chemistry Analyser	Siemens Healthcare
*CLINITEK Advantus ®Urine Chemistry Analyser	Siemens Healthcare
*CLINITEK Status® Urine Chemistry Analyser	Siemens Healthcare
• CoaguChek® XS Plus	Roche Diagnostics
• Cobas® b 221 and b 123	Roche Diagnostics
• Cobas® IT 1000	Roche Diagnostics
• DCA Vantage® Analyser	Siemens Healthcare
epoc®	Alere™
• Gem Premier® 3000, 3500, 4000	Instrumentation Laboratory
*HemoCue® Hb 201 DM System	HemoCue®
*In2it™ A1c	Bio-Rad Laboratories
IRMA TruPoint®	LifeHealth
• *i-STAT® Via CDS5	Abbott Point of Care
*Piccolo® xpress	Abbott Point of Care
Radiometer ABL700 Series	Radiometer
StatSensor® Creatinine	Nova
• StatStrip® Glucose	Nova

• *Triage® Meter	Alere™

Bidirectional * Requires serial to network adaptor

Benefits of connectivity

Flow of information to and from the POCT device

A major benefit of connectivity is its ability to improve the flow and management of information to and from POCT devices, enabling faster, more informed and coordinated clinical decisions to be made. Seamless transfer of data reduces the amount of time spent on clerical transcription whilst reducing the possibility of clerical error and loss of results. Devices which have the option of bi-directionality allow information, such as alerts and software upgrades, to be relayed back to the point-of-care device. Additionally, where customised clinical reference ranges have been set and where test results fall outside the acceptable range, connectivity can allow a warning to be sent to a clinical expert who can take action if required (Travanty 2011). Some devices have a laser scanner which can scan the patient's bar code to assist the direct uploading of results into the patient's medical record. This further reduces data entry error and administration time. To reduce the possibility of results being sent to the wrong medical record, second and third unique identifiers confirm the patient's ID before data is uploaded. Typically, results with invalid patient identifiers will not enter patient records until reviewed, corrected and re-sent (Travanty 2011).

From the data management system, data can be stored, transformed if required, organised and backed up. Reports can be generated and may include external quality assurance (EQA), quality control (QC), operator competency and individual and cohort patient reports. Some systems can automate data analysis and prepare and distribute reports automatically (POCT Consultative Group 2007). Data collection using connectivity allows for audit controls, logs, accountability and can be used to inform consumable orders. In addition, when POCT data is uploaded to a LIS, the results can be integrated with other laboratory results to enable the provision of coordinated care. Connectivity can also enable automated billing with the benefit of streamlining the financial administration process (Yu *et al*. 2010).

The functionality of the data management system can be limited by the POCT device itself; for example, how the incoming data is organised will depend on the labels associated with that

incoming data. The label attached to the incoming results may, for example, be an operator identifier (ID), unique patient identifier(s) or a quality control lot number. Labelling of incoming data allows for easy identification of the type of test and for differentiation between incoming patient test results, quality testing results or errors.

Treatment and medication compliance

Connectivity was shown to support medication compliance in a network of 10 anticoagulation clinics using connected INR devices at the Giesinger Health System, Pennsylvania. Connectivity facilitated a more streamlined, or 'lean', patient workflow which in turn assisted in improving compliance rates and avoided adverse clinical events (Jones 2010). POC test results were immediately uploaded to the LIS and reviewed by clinic pharmacists who made changes to medication dose based on the current test result as well as a comparison to previous results (Jones 2010).

POCT connectivity has also been linked to reducing turnaround time for patient results, leading to earlier medication intervention and improving the ability to be able to flag, track and follow-up test results (Dabkowski 2009 and Kost 2001). Not only can connectivity help reduce turnaround time but patient results can be shared instantaneously with all members of a medical team to facilitate coordinated care.

POCT connectivity also permits faster clinical decision making in life threatening situations such as disaster management where the bi-directional exchange of diagnostic data between device and medical personnel permits real-time, evidence-based treatment and disaster response coordination (Yu *et al.* 2010).

Operator competence and lockout

To ensure appropriate clinical decisions are being made, compliance with regulations is met and the possibility of technical errors reduced, POCT operators should be trained and competent in both test performance and data entry procedures for each POCT device (POCT Consultative Group 2007; Travanty 2011). Assigning a unique operator ID when a POCT device is connected allows the benefit of traceability and accountability and enables maintenance of operator competency records. Reports on operator competency (certification date and date of certification expiry) can be regularly reviewed by POCT Coordinators. A bi-directional interface can include a lockout system which prohibits an operator with expired competency or an unauthorised operator from using a device.

Operator compliance has been shown to be improved with operator lockout functions (Salka and Kiechle 2003). Lockouts can additionally discourage fraudulent use including tampering and theft (Kost 2001).

Monitoring of quality testing and reagents

For there to be confidence in the accuracy and precision of test results, the POCT device must be properly configured, should be in sound working order and meet the manufacturer's specifications and recommendations (POCT Consultative Group 2007). Connectivity can be used to monitor, track and record the performance of quality testing of each POCT device (Kost 2001). POCT Coordinators and /or medical staff can remotely monitor EQA and QC results to be certain the device conforms to acceptable analytical standards (Gramz *et al*. 2013 and Travanty 2011).

Connectivity can also be used to monitor reagent and control lot numbers as well as expiry dates, and if reagents are out of date or have incorrect lot number, lockouts can be applied.

Challenges for connectivity

Information technology

POCT with connectivity represents a departure from traditional laboratory medicine, especially with results potentially by-passing the laboratory and being accessed in real-time by clinical decision makers. For connectivity to be implemented successfully, the set-up process must be seamless, reliable and involve both clinical and technical professionals.

One of the first challenges to operating a connected POCT program is the time, cost and effort associated in selecting a device which is analytically sound, meets the organisation's clinical and operational needs, and has interface compatibilities with the organisation's IT infrastructure (Gramz *et al*. 2013).

Transfer of data requires an internet connection (wireless or cabled) via a network to a secure server, where the data management system holds the data which is made accessible to authorised personnel only. In order for data to be held on the database and accessed, there must be a well-planned, systematic approach involving collaboration between multiple stakeholders, including device manufacturers, health service managers, POCT Coordinators, IT personnel, internet service providers and data management system vendors.

Importantly, the IT department must be skilled enough to manage the device connections, information system and the network operations. They must be able to ensure security over the network and be able to support device operators and data management system vendors as required. The IT department will need to supply and/or install ports and network cabling for devices and be able to configure networks for wireless devices. Not all POCT devices share the same functionality so the IT department may need to interface multiple devices with the one information system. There must also be consideration and preplanning for growth in the number of devices and the addition of new and different devices as the POCT network expands (Moorman 2010).

The data management system vendor must have the architecture in place to store, organise and manipulate auditable data. To ensure patient confidentiality, the system must have the ability to restrict access to include authorised personnel only. The data management system must be able to meet the required specifications of the device in order for it to be able to accept the data. It must also have the capacity to regularly back up data and allow ready access to that data.

Finally, for the seamless transfer of data, internet access should be available, reliable and be able to deliver data in real-time so that clinical decisions can be made immediately. Where internet connection has been lost, the health service should expect timely notification, re-connection and the recovery of any missing data (Gramz *et al*. 2013).

Operator

A major challenge to maintain the viability/accuracy of data is correct data entry. Data entry errors in relation to patient identifiers by device operators (particularly if the data entry is performed manually) can result in risk to patients and loss of information. Operator training and competence is the key to good data entry and therefore valid and viable data. POCT Coordinators are likely to have responsibility for performing software updates and will also be undertaking the day to day troubleshooting. Consequently, selecting suitable and proficient device operators and POCT Coordinators is vital (Gramz *et al*. 2013).

Cost

The initial cost of setting up a connected POCT program can be expensive. The ongoing maintenance and system upgrades can also be costly in both time and money and may interrupt patient care (Travanty 2011).

The unavoidable push for cheaper, faster, smaller devices by consumers also presents a challenge to the success of connectivity. Manufacturers must not compromise accuracy and reliability but bear in mind the desired outcome of connected POCT devices is to improve the flow and management of information to and from devices to enable faster, more coordinated clinical management and to improve patient outcomes (Travanty 2011).

The future for connectivity

Recently POCT devices capable of transmitting data wirelessly have been adopted at a fast rate. Wireless technologies enable devices to be more portable and patients more mobile. In a hospital setting, vital signs, blood pressure, electrocardiogram and temperature can be continuously monitored allowing patient mobility (McClintock 2014).

Wireless POCT devices are also available for home monitoring, minimising patient trips to the general practices or hospitals and saving time and expense. For instance, the Nova StatStrip (Nova Biomedical, Waltham MA, USA) blood glucose meter has a docking station allowing POC results to be uploaded, either by wireless modem or ethernet connectivity directly to a data management system. The Accu-Chek Inform II glucose meter (Roche, Basel, Switzerland) can send POC test results to the data management system immediately and automatically without the need to even be docked. The new i-STAT 1 Wireless Analyser (distinguished from the original i-STAT by its blue cover) is portable and results can be transferred to the data management system via the docking station either wirelessly through a wide-area network (WAN), by using a 3-4G wireless telephone network or by ethernet cable (Francis *et al.* 2010). This seamless, immediate transfer of test results facilitates patient self-monitoring and/or external monitoring by a clinician (McClintock 2014).

Figure 6.2: Example of wireless POCT devices currently available. a) Roche ACCU-CHEK® Inform II, b) epoc ®Blood Analysis System (figures reproduced with permission from Roche Diagnostics Pty Ltd and Alere™ ©2015 Alere).

Heart rate and blood pressure are also frequently monitored wirelessly in the home by patients receiving cardiac care (Francis *et al.* 2010). Data can be sent to a general practice for review using a software application installed on a computer, smartphone or tablet in the patient's home.

Recently, implantable glucose monitors have been developed that continuously transmit results to a networked computer at the patient's home with the results being able to be accessed and monitored remotely by health professionals (GlySens 2015). Even critical life-sustaining devices, such as pacemakers, can now be checked by doctors using wireless technology. Wireless technology enables configuration updates to be sent directly to devices and has been associated with better availability, easier use, lower costs and easier access to patient data for health professionals whilst allowing timely critical care decisions to be made (DuBois 2010).

Bluetooth is the most recent wireless protocol in POCT devices (Velez and Shanblatt 2011), where mobile phone networks are used to immediately transfer data to a mobile phone, computer or information system from where the data can be monitored. Examples of Bluetooth POCT devices include the Accu-Chek Aviva Connect (Roche, Basel, Switzerland) wireless glucose monitor, the VivaChek®Smart glucose meter (Wilmington DE, USA) and the epoc device (Alere, Waltham, MA, USA) which is a handheld, wireless solution used for testing gases, electrolytes and metabolites.

Remotely monitoring patients using wireless technology can be used to identify trends and send bi-directional alerts when necessary. It allows health professionals to intervene early and potentially prevents hospital admissions. Remote monitoring allows regular communication between clinician

and patient and facilitates coordinated care and improved self-management. It helps reduce travel time and costs for patients and can reduce the number of home visits as well as prevent admissions to aged care facilities by helping keep elderly patients in their homes longer (RACGP 2015).

The rapid growth of wireless connectivity allows instantaneous bi-directional transfer of information. However, not all wireless networks are of the same standard; there can be dead spots, connection issues, and downtime and bandwidth limitations. Wireless technology, at this stage, is not as reliable as hard-wired systems; however its benefits may outweigh the limitations (McClintock 2014). Additionally, patients may be reluctant to use this new technology as they may feel more at ease visiting a health professional face to face. They may also experience anxiety with having some responsibility for monitoring of their treatment and medications (RACGP 2015).

Role of the POCT Coordinator in connectivity

Surveillance of incoming data

A POCT Coordinator has the responsibility of overseeing a network of POCT devices, ensuring those devices are being used in the manner for which they were intended and are producing results of the required analytical quality to ensure patient safety. This role may include surveillance of incoming patient data to ensure there are no errors in measurement or any gross abnormalities in pathology results. If such errors or abnormalities are found, this information can then be reported back to the health service manager or discussed with the POCT operator (if an operator ID is included in the data label). The frequency of surveying incoming POCT data by the POCT Coordinator will depend on the size of the network and the coordinator's designated responsibilities. For example, the POCT Coordinator may survey the incoming data daily to check for a pattern of errors from a particular operator ID to inform if more education or training is needed, or weekly to check for error patterns on a particular POCT device to determine if maintenance is required.

Surveillance of incoming data can be enhanced if the data storage system has an alert system inbuilt which can be customised to notify the POCT Coordinator (via phone SMS or email) if an incoming result is within or outside a particular range. The customisation of an alert system may also include the timing of the alert which may be instantaneous for critical errors so they can be followed up immediately, or daily, for results within a particular target range of interest. As an example, the POCT Coordinator may set up an immediate alert system if a grossly high potassium (>8.0mmol/L) result is recorded, as this result may be caused by incorrect sampling technique, e.g. the blood was

collected into the wrong preservative tube (containing di-potassium EDTA) or the blood sample was grossly haemolysed. A less critical daily alert system may include all incoming results without a valid patient identifier so these results can be followed up with the operator who performed the test and the correct information entered.

Reporting on incoming data

As part of continuing quality management processes, the POCT Coordinator may be required to provide a feedback summary of the incoming data to key stakeholders within a POCT network. Considerations for reporting this data include:

- what data is to be reported
- to whom the feedback report will be provided (eg the medical director, health service manager, or multidisciplinary POCT management committee)
- an appropriate frequency to provide feedback (e.g. daily, weekly, monthly or annually).

The types of information that the feedback report may include are:

- total number of patient tests
- total number or percentage of errors produced
- common or re-occurring errors
- individual POCT operator usage (for the health centre manager or individual to inform if further training/education is required)
- total number of individual test cartridges/strips performed (to inform ordering processes)
- number and type of quality tests performed on each POCT device (to monitor the rate of participation in quality testing procedures)
- individual patient report [based on a unique patient ID] (for the treating medical professional).

Table 6.2 provides an example of an individual health centre feedback report used in the Northern Territory Point-of-Care Testing Program in Australia (Shephard *et al.* 2014). These individual health centre feedback reports are a useful means of providing information to senior management at participating health services about the real-time field use of their POCT device in this program.

Table 6.2: Example of a Feedback Report for an individual health service.

Health Service Name - POCT Device Name - Month				
Total Tests	**Cartridge A**	**Cartridge B**	**Cartridge C**	**Cartridge D**
48	22	13	8	5
Patient Tests				
35	15	9	8	3
Quality Tests				
9	4	3	0	2
Errors				
4	3	1	0	0

Tests by Operator	**Total Tests**	**Patient Tests**	**Quality Tests**	**Total Errors (%)**
Operator 1	25	24	1	0 (0%)
Operator 2	13	8	4	1 (8%)
Operator 3	10	3	4	3 (30%)
Total	**48**	**35**	**9**	**4 (8.3%)**

Errors by Type	**Number of Errors**	**Comment**
Overfilled Cartridge	1	Caused by operator 2
Underfilled Cartridge	1	Caused by operator 3
Interference between cartridge and device	2	Error caused by operator 3, device requires cleaning

Quality Testing	**Cartridge A**	**Cartridge B**	**Cartridge C**	**Cartridge D**
Quality Control (2 required for each cartridge)	2	1	0	1
Quality Assurance (2 required for each cartridge)	2	2	0	1

Summary of Recommendations to Health Service Manager

1	Operator 3 has produced a high error rate (30%), however 2 of these errors relate the maintenance requirements for the POCT device; please perform cleaning procedure
2	Discuss correct cartridge filling procedure with operators 2 and 3
3	Quality testing was not performed on cartridge C; perform QC and QA checks immediately to ensure patient safety

Table 6.3 provides an example of a monthly summary report of the total number of tests performed in a POCT network for management committee personal. This type of report is useful to provide the total cartridge usage by site as well as monitoring high error rates for individual services.

Table 6.3: Example of a monthly management statistics report for a POCT network.

Health Service Name	Total Tests	Total Errors	% Error Rate	Cartridge A	Cartridge B	Cartridge C	Cartridge D
Site 1	48	3	6.2%	21	16	8	3
Site 2	56	2	3.6%	10	25	6	15
Site 3	20	8	40.0%	5	4	9	2
Site 4	88	2	2.5%	41	32	7	8
Site 5	33	0	0%	5	3	4	21
TOTAL	**245**	**15**	**6.1%**	**82**	**80**	**34**	**49**

Conclusion

Information technology is the single most rapidly advancing industry in the world. Every day new technologies are developed while old technologies are retired or improved. This too will be the case for POCT devices and their connectivity capabilities. Already there has been dramatic change over the past thirty years and no doubt there will be more. POCT is becoming more mobile, sophisticated and accurate. Costs of devices and tests are reducing and, with this, demand will continue to increase at a dramatic rate. Providers, manufacturers and regulators should look five to ten years in the future and work together to plan for new and novel technologies, connectivity systems and processes (DuBois, 2010). Manufacturers, alongside independent IT vendors, need to continue evolving data management solutions to better support all aspects of POCT as the new generation of products will need to incorporate new and evolving communication and information technologies. The ideal POCT data management system is a comprehensive and powerful single-platform system for POCT connectivity which is a truly open (non-vendor specific) platform and able to interface with all types of analysers, irrespective of manufacturer. Such POCT data management systems must be web-based and which can be learnt quickly and relatively easily. Attributes of a connectivity solution should allow control and management all aspects of remote POCT, from quality control, calibration and maintenance protocols through to result validation, including training records for all certified operators, POCT site accounts and workload statistics, a complete audit trail and traceability of testing pathways for individual POCT sites.

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Appendix B:

Point-of-care testing for drugs of abuse

Santiago Vazquez and **Brooke Spaeth**

Summary

246 million people between the ages of 15 and 64 years used an illicit drug in 2013. The advantages of POCT for drugs of abuse are the ability to have results without delay and reduced cost of testing. Urine and oral fluid (saliva) are the preferred matrix analysed by POCT drugs of abuse devices which use immunochromatography to detect the drug or drug metabolite. With these POC drug tests, a positive result is termed a "negative read" meaning the absence of a test line formed is indicative of a positive result. POCT for drugs of abuse can be used in roadside drugs testing, workplace testing, judicial drug testing and rehabilitation clinics. The limitation of POCT for drugs of abuse is that a positive result needs confirmatory testing by a laboratory.

Global drug use trends

According to the United Nations Office on Drug and Crime World Drug Report (2015), 246 million people between the ages of 15 and 64 years are estimated to have used an illicit drug in 2013. This equates to 1 in 20 people globally. Of these drug users, more than 1 in 10 is considered a problem drug user, suffering from drug use disorders or drug dependence. General U.S. workforce urine drug test data released by Quest Diagnostics® showed that the percentage of American workers testing positive for illicit drugs including marijuana, cocaine and methamphetamine has increased for the second consecutive year. These are the first increases observed since 2003 (McKetin *et al.* 2014).

Cannabis is the most commonly used illicit drug and its use continues to rise. Improvements in cannabis plant cultivation techniques and the use of genetically selected strains have produced increases in yield and potency of cannabis. This has led to a growing concern that cannabis may be becoming more harmful, with increasing numbers of users seeking treatment for cannabis use disorders (United Nations Office on Drugs and Crime 2015).

Opiate use remains the most problematic form of drug use globally due to the relationship between opiates and injecting drug use, blood-borne viruses (BBV) and overdose deaths. In 2014 opium poppy cultivation reached the highest level since the late 1930s. The effects of these record crops are yet to be seen on the global opiate market (United Nations Office on Drugs and Crime 2015).

Cocaine use continues to decline in Western and Central Europe and North America although it remains the primary drug of concern in Latin America and the Caribbean. Supply reduction measures may have contributed to the decline in coca bush cultivation in coca-producing countries, now with the lowest levels of cultivation since the mid-1980s, leading to a reduction in the availability of cocaine and the reduction of some of the principal cocaine markets (United Nations Office on Drugs and Crime 2015).

Methamphetamine continues to dominate the global market for amphetamine type substances (ATS). In North America, Europe and Australia there are increasing trends towards the use of methamphetamine in its purest form known as crystal methamphetamine or 'ice' rather than methamphetamine in its powdered form known as 'speed' (United Nations Office on Drugs and Crime 2015; AIHW 2014). The 'high' experienced from ice is much more intense than other drugs and has a greater potential for the user to develop dependence (addiction), psychosis, as well as long-term physical and mental health problems.

New psychoactive substances (NPS) are relatively new to the recreational drug market and are marketed as alternatives to traditional drugs. NPS often have chemical structures similar to

'traditional' illicit drugs and are purported to mimic their mind-altering effects; however, they are generally not detectable by conventional drug screening tests. Marketing as legal or herbal highs has yielded market acceptance. NPS continue to proliferate; by the end of 2014 a total of 541 NPS had been reported in the global marketplace. Information and research on the potential harm caused by NPS is limited; however, worrying developments such as the injecting use of NPS and poly-drug use involving NPS have the potential to pose serious risks to public health and safety (United Nations Office on Drugs and Crime 2015).

Prescription drug misuse is greater globally in the female population compared with the male population (United Nations Office on Drugs and Crime 2015). Women are twice as likely as men to use tranquillisers, but both have roughly equal levels of use of prescription opioids. Data from the National Drug Strategy Household Survey 2013 found that pain-killers/analgesics (for example, over-the-counter and prescription codeine combination products) were the most commonly misused pharmaceutical drugs followed by tranquillisers/sleeping pills (for example, benzodiazepines) as the second most commonly misused pharmaceutical drug (AIHW 2014).

The health burden of drug use

Globally, drug use accounted for an estimated 187,100 drug-related deaths in 2013 (United Nations Office on Drugs and Crime 2015). Illicit drug use is an increasingly significant contributor to the global burden of disease/illness rising in ranking from 25th to 19thranking between 1990 and 2010 (Degenhardt *et al.* 2010; Lim *et al.* 2010). Drug abuse is associated with numerous health impacts ranging from the mild, such as headaches and altered mental states, to life-threatening situations such as suicide, coma, seizures and violence towards others. The health risks of drug use increase with the frequency, quantity and number of drugs used. Intravenous drug use amplifies the potential for deleterious health effects through the potential transmission of blood-borne viruses, including HIV, hepatitis C and hepatitis B, as well as bacterial infections including bacterial

endocarditis, osteomyelitis and abscesses (Karch 2007). In fact, the level of mortality among injecting drug users is nearly 15 times higher than would be normally expected among people of comparable age and gender in the general population. There is no “quick fix” for drug dependence; it is a chronic health condition. Affected persons may remain vulnerable for a lifetime and require long-term and continued treatment.

Historical milestones of drug testing

Workplace drug testing has developed steadily through a series of events and technological developments. The most significant milestones are detailed in Table 26.1.

Table 26.1: Major historical events in the development of drug testing.

Year	Event	Comments
Pre 1960s	Limited ability to drug test	Capacity to chemically identify the use of common drugs has been available for approximately a century; however, the ability to engage in mass drug screening was limited primarily by inefficient and non-specific techniques (Lewis 2001).
1966	Drug Testing for methadone substitution therapy	Drug testing was introduced in the United States as a means of monitoring patients who were undergoing methadone substitution therapy for heroin addiction. Testing was carried out primarily by performing thin layer chromatography (TLC) (Dole *et al.* 1996).
1971	Nixon declares war on drugs	US President Nixon names drug abuse as "public enemy number one in the United States." During the Nixon era, for the only time in the history of the war on drugs, the majority of funding goes towards treatment, rather than law enforcement (Kuzmarov 2009).
	Operation Golden Flow	In June 1971, following the public relations fallout surrounding drug addicted army personnel in Vietnam, President Nixon enacted a urine drug testing program on U.S. military personnel known as Operation Golden Flow (Kuzmarov 2009).
1972	First Immunoassay Drug Screening Assay Released	Originally developed to be used in the methadone maintenance treatment programs the Enzyme Multiplied Immunoassay Technique (EMIT®) assay, developed by Syva®, was automated, didn’t require separation and utilised easily available spectrophotometers (Schneider *et al.* 1973).
1986	President Reagan signs The Anti-Drug Abuse Act of 1986	US President Reagan's Executive Order 12564 required all federal agencies to develop programs and policies to

		achieve a drug-free federal workplace (Normand *et al.* 1994).
1988	Micro-particle Based Drug Screening Devices FDA Approved	The first wave of practical, micro-particle-based, POCT drug screening devices received FDA approval. These devices, utilising latex agglutination-inhibition, allowed results to be visually read in 4 minutes rather than after 2 hours of incubation (Karch 2007).
	The first mandatory guidelines for workplace drug testing published	The U.S. Department of Health and Human Services (HHS) drug testing standards "Mandatory Guidelines for Federal Workplace Drug Testing Programs" were published.
Mid-1990s	Proliferation of Membrane based Lateral Flow Drug Screening Devices	By the mid-1990s as many as twelve membrane based lateral flow devices for screening drugs of abuse in urine were available. These devices have further evolved and have become the primary technique for point-of-care drug testing (Karch 2007).
1995	Australian Standard for Urine Drug Testing Published	Standards Australia published AS 4308 “Procedures for specimen collection and the detection and quantitation of drugs of abuse in urine” (Standards Australia 1995).
Late 1990s	First lateral-flow POCT Oral Fluid (OF) Device available	The first on-site screening devices for drug testing in oral fluids were developed in the late 1990s. By 1999 three on-site oral fluid devices were available (Verstraete 2005).
2001	ROSITA study released	The 21-month Roadside Testing Assessment (ROSITA) project included the on-site immunoassays detection of drugs in urine, oral fluid and/or sweat in 2968 subjects in European Union countries.
2002	European Guidelines Released	European guidelines for legally defensible workplace drug testing prepared by the European Workplace Drug Testing Society (EWDTS) were released.
2006	Australian Standard for Oral Fluid Drug Testing Published	Standards Australia publishes AS 4760 “Procedures for specimen collection and the detection and quantitation of drugs in oral fluid” (Standards Australia 2006).

The drug testing process

Drug testing is generally a two-step process: an initial drug screen; and, if required, a confirmatory test. The drug screen is a qualitative analysis that does not measure the quantity of a drug group drug or its metabolites, but quickly establishes the presence or absence of a drug/drug group and/or its metabolites in a particular specimen. This is usually an immunoassay either performed on an automated instrument in the laboratory, or by a POCT device. Immunoassays are calibrated at the

cut-off concentrations, and a specimen that yields a response greater or equal to this calibration point is positive, and negative if the response is less. Initial immunoassay positive results should be referred to as 'presumptive positive' until confirmatory testing is performed. This is necessary as screening assays do not have a high degree of specificity and substances chemically similar to the drug/s being tested can cross-react yielding false positive results. For example, the consumption of poppy seeds can yield a false positive result.

The purpose of the confirmatory test is to unequivocally verify or negate the drug screen result. If present, the specific drug and/or its metabolite are identified and quantified. Confirmatory tests are performed in a laboratory setting and employ analytical techniques that have a higher degree of specificity and sensitivity than the initial screen. The use of mass spectrometric techniques coupled with chromatographic techniques such as liquid chromatography (LC) or gas chromatography (GC) are required to achieve the near absolute specificity essential for confirmatory work. These tests involve higher costs due to the high degree of skill and effort required as well as higher cost of instrumentation. Confirmation is essential where punitive consequences may follow a positive result such as in workplace or judicial settings.

Drugs of abuse testing standards and guidelines

Every form of drugs of abuse testing is contingent on the use of a cut-off. Functionally, it is an administrative decision point. If a specimen contains a target drug above this threshold concentration value the specimen is reported as positive. Below this concentration a specimen is reported as negative. Prior to 1988, when the US government published "Mandatory Guidelines for Federal Workplace Drug Testing Programs", guidelines and standards for drugs of abuse testing did not exist. Standardised cut-offs did not exist. Screening cut-offs were established by individual manufacturers of POCT devices while confirmatory cut-offs were determined by the laboratory

performing confirmatory analysis. Confirmatory cut-offs varied from laboratory to laboratory and depended upon the sensitivity of the laboratory's equipment.

Setting standardised cut-offs aimed to minimise the risk of a positive result from incidental exposure to a target drug, for example, passive marijuana smoke, and ensure uniformity of testing and reporting across laboratories. Initially, guidelines were only developed for urine drug testing with guidelines for oral fluid testing preceding the advent of oral fluid POCT devices.

Screening and confirmation cut-offs for urine and oral fluid guidelines and standards used in the USA and Australia are listed in Tables 26.2 to 26.5. Similar guidelines are also available for Europe (European Workplace Drug Testing Society 2015a and 2015b). Confirmatory cut-off concentrations are generally lower than screening cut-offs because confirmation targets a particular drug while a screening cut-off accommodates immunoassay testing in which the total response is the sum of the response by the target drug as well as any cross reacting drugs and/or metabolites. Cut-offs are largely quite closely aligned across all regions where testing is performed; however, differences do exist. The most significant differences exist between US guidelines for urine screening cut-offs for amphetamines and opiates, where they are significantly greater than those used in other countries such as in Europe and Australia. These differences may become an issue when POCT devices are purchased from uninformed device suppliers who source product intended for markets in foreign countries where different cut-offs are used. For example, kits developed for the US market, if used in Australia, may cause false negative screening results for opiates and amphetamines because of the higher cut-offs for these target drugs.

Currently, with the exception of the AS/NZS 4308:2008, all standards and guidelines mentioned in this chapter are under review or open for public comment. With the increasing concern that drug abuse is not limited to illicit substances, guidelines and standards are including additional substances particularly pharmaceutical drugs.

Table 26.2: Screening and confirmation cut-off concentrations, in urine, as stated in the US Mandatory Guidelines for Federal Workplace Drug Testing Programs. Cut-offs are subject to change as revision of mandatory guidelines is currently under consideration (Substance Abuse and Mental Health Services Administration 2015a; Substance Abuse and Mental Health Services Administration 2015b; Substance Abuse and Mental Health Services Administration 2008).

Screening Test Analyte/s	Screening Cut-off Concentration (ng/mL)	Confirmatory Test Analyte	Confirmatory Cut-off Concentration (ng/mL)
Marijuana (THC-COOH)	50	THC-COOH*	15
Benzoylecgonine	150	Benzoylecgonine	100
Codeine/Morphine	2000	Codeine	2000
		Morphine	2000
Hydrocodone/Hydromorphone	300	Hydrocodone	100
		Hydromorphone	100
Oxycodone/Oxymorphone	100	Oxycodone	50
		Oxymorphone	50
6-MAM	10	6-MAM	10
Phencyclidine	25	Phencyclidine	25
Amphetamine/Methamphetamine	500	Amphetamine	250
		Methamphetamine	250
MDMA/MDA/MDEA	500	MDMA	250
		MDA	250
		MDEA	250

***** Delta-9-tetrahydrocannabinol-9-carboxylic acid.

Table 26.3: Screening and confirmation cut-off concentrations, in oral fluid, as stated in the US Mandatory Guidelines for Federal Workplace Drug Testing Programs. Cut-offs subject to change as revision of mandatory guidelines is currently under consideration.

Screening Test Analyte/s	Screening Cut-off Concentration (ng/mL)	Confirmatory Test Analyte	Confirmatory Cut-off Concentration (ng/mL)
Marijuana (THC)	4	THC	2
Cocaine/Benzoylecgonine	15	Cocaine	8
		Benzoylecgonine	8
Codeine/Morphine	30	Codeine	15
		Morphine	15
Hydrocodone/Hydromorphone	30	Hydrocodone	15
		Hydromorphone	15
Oxycodone/Oxymorphone	30	Oxycodone	15
		Oxymorphone	15
6-MAM	3	6-MAM	2
Phencyclidine	3	Phencyclidine	2
Amphetamine/Methamphetamine	25	Amphetamine	15
		Methamphetamine	15
MDMA/MDA/MDEA	25	MDMA	15
		MDA	15
		MDEA	15

Table 26.4: Urine screening and confirmation cut-off concentrations as stated in the Australian and New Zealand standard AS/NZS 4308:2008 (Standards Australia and Standards New Zealand 2008).

Screening Test Analyte/s	Screening Cut-off Concentration (ng/mL)	Confirmatory Test Analyte	Confirmatory Cut-off Concentration (ng/mL)
Amphetamine Type Substances	300	Amphetamine	150
		Methamphetamine	150
		MDA	150
		MDMA	150
		Benzylpiperazine*	500
		Phentermine*	500
		Ephedrine*	500
		Pseudoephedrine*	500
Benzodiazepines	200	Diazepam	200
		Nordiazepam	200
		Oxazepam	200
		Temazepam	200
		α-Hydroxyl-alprazolam	100
		7-Amino-clonazepam	100
		7-Amino-flunitrazepam	100
		7-Amino-nitrazepam	100
Cocaine metabolites	300	Benzoylecgonine	150
		Ecgonine methyl ester	150
Opiates	300	Codeine	300
		Morphine	300
		6-MAM *	10
Cannabis metabolites	50	11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid	15

*These drugs may be optionally tested within each class.

Table 26.5: Oral fluid screening and confirmation cut-off concentrations as stated in the Australian standard AS 4760-2004 oral fluid (Standards Australia 2006).

Screening Test Analyte/s	Screening Cut-off Concentration (ng/mL)	Confirmatory Test Analyte	Confirmatory Cut-off Concentration (ng/mL)
Amphetamine-type stimulants	50	Amphetamine	25
		Methamphetamine	25
		MDA	25
		MDMA	25
Cocaine and metabolites	50	Benzoylecgonine	150
		Ecgonine methyl ester	150
Opiates	50	Codeine	25
		Morphine	25
		6-MAM	10
Δ9-tetrahydrocannabinol (THC)	25	Δ9-tetrahydrocannabinol	10

Specimens for drugs of abuse testing

Almost any biological matrix can be used for testing for the presence of drugs or their metabolites; however, matrix selection is essential in evaluating an individual's likelihood of impairment or historical drug use. The more common matrices include: blood, urine, oral fluid and hair. Other matrices which are not widely used include: sweat, meconium, breast milk, vernix caseosa (a waxy cheese-like substance found coating the skin of newborn babies), semen and nails. Only urine and oral fluid are commonly analysed using POCT devices.

Blood

Blood is widely regarded as the specimen offering the best correlation with the degree of impairment. However, not all drugs of abuse have been subjected to controlled studies to define this relationship. Drugs are present in blood most commonly as the parent compound and not the respective metabolites which may be present at low concentrations and are relatively short-lived.

The analysis of drugs in blood is complex and time-consuming. Collection of specimen is invasive and the possibility of transmission of infectious disease is greater than with other matrices.

Urine

Urine is the biological matrix of choice when it comes to the detection of drug use in an individual. It offers numerous distinct advantages including: large specimen volumes; drugs/metabolites bio-concentrate into urine (up to 100 fold); variety of POCT devices available; extensive literature regarding analytical methods and long history of case law regarding workplace use. Drugs are generally present in the urine as phase I and phase II metabolites of the respective parent compound.

Some of the challenges include: invasion of privacy; potential for adulteration, potential for physiological dilution; also correlation between urine drug/metabolite levels and the likelihood of impairment is difficult.

Oral Fluid

Oral fluid is a mixture of various fluids, including saliva, from the oral cavity and is effectively an ultra-filtrate of blood and consequently the drug in circulation, usually the parent drug, is found in oral fluid. The major factors affecting drug entry into oral fluid are a drug's lipophilicity and ionisability at typical oral fluid pH (normal pH is approximately 6.7). Oral fluid is increasingly becoming the drug testing matrix of choice spurred on by: the global experience with roadside drug testing programs; availability of POCT devices; collection process which minimises privacy and gender related issues; and specimens present fewer opportunities for adulteration or substitution and the perception that results are more closely correlated with impairment.

Some of the challenges include: volume of oral fluid collected is limited; drug concentrations are low; and some medications, illegal drugs, and medical conditions cause dry mouth syndrome (or

xerostomia) making specimen collection difficult (Drummer 2006). Additionally, detection of cannabis use can be challenging as cannabinoids are not secreted from blood into oral fluid and detection is generally considered to be the result of relatively short-lived contamination of the oral cavity following smoking or ingestion. Anecdotally, this may be beneficial where the goal of drug testing is the demonstration of possible impairment. Analysis of benzodiazepines can also be challenging for analysis due to their low therapeutic concentrations in blood.

Hair

Hair testing appears to be best suited for detecting prior frequent heavy use rather than for detection of very recent or occasional drug use (Dolan *et al.* 2004). Drugs and/or metabolites are assumed to be incorporated into the hair shaft during growth, by direct transfer from the bloodstream through hair follicles and secretions of the sebaceous and sweat glands in the scalp (Musshoff and Madea 2006). Drugs can be detected in the hair shaft approximately 7–10 days after drug ingestion.

Specimen collection is relatively easy and non-invasive and hair has the longest window of detection compared to other matrices. Furthermore, it may give an indication of the chronology of drug use or abstinence if segmental analysis along the length of the hair shaft is performed.

Challenges of hair based drug testing include: analysis is very costly and labour intensive; few laboratories are capable of performing analysis; POCT devices are unavailable; specimen can be removed by shaving; and, significantly, results can be difficult to interpret since drugs may also be incorporated into hair through environmental drug exposure (Wong and Tse 2005).

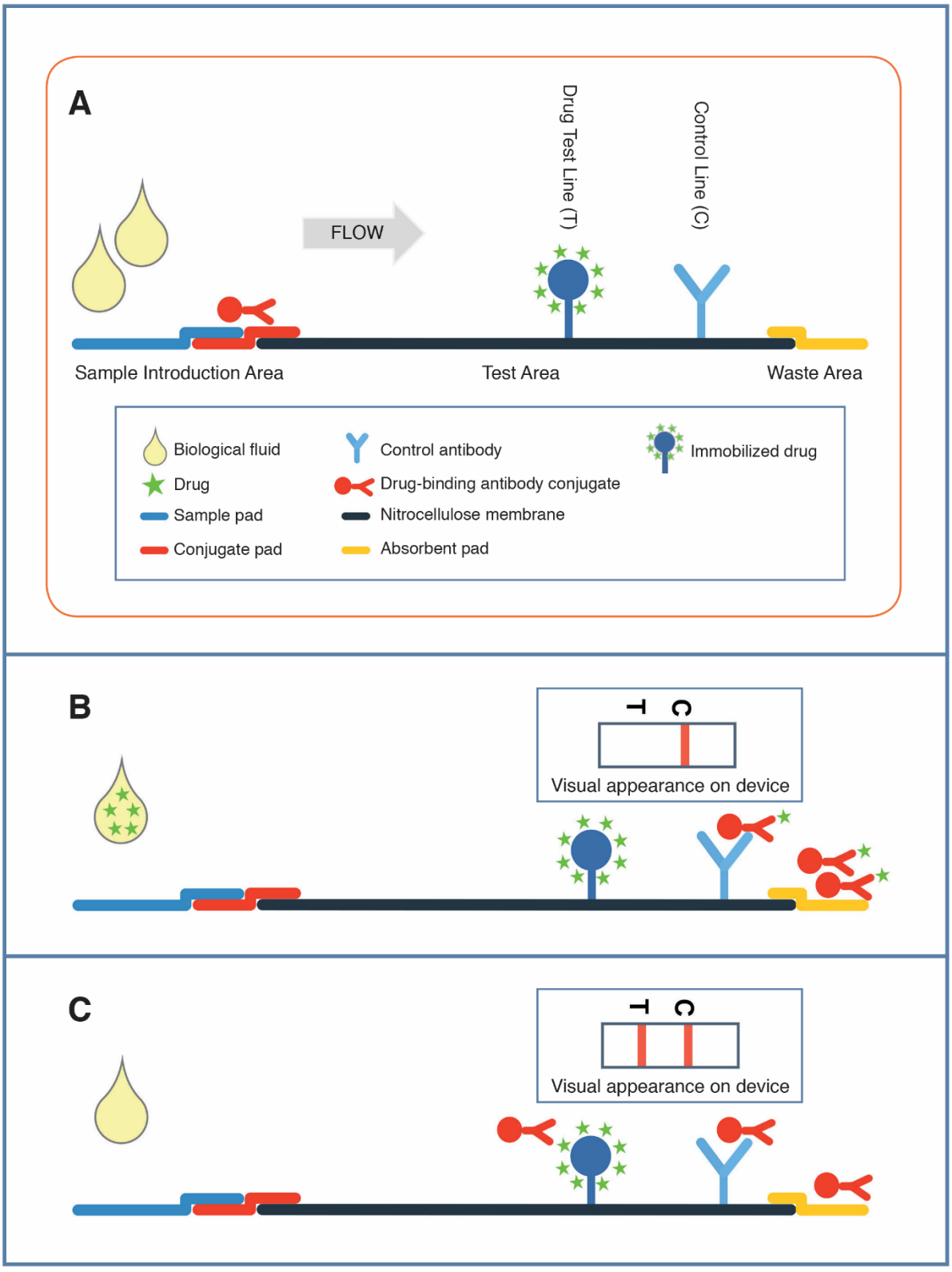
Additional controversies exist about effect of biophysical attributes on the concentrations of drugs in hair. Studies have shown that hair structure, growth rate, melanin content, hygiene, and cosmetic hair treatments, such as bleaching, have an effect (Dasgupta 2008).

POCT devices - lateral flow methods

A range of devices is now available for POC drug testing, from simple dipsticks, to cups with incorporated test strips, to instrument-based readers. The appeal of modern lateral flow devices for drugs of abuse testing lies in the specificity and rapidity of result delivery, anywhere from a few to 15 minutes. Devices are available in single assay or multi-assay formats with adulterant and creatinine testing. Devices use well established immunoassay technologies, which involve antigen-antibody reactions in chromatographic strips, with this form of immunoassay testing referred to as immunochromatography. Antibodies are directed to the specific drug and/or metabolites to be detected and are labelled with either colloidal gold or coloured latex spheres as a means of visualisation.

A point-of-care drug testing device consists of three regions: sample introduction, test and waste areas as shown in figure 26.1.

Figure 26.8: A) Layout of a point-of-care drug testing device; B) Addition of a specimen containing drug at a concentration at or above the cut-off producing a single line result; C) Addition of a specimen free of drug or containing drug at a concentration below the cut-off concentration produces a two line result.



The sample introduction area consists of a sample pad, which overlaps the conjugate pad which in turn overlaps the nitrocellulose membrane. This membrane acts as the separation and reaction

medium. The sample pad is impregnated with a buffer and surfactant matrix, to ensure optimal immunoreactions, and the conjugate pad is impregnated with the drug-binding labelled-antibody. The test area is situated on the nitrocellulose membrane and is comprised of a drug test line and a control line. The drug test line consists of a drug covalently bound to a large molecular weight carrier protein (drug conjugate) immobilised on the nitrocellulose membrane. The control line is a single line of immobilised antibodies specifically directed to bind to the labelled antibody. This control line is a functional control and only determines serviceability of the device. It is not a drug based quality control test of assay performance. The waste area consists of a final porous pad which overlaps the nitrocellulose membrane and acts as a waste capture container.

When sample is introduced to the sample pad it rehydrates the buffer and surfactant compounds. The sample then migrates to the conjugate pad where it rehydrates and mixes with the labelled antibody. The mixture then migrates along the nitrocellulose membrane through the test area by capillary action to the waste area. Once the test has been performed, the test result is evaluated visually by the presence or absence of a coloured line at the drug test and/or control line.

When a drug is present in the test sample above the cut-off concentration, the drug populates all possible binding sites on the labelled antibody and prohibits it from binding to the drug conjugate. The labelled antibody is still able to bind to the control line giving the single line at the control line, as shown in figure 26.1(b), indicative of a non-negative result. In contrast when no drug is present in the specimen or is present below the cut-off concentration, binding sites on the labelled antibody are available to bind to the immobilised drug conjugate on the membrane as well as with the control line giving rise to two lines which corresponds to a negative result, as depicted in figure 26.1(c), which is why results are often referred to as ’negative read’. The absence of any line is indicative of a failed test possibly due to either: incorrect application of the test; poor storage of the device; or

manufacturing issues. In such cases testing of the specimen should be repeated (Ropero-Miller *et al.* 2009).

A limitation of these devices is the necessity for the operator to visually interpret the result which is subjective and can be influenced by the individual's visual acuity, level of training and adherence to the device manufacturer's operating instructions. Increasingly, vendors are developing instruments and readers of point-of-care devices to provide objective interpretation of results.

Table 26.6 lists representative examples of some qualitative and quantitative drugs of abuse devices that are available on the global market.

Table 26.6: The POCT drug testing market can be divided into two major categories. Those supplied by prominent companies and those supplied by manufacturers in China (these are too numerous to list).

Company	Qualitative Urine POCT	Quantitative Urine POCT	Qualitative Oral Fluid POCT	Quantitative Oral Fluid POCT
Branan Medical Corporation™+	Fastect®II, ToxCup®, QuickTox®, Monitect®		Oratect®, OratectPlus®, Oratect® III	
Alere™	SureStep™ Drug Screen Cassette, SureStep™ Drug Screen Cup	Alere Triage® MeterPro	Alere iScreen® OFD Test	Alere™ DDS®2
Bio-Rad™	TOX/See Rapid Urine Drug Screen Test+			
US Diagnostics Inc.*	ProScreen® Cup, ProScreen® Dip, ProScreen® Cassette, UScreen Cup, UScreen Dip, E-Z Cup		UScreen Oral, USD Oral	
Clonal Technologies			Clonal Oral Fluid DoA	
Dräger				Dräger DrugTest® 5000
Thermo Fisher Scientific	MicroScreen™ Drug testing Cup+, MicroTox 6 Panel Drug Test Cassette+			
Securetec AG			DrugWipe 5S, DrugWipe 6S	

* An Alere Subsidiary + Manufactured by Alere or Alere subsidiary

Limitations of POCT

The utility and ease-of-use of POCT devices has enabled access to drug of abuse testing across all sections of society. Consequently, non-technically trained or inexperienced operators have the confidence to apply testing. However, deficiencies in the understanding of POCT device limitations,

performance and troubleshooting of problematic specimens can compromise the accuracy of the results reported.

Result reading from POCT devices, in the main, is quite facile since the test line will be: intense when drug is not present in the specimen; or not visible when the concentration of drug is well above the cut-off. In situations, however, where the drug concentration in the specimen is present at a concentration near its respective cut-off, either above or below, the test line may appear very faint and difficult to determine if present or absent. This situation is often referred to as a 'near cut-off' concentration reading. Factors such as the visual acuity of the reader, lighting conditions and colour vision deficiency, such as protanopia (inability to perceive red light) could all have an impact on the ability of the user to read a result and thus give rise to the subjective nature of result reading. This is a concern for test accuracy. In a study by Kadehjian, the near cut-off performance of five POCT devices was evaluated. Sixty clinical specimens for each of the five SAMHSA-specified drug categories (Cocaine, THC-COOH, Amphetamines, Opiates and Phencyclidine) were selected with drug concentration near the POCT device screening cut-offs. POCT device results were read independently by both a scientist and a non-scientist and compared to results from an immunoassay analyzer (Emit reagents) and gas chromatography-mass spectrometry (GC-MS). An overall accuracy of only 70% (66-74%), compared with GC-MS was found (Kadehjian 2001).

Adulterants can affect immunoassay testing by affecting drug-antibody interactions. Most POCT device manufactures offer the option to manufacture devices with on-board adulterant testing strips, for example, the detection of dilution and oxidants. In addition to chemical adulterants (including glutaraldehyde, nitrites, chromium VI compounds or bleach) which instrumental based immunoassays systems are susceptible to, POCT devices are also at risk from adulterants that can impede flow, such as particulate matter. Such adulterants prevent the development of a control line and thus invalidate testing. Oral fluid, as a matrix, is susceptible to poor flow of matrix through POCT

membranes due to viscosity issues and debris in the oral cavity without attempts at adulteration. In situations where possible adulteration is detected or suspected, operating procedures should allow for re-collection of a specimen and referral of both to the laboratory for analysis.

A significant challenge for oral fluid-based POCT devices is the non-specific binding of drug to device surfaces limiting drug recovery from the device and therefore the usability of some devices. Numerous devices, for example, demonstrate poor THC recoveries (Drummer 2006).

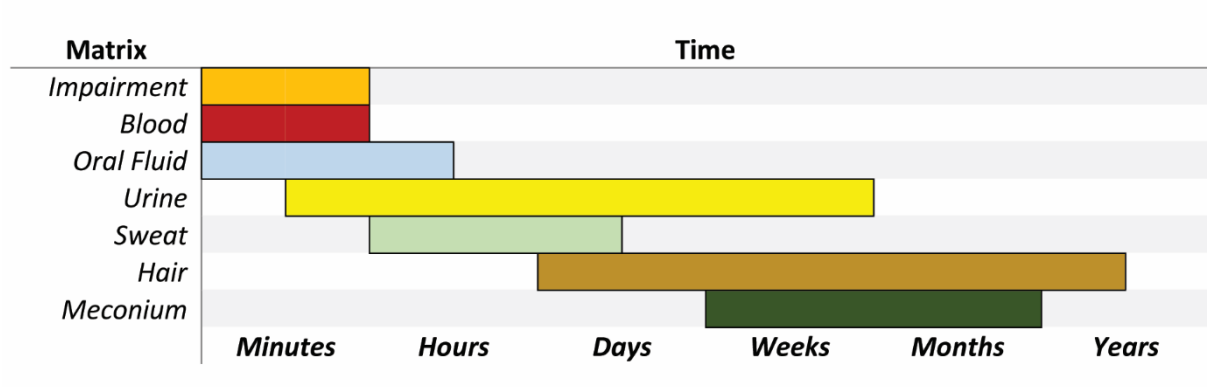
Window of detection

The length of time that a drug or its metabolites can be detected in a biological specimen, or matrix, is referred to as the detection time or the window of detection. Many factors influence the window of detection for a drug and, as such, only an estimate of this length of time can be given. Factors that influence the window of detection include:

- Drug half-life
- Frequency of drug use
- Quantity of the drug ingested
- Individual metabolism rates and excretion routes
- Route of administration
- Sensitivity and specificity of the test
- Cut-off concentration used
- The individual's health, diet, weight, amount of body fat, gender, fluid intake, and pharmacogenomic profile
- Matrix tested.

Figure 26.2 shows a comparison of the detection times in various matrices.

Figure 26.9: Windows of detection of drugs in various matrices. Time ranges are very broad and are dependent on numerous factors including: drug taken; frequency of use; drug half-life and the individual (Dasgupta 2008).



Pharmacology and metabolism of major classes of drugs measured by POCT

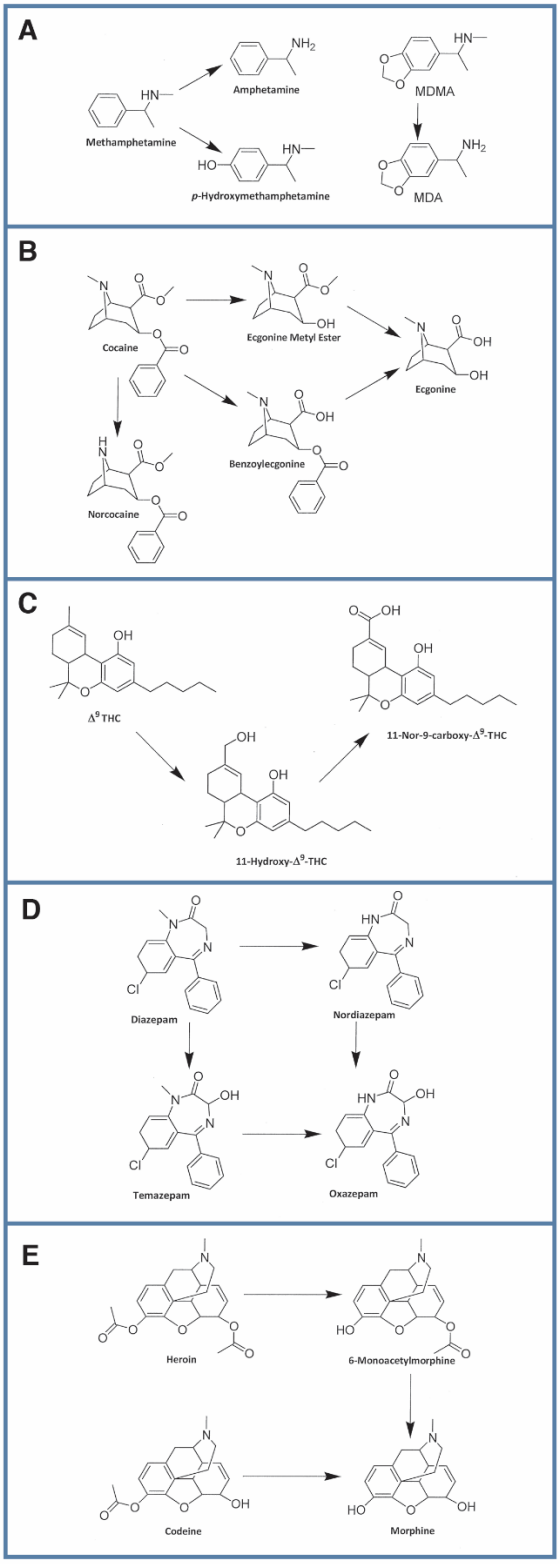
Amphetamines

Amphetamines refers to the group of substances that primarily include methamphetamine, amphetamine, methylenedioxyamphetamine (MDA) and methylenedioxymethamphetamine (MDMA).These low-molecular weight drugs are abused for their central nervous system (CNS) and cardiovascular stimulant activity. These effects are mediated by increasing synaptic concentrations of noradrenalin and dopamine either by stimulating neurotransmitter release or inhibiting uptake or both. The effects are longer lasting than cocaine and may prevent fatigue and suppress appetite. Heavy users of the drug may consume up to 2000 mg per day.

Amphetamine is metabolised by deamination, oxidation and hydroxylation as shown in Figure 26.3. Methamphetamine in humans primarily undergoes N-demethylation to yield amphetamine, the major metabolite of methamphetamine. Methamphetamine may also undergo hydroxylation to give *p*-hydroxymethamphetamine. Under normal conditions approximately 40% of a D-methamphetamine dose is excreted in urine in the first 24 hours and less than 10% is present as amphetamine. MDMA is metabolised to MDA with approximately 70% of the dose excreted as the

parent drug within 3 days. Both MDMA and MDA are hydroxylated to mono and di-hydroxy derivatives prior to conjugation and elimination (Karch 2007).

Figure 26.10: The major metabolic pathways of (A) methamphetamine and MDMA, (B) cocaine, (C) THC, (D) benzodiazepines and (E) opiates.



Cocaine

Cocaine is a naturally occurring alkaloid obtained from the plant *Erythroxylon coca*. Cocaine inhibits the presynaptic reuptake of the neurotransmitters noradrenalin, serotonin and dopamine at synaptic junctions resulting in stimulation of the sympathetic nervous system. This drug is abused for its euphoria, increased alertness and energy, heightened sexual excitement, and self-confidence. The physiological effects of this stimulation include tachycardia, hypertension, vasoconstriction, mydriasis (prolonged dilation of the pupil) and hyperthermia. Cocaine also acts as a local anaesthetic through its ability to block sodium channels in neuronal cells.

In humans the primary route of metabolism of cocaine is through hydrolysis of the ester linkages to give benzoylecgonine (BE) and ecgonine methyl ester (EME). Further metabolism of these metabolites produces ecgonine. Cocaine can also be *N*-demethylated to give norcocaine. It is estimated that up to 90% of cocaine dose is excreted in the urine in 24 hours. Parent, un-metabolised, drug accounts for less than 10% while the amount of BE and EME can each account for approximately 30% to 50% of the dose depending upon urine pH (Karch 2007).

Marijuana

Marijuana refers to all parts of the plant *Cannabis sativa*; the leaf, seed and resin; the primary active constituent being tetrahydrocannabinol (THC). The pharmacological effects of marijuana include sedation, euphoria, hallucinations and temporal distortion. THC binds to the cannabinoid receptors in the brain and in immune tissues such as the spleen, tonsils and thymus. In addition THC possesses activity at benzodiazepine and opioid receptors. THC may act as a direct or indirect dopamine agonist to stimulate the brain's reward circuits (Shaw *et al.* 2001). Over 20 metabolites of THC have been identified in human urine and faeces.

More than 60% of the drug is excreted in faeces while approximately 20% of the drug is excreted in urine. Following a single dose 80-90% of the drug is excreted within 5 days - mostly as the

hydroxylated and carboxylated metabolites (Shaw *et al. 2001)*. However, clearance times may extend to weeks or months with chronic users.

Benzodiazepines

Benzodiazepines are the most commonly prescribed medications encountered in drug screening. Abuse of these drugs usually occurs either through long term use, longer than recommended use, or illicit use. Long-term prescription use typically involves use at low doses while illicit use involves high doses and clear indications of intoxication. The effects of benzodiazepine intoxication are similar to those of alcohol intoxication. Benzodiazepines have central nervous system (CNS) depressant effects and they are used as muscle relaxants, anticonvulsants, sedative-hypnotics and anti-anxiety medications.

Metabolism of benzodiazepines produces numerous metabolites. Metabolism typically involves hydroxylation, demethylation and glucuronidation. Diazepam undergoes N-demethylation to nordiazepam both of which can undergo hydroxylation to yield temazepam and oxazepam, respectively. In urine only small amounts of diazepam or nordiazepam are detected. From a single diazepam dose typically both temazepam and oxazepam and sometimes nordiazepam are observed, and occasionally diazepam. (Karch 2007).

Diazepam, nordiazepam and oxazepam are long acting benzodiazepines and are typically prescribed at high doses. Following chronic use, they can be detected in urine for weeks or months after chronic use. Short acting benzodiazepines such as in urine for only a few days (Karch 2007).

Opiates

Opiates produce their pharmacological effects by binding to opiate receptors in the body. Three types of opiate receptors are recognised with the μ receptor considered to be the most important. Opiates act as μ-receptor agonists and exert a direct effect on brain stem respiratory centres

reducing their responsiveness to carbon dioxide causing respiratory depression. μ receptors are responsible for euphoria, supraspinal analgesia, respiratory depression, reduced gastrointestinal motility and physical tolerance and dependence.

Heroin is very rapidly metabolised by deacetylation to 6-monoacetylmorphine (6-MAM) which is further metabolised to morphine. The presence of 6-MAM in urine is definitive evidence of recent heroin use. Codeine is metabolised by *O*-demethylation to morphine and *N*-demethylation to norcodeine. Codeine concentration in urine is usually highest in the initial phase of elimination but morphine conjugates are the major products found in urine over the 20 to 40 hour period. Morphine is metabolised by conjugation to its glucuronide and by sulfation. It can also undergo *N*-demethylation and *N*-oxide formation. Approximately 90% of a morphine dose is excreted within 72 hours (Shaw *et al.* 2001). The presence of morphine in urine can be attributed to morphine use itself or the metabolism of codeine or heroin to morphine. Therefore, it can be difficult to determine the source of morphine without further information. This can be further complicated, as the consumption of poppy seed can also produce codeine and morphine concentrations in urine above screening cut-offs.

POCT drug testing in different settings

Clinical

In the clinical setting, urine is the preferred biological matrix for testing. Clinical situations where drug POCT can be useful include: emergency medicine; mental health management and identifying substance use disorders; prevention of dangerous medication interactions; identifying/refuting maternal drug use; and monitoring patient compliance (Substance Abuse and Mental Health Services Administration 2012). However, controversy exists regarding the value of drug testing in clinical settings. Reasons include: methods used; targeted analytes; and the level of understanding

of the physician using the data (Hammett-Stabler *et al.* 2002). Additionally, testing is often limited to screening without the benefit of confirmatory testing and tests are commonly optimised for workplace testing where cut-offs are set high enough to be indicative of drug abuse. Therefore, therapeutic concentrations of medications may not be detected. Nevertheless, the rapidity of result production together with the cost of laboratory-centric drug screening has made POCT a valuable option particularly in emergency medicine and mental health settings. Clinicians should be guided on the range of detectable analytes and cut-off concentrations used in drug testing of their patients.

Workplace

Worldwide, workplace drug testing is not legislatively mandated, except in the USA where workplace drug testing is mandated for all government sector workers. Due to the liabilities associated with unsafe workplaces, many private sector corporations particularly those involved in safety-sensitive areas have drug testing policies. These policies are generally directed towards: pre-employment screening; random screening as a workplace deterrent; reasonable suspicion; post incident investigation; and return to duty following detection. The immediacy and timely delivery of results is of concern since workers are often stood down on full pay until results are confirmed by a laboratory. As such, POCT is almost exclusively used in these settings. While urine is the biological matrix commonly selected for testing, increasingly, negotiations between unions and individual corporations are favouring oral fluid as the testing matrix, due to the belief that detection of drugs in oral fluid may be a better indication of possible impairment. The move towards drug screening in oral fluid has been facilitated by increasing numbers of laboratories gaining accreditation for the provision of confirmation services in oral fluid. The menu of target analytes is directed towards the detection of illicit substances and pharmaceutical drugs such as benzodiazepines opiates and opioids. Due to the medico-legal implications and potential impact of non-negative results, confirmatory testing should follow.

Judicial

The criminal justice setting encompasses drug courts, probation and parole and correctional facilities. Carried out under supervision of the courts or parole boards, sample collection and testing is scheduled and directed by the relevant judicial authority. Financial resources for testing are limited because funding is provided by the federal, state or local governments. Depending on the country or state, the drug testing of individuals in the criminal justice setting is often covered by specific legislation. Cut-offs used are often aligned with recommended workplace cut-offs in the respective country. Due to time and budgetary constraints there is an increasing shift towards POCT for drugs of abuse in these settings.

Urine is the biological matrix of choice; however, there is movement towards the testing of oral fluid particularly in the community setting where corrections officers may randomly turn up at an offender's residential address for testing. Depending on the severity of the offence, the rigor of testing may vary; for example with lower level offenders, judicial monitoring is focussed on rehabilitation of the individual, non-negative results may not be confirmed and are treated as positives. In monitoring high risk offenders, where judicial intervention may be required, non-negative results are confirmed and certificates of analysis are provided to the requesting organisation by the issuing laboratory.

In judicial settings, the range of illicit substances abused reflects patterns of abuse in the general population. However, in the custodial environment where access to illicit substances is limited, abuse of pharmaceutical substances is equally if not more prevalent. Depending on the class of drug, the detection of abused of pharmaceutical substances using POCT can be limited due to available of a test for that particular pharmaceutical.

Roadside

While roadside alcohol breath testing has, undeniably, reduced the number of alcohol associated fatalities, the same cannot be said about driving while under the influence of drugs. Increasingly, governments are establishing roadside drug testing programs and these programs are yielding surprisingly high drug detection rates. For example, the New South Wales Police force, in Australia, started testing for cannabis, methamphetamine and ecstasy by the roadside in 2007 (Centre for Road Safety 2015). During 2013, roadside drug tests detected the presence of illicit drugs in oral fluid in about one in 40 light vehicle drivers. Since 2013 roadside drug testing has become more targeted and, during 2014, as many as one in 10 drivers were detected with the presence of one of the three targeted drugs. Comparatively, only one in every 236 drivers randomly tested for alcohol returned a positive reading in the period from 2010 to 2013 (Centre for Road Safety 2015).

Screening is performed by the roadside generally utilising POCT devices and specimens are sent to the laboratory for confirmatory analysis when necessary. While numerous matrices have been investigated, oral fluid is the preferred matrix in this setting as it offers the advantages of ready availability; less invasive collection; and results are more likely to be reflective of impairment.

Quality practices

Good quality practices are necessary throughout the entire drug testing process from the point of collection through to the issuing of results. Manufacturers of POCT devices that follow good manufacturing practices typically employ lot-based quality controls (QC) throughout each stage of the manufacturing process from test strip production to the device assembly stage. Nevertheless, lot-to-lot variations in performance can be seen from time-to-time at the end-user stage. In addition, poor storage or use of devices in temperature extremes; and new or poorly trained users can also cause variations in performance. End-users should be aware of these factors and at a

minimum use QC material to regularly monitor the ongoing performance of POCT devices and testing programs. This is one of the many quality management practices necessary to maintain an effective drug testing program. There is often resistance to QC procedures due to the additional cost. If, however, the potential costs and impacts of failed testing are considered, the additional cost of QC is only a minor concern. Furthermore, standards and guidelines mandate the use of quality management processes in testing; and participation in nationally or internationally recognised proficiency testing (PT) programs. Participation in PT programs provides independent assessment of an end-users performance and comparison of performance with other end-users. PT programs are readily available for urine as are QC materials. On the other hand, PT programs and QC materials to support oral fluid testing are difficult to find and the range of target drugs offered may be limited. The end-user's QA processes should allow for evaluation of QC and PT program results and detail acceptance criteria and the course of action to be taken should performance fail to meet the acceptance criteria.

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Appendix C:

Stakeholder perspectives on point-of-care testing

Wilton Braund, **Brooke Spaeth**, Malcolm Auld, Lauren Foohey, Connie Mardis

Summary

There are a number of key stakeholders involved in the day-to-day operation of point-of-care testing (POCT) in primary care and hospital settings; depending on the size/scope of the POCT program, stakeholders may include: the doctor actively managing the patient based on the POCT result, the POCT Coordinator or Regional Supervisor responsible for the organisation and management of POCT services at the network/regional level; the POCT operator who performs the POC test in situ, the patient, who is the consumer of the POCT service, and the industry partner who provided the POCT device and consumables for testing. This chapter provides a brief personal perspective from a representative of each of these stakeholders.

A clinical perspective (Dr Wilton Braund)

I write as a physician/internal medicine specialist who has practiced in endocrinology, diabetes and as a general internal medicine specialist in acute hospital practice and office practice for 35 years. The last 15 years have been with benefit of point- of-care testing (POCT).

What are the day-to-day experiences that make me want to have POCT available in my rooms? Let me give a scenario:

A 32 years old woman who has had Type 1 diabetes since her early teen years arrives, saying: "'I don't think you will be pleased with my HbA1c: I haven't really been taking care of myself well enough." Naturally, she has not remembered to attend the laboratory a few days before the appointment to use the HbA1c request form with which I supplied her at the last appointment.

Why have I used the word 'naturally'? It is very common and very natural for a patient to forget to have the blood test in advance. It requires two episodes of leave from work: one to have the test and one to visit my office to discuss the result. People with diabetes have increased 'sick' leave from work – not because they are actually ill, but because they have many appointments to go to. Attending a laboratory can come a long way down the agenda for a busy or a financially-straitened person. Omitting to have laboratory tests can also be a feature of being fed up with the whole nuisance and rigmarole of having diabetes.

After that opening sentence of her conversation, "'I don't think you will be pleased with my HbA1c; I haven't really been taking care of myself well enough", it is all too easy to devote the remaining minutes of my consultation to ways in which her diabetes control might be made tighter. But what if she has had a POC test for HbA1c? A high result (eg 9.8%) might confirm the intended thrust of the consultation; but a tight-control result (eg 6.8%) would mean the consultation can be completely redirected. It might create time and opportunity to re-examine her for any emerging complications. Or the consultation might be directed towards why she made such a remark; why her self-esteem is low; whether she has depression. This 'change of frame' effect of a POCT results has been a common scenario in my diabetes practice.

It is these aspects of POCT that are so important. The diagnosis or assessment of the patient's current need is so rapidly clarified or altered that maximum value can be extracted from the consultation – a consultation that has already been paid for. And, in addition, the patient makes savings in time, effort and absence from work.

Point-of-care testing is a 'disruptive' technology. But does it cause a disruption in the doctor's offices? It does indeed require staff time for the tests to be performed – most POC tests take 5 to 10 minutes. Most patients, however, have a few minutes to spare in the waiting room and prefer this small delay to the idea of a separate trip to the laboratory.

What is the downside? Firstly POCT is expensive. Laboratories need have no fear of a tsunami of POCT that will destroy their revenues. Secondly, a clinician needs to identify a small group of POC tests that suit his or her practice. In a remote area, this might include tests that are usually the province of emergency departments, such as troponin. To have an unlimited number of POCT devices is expensive and exhausting. Finally, results are only clinically useful if they are analytically reliable. Someone in the practice must perform QC and/or PT testing. Indeed, if POCT is to be reimbursed by anyone other than the patient, QC and PT are essential steps to obtain accreditation and, in turn, should the reimbursement come from insurers or from government?

Has POCT's moment arrived for general and specialized specialised clinicians? In those countries where these tests are reimbursed, there has been rapid adoption of POCT. This is not only by general practitioners, but also by domiciliary nursing services and by aged care centres.

Further evidence of the value of POCT lies in the predictive algorithms that are now in use in haematology and cardiology (with for example D-dimer and troponin). Finally, the adaptation of molecular testing to POCT platforms means that infectious disease can now be diagnosed accurately at the point of care, while antibiotic stewardship can now be supported by POCT in sexual health clinics. Because there is a strong chance that the patient will not return for the results of their tests, immediate results, within around one hour, assume great importance in the decision whether to treat with antibiotic. If the latter decision is made empirically, without benefit of POCT, the majority of those treated will not actually need antibiotic.

A POCT Coordinator perspective (Brooke Spaeth and Malcolm Auld)

Brooke Spaeth is POCT Coordinator for the Northern Territory POCT Program operating in a very challenging environment in remote Australia (see Chapter 28). Malcolm Auld supports the program as on-ground Regional POCT Supervisor, based in Alice Springs.

What I enjoy as a POCT Coordinator working with remotely located health services and staff is knowing that I am assisting with providing a service to patients with both acute and chronic illnesses that was not accessible previously to these patients. The contact I have as a POCT Coordinator with the remote health centre staff is something I really enjoy and it makes me want to ensure their POCT work is as streamlined and easy as possible, as I know that the staff are already dealing with a huge workload of usually very sick patients with multiple comorbidities. As part of my role I have developed a deep respect for the remote staff who work in some of the most isolated areas in Australia where the appropriate resources to assist patient care are often not available or difficult to access.

As a POC Coordinator for 7 years now, some of the most rewarding comments I have received from remote staff/operators have been along the following lines:

From remote nurse 1: *'Thank you for helping us to get our POCT device and providing all of the support, we were just now able to perform our first troponin test on a patient with chest pain and rule out a heart attack and the patient was able to remain in community. Normally we would have to evacuate any patients presenting with chest pain'*.

From a remote doctor 1: '*The ability to get the HbA1c test result immediately on the DCA device allows me to fully engage the patient in discussing how best to treat their diabetes and help them make healthier lifestyle choices. The golden 6 minutes to the result popping up on the screen is the best opportunity to fully grasp the patient's attention and discuss their diabetes care'.*

From a remote doctor 2: *'Before we were able to perform electrolyte testing on-site we had a patient with chronically low potassium (due to the medication he was taking) who had to be evacuated by air every time he presented unwell and needed a laboratory potassium test as we could not confirm his status on-site. This evacuation cost approximately $20,000 each time and was a 2,000 km return journey for the patient. Now we can perform the test and get his potassium result in 2 minutes'.*

The most satisfying component of being a regional POC Supervisor in the Northern Territory POCT Program is being able to work cooperatively and collaboratively with health service managers, clinicians, remote area nurses, administrators, technicians and other health professional across multiple agencies to ensure the POCT program runs successfully. This has included many conversations in-person, by phone and email around training sessions, dissemination of reagents and consumables and establishing reliable systems/processes; and finally seeing clinicians at the point of health care delivery being able to use and manage the POCT device effectively as an adjunct in providing clinical care in the most cost-efficient manner for the health of patients we serve.

A POCT operator perspective (Justin Busbridge)

For over two decades I have worked in remote healthcare settings in both Scotland (Outer Hebrides) and Australia (Northern Territory) and have seen how POCT has completely transformed the patient and clinician experience.

Many blood pathology tests require rapid analysis and need to be performed frequently, but the logistics of getting these samples to the laboratory is often difficult. In such cases the only option is to move the patient closer to the testing, which is facilitated by POCT. A good example is the INR test for monitoring warfarin therapy.

Before the introduction of POCT to our remote general practice clinic in the Outer Hebrides, Scotland, we could only test those patients with relatively stable INR results. The venous sample was taken by the nurse and then transported by road to the nearest laboratory only once or twice per week along with the groceries and parcels going to town. Test results took at least another two days before being reported to the treating GP (making the total time between blood collection and return of results approximately a week. Such a time-lag was too long for patients requiring frequent monitoring (twice per week); so those patients would have to travel to the main hospital, a return journey that could be up to 200 km. There the patient would attend a warfarin clinic where venous blood samples were tested immediately in the laboratory and drug doses titrated on the spot. However the journey on slow rural roads might take four hours of a patient's time, if the patient had their own transport. This was impractical for many patients and to initiate warfarin we would have to admit patients to hospital, perhaps for many weeks at a time until stable INR results were achieved. This time commitment meant some patients refused to accept warfarin medication, and by doing so increased their risk of a heart attack or stroke.

In remote Australia, pathology laboratory handling requirements made our clinic samples unreliable. For example sample tubes needed to be completely filled, then centrifuged to separate the serum before being frozen and packed in insulated boxes ready for transport by the local bus to the nearest laboratory, a process which involved many hours and hundreds of kilometres in transit. During this summer, these processes occurred in temperatures reaching 48 degrees Celsius. Attempting to transport Indigenous patients to a laboratory was not possible due to cultural and economic barriers, as traditional Indigenous people often refuse to go to urban hospitals and prefer no medication at all rather than leave their desert communities.

POCT has dramatically changed the human and logistic faces of those Scottish and Australian experiences. In remote Scotland, what was a long drive or extended hospital stay has become an

approximately ten minute encounter at the local GP clinic. In remote Australia I am now able to get an almost instant INR result based on a simple finger-prick POC test. After relaying the INR result to the doctor I can then immediately adjust the warfarin dose as required. In very remote Australia, POCT has meant that what was not possible at all is becoming increasingly common place and the use of warfarin in cardiac patients is now a viable option.

Apart from INR, POCT is providing a whole raft of new blood tests that we (nurses) can use to manage both chronic diseases and critically-ill patients. (As a remote area nurse working in these areas there is only so much I can diagnose with simple assessment tools such as blood pressure, oxygen saturation, temperature, perhaps ECGs as well as my own clinical skills). POCT is now available in remote Australia for tests like troponin, blood gases, white cell and differential count, electrolytes and renal function tests and HbA1c have been invaluable. Tests like cardiac markers and blood gases can assist in avoiding an unnecessary air evacuation (a risky undertaking, let alone extremely expensive), as well as buying valuable time in an acute emergency, and where I have seen POCT save lives. Creatinine and potassium can help us evaluate the deterioration of an Indigenous renal patient who has stayed overlong in the remote homeland and missed their dialysis session. A POC HbA1c result is available from a finger prick of blood in the consultation room, giving it immediate impact and relevance, and enabling me to negotiate future management plans with the patient. The POC HbA1c test is another tool for the clinician and has been invaluable in facilitating real improvements in diabetes control.

For a nurse or doctor working in remote desert Australia it is easy to see how POC testing is valuable. The isolation of remote clinics and harsh climate make laboratory samples unreliable, and the time lag in receiving results devalues their relevance. In contrast I can use POCT results immediately to help manage both emergency treatments and chronic diseases, plus it is a mode of testing that overcomes the cultural barriers faced by Indigenous people accessing urban-based services.

A patient's perspective (patient with diabetes)

From a personal perspective, I was diagnosed with diabetes some 25 years ago now as a result of follow-up for a high cholesterol result that was performed opportunistically on a POCT device; this is somewhat ironic as POCT was very much in its infancy in our country at that time. The diagnosis of diabetes was made following an oral glucose tolerance test (OGTT), an experience I found most uncomfortable and 'unpalatable'. This was my first encounter with laboratory pathology testing and I'd like to make several points regarding this form of testing. The laboratory-based person may often view the patient as 'just another blood sample for analysis', with their main concern being eg 'has the request form been filled in appropriately and is the sample suitable for analysis? I'd ask the lab person to stop and think for a moment that there is indeed a real person, with feelings and worries, at the 'front end' of that sample.

I am undoubtedly one of the world's worst patients. The actual act of venipuncture every 3 months for my management review holds no fears, but (like I'm sure is the case for many others with diabetes) I endure considerable stress and worry in the days leading up to the blood taking and then in the days after the event before I visit my specialist to get my results. Will my HbA1c level be good or has it shifted upwards, as it inevitably seems to do? Are my kidneys OK? Will I have protein in my urine this time? Has something changed for the worse in my biochemical profile? My biggest long-term concern about living with diabetes is the perhaps inevitable onset of complications – especially kidney disease and retinopathy. I've always thought that life without sight would be the worst possible thing to experience and so the regular visit to the eye specialist is just as traumatic as the three-monthly blood-taking episode.

After progressing through oral medication and now onto insulin, fingerprick blood glucose testing has become part of my daily routine. Yes, it is a chore and an imposition in the morning and at meal time, but these POCT results gives me instant awareness of my diabetes status, with a sense of

immediate gratification if the results indicate my glucose levels are within 'good' limits. POCT provides me with strong messages of positive reinforcement that my diet and exercise regimes are working well and makes me want to be compliant with my medication taking because I know my POCT results will be good if I do the right thing. I've particularly noted when I stick most rigidly to my exercise regime (which includes the gym, tennis and cycling), then my HbA1c results are always very good. Now my doctor has access to a POCT device for HbA1c too, and it is just so simple and convenient to have the test done while you are at your appointment.

So living with diabetes is not all doom and gloom. You can definitely live comfortably and happily with diabetes, as I have done for many years and POCT is a critical factor in daily life for me; but I do acknowledge that the diabetes patient does have a never-ending uphill battle to keep ahead of the disease (and I'll need my POCT and medications for the rest of my life)!

An industry perspective (Lauren Foohey and Connie Madris)

With POCT at the forefront of healthcare delivery, our industry acknowledges that POC solutions can immediately impact the lives of patients who may be suffering from a chronic disease or a life-threatening critical illness. We believe that, whether a patient is dealing with the day-to-day challenges of a chronic disease or facing a life-threatening situation, every moment counts. Getting test results quickly and accurately – in the doctor's office, at the hospital bedside, or in the emergency department – is vital; because less time spent on tests means more time focused on patient care. For millions of chronically or critically ill patients around the world who depend on the right results at the right time, POCT matters.

With the ultimate goal of improving patient care, adoption of POCT continues to grow at a high rate and industry needs to be at the forefront of diagnostic innovation and opportunity. Emerging markets need to focus on cost-effectiveness and scalability to meet high patient volumes.

Efficiently managing all aspects of a POCT program requires close collaboration among health care institutions, device manufacturers, and information technology vendors. Although the present growth of POCT is strong, further adoption of POCT depends on how well the industry manages to overcome the challenges POCT Coordinators face in managing their programs.

Appendix D:

Simply* better access to pathology diagnostics *is not so simple*

Brooke Spaeth BMedSc (Hons), POC Coordinator – Northern Territory Point-of-Care Testing Program, Flinders University International Centre for Point-of-Care Testing

In rural and remote health, we know that one of the most difficult obstacles to health equity is access to services that may only be available in the larger urban or metropolitan centres, such as cancer treatment and mental health specialists. However, the service that is not widely mentioned is pathology, which can provide clinical tools for the diagnosis and management of a range of acute, chronic and infectious diseases. Health professionals working in rural and remote health will be well aware of the long turn-around time for pathology results for their clients, some waiting more than a week for the results to become available to be acted upon, if the patient returns to discuss their results.

Surprisingly, in the remote Northern Territory (NT) many pathology samples are sent to the major hospitals in Darwin and Alice Springs (a process that already takes a few days in many instances) and some of these samples are then sent on to Perth, taking further time before they are analysed and the results become available. Unfortunately, this means that a higher number of pathology reports are now being returned with comments such as “The sample was received and processed more than three days after sample collection, some time delay effects have been detected, results may not be reliable”. This means the health professional in the remote location needs to re-contact the patient, take the same blood sample again, prepare and package it, and send it on the same journey, hoping that this time it will arrive within a suitable timeframe for analysis.

There is a simple* solution to this issue, which many health professionals will already be aware of and which already operates in many rural and remote areas across Australia, albeit not consistently. This solution is point-of-care pathology testing (POCT) which offers a way for non-laboratory trained staff to employ a simple-to-use device to obtain immediate pathology results for a variety of acute, chronic and infectious disease markers.

At the 14th National Rural Health Conference in Cairns, I delivered a presentation on the Northern Territory POCT Program, which has recently been rolled out to all remote health services across the Territory. This program now ensures that all remote Territorians have access to immediate pathology results, primarily for acute care markers, such as Troponin I for acute coronary syndrome, electrolytes, blood gases and lactate. The POCT device used in the NT Program also tests for a number of chronic disease markers such as creatinine and urea for kidney disease and international normalised ratio (INR) for patients on warfarin anticoagulation therapy. The presentation, titled 'Immediate pathology results now available for all remote Northern Territorians', also discussed the significant benefits POCT had on patient safety and substantial cost savings to the Government through prevented unnecessary medical evacuations.

After the presentation, I was approached by several conference delegates who asked "Why has this program not yet been rolled out to all rural and remote locations more widely?". One of the 'Priority Recommendations' that came from the conference around digital health also suggested that partnerships be made to facilitate access to consumer-held technologies such as POCT equipment.

To at least partly address these comments I will come back to the word simple* I highlighted earlier. While the technology is simple to use and has obvious benefits, with the most important being increased patient safety, there are many implementation and management issues to consider including:

1. What are the priority diseases in the local area for which a POCT test is required?
2. Which POCT device should you choose and has it been evaluated for use in the intended setting?
3. Operator training and quality testing must be implemented as per the recently released guidelines on POCT (http://www.health.gov.au/internet/main/publishing.nsf/Content/health-npaac-poctguid) to ensure the device is used correctly and the results are reliable.
4. The cost of implementing a POCT program as well as the ongoing costs of consumables as many POC tests do not attract a Medicare rebate.

Cost is probably the most significant obstacle to implementing POCT. A Medicare rebate for POC tests conducted in rural or remote areas is required to allow POCT technology to be affordable and thus accessible for patients living in for these geographically isolated areas. However, the Medicare Rebate should be contingent on considerations 1, 2 and 3 having been addressed.

More information: http://www.flinders.edu.au/medicine/sites/point-of-care/

The findings of the 'Immediate pathology results now available for all remote Northern Territorians' study will be published in the conference proceeding for the 14th National Rural Health Conference.

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