The Development And Application Of Point-Of-Care Pathology Testing (POCT) Models For The Early Detection And Management Of Diabetes And Renal Disease In Indigenous Medical Services

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TABLE OF CONTENTS

INDEX OF TABLES

PAGE NO.

INDEX OF FIGURES

ABSTRACT

The peer-reviewed publications presented in this thesis describe my program of research conducted over the past 10 years in the field of point-of-care pathology testing (POCT) for the early detection and management of diabetes and renal disease, principally in the Australian rural and remote Indigenous health care setting. POCT is defined as pathology testing performed on-site in a clinical setting at the time of patient consultation, with the test result being immediately available for the treating medical practitioner. When this research was commenced, POCT as a medico-scientific discipline was in its infancy in Australia. Its application in the Australian Indigenous primary care setting had never before been attempted, despite numerous cultural and epidemiological factors indicating this setting represented a suitable niche.

The key research question examined in this thesis was: Could POCT models that were analytically sound and clinically and culturally effective be established in Australian Indigenous medical services for the prevention and management of diabetes and renal disease? The systematic approach to answer this overarching research question included the scientific validation of the analytical performance of suitable point-of-care (POC) devices, the development of a culturally appropriate education and training program for Aboriginal Health Workers (and nurses) as POCT operators, the implementation of a quality management framework for maintaining surveillance of the analytical quality of POCT results, and an assessment of qualitative and quantitative research outcomes to determine the clinical and cultural effectiveness of POCT.

POCT models for the prevention and management of diabetes and renal disease were conceived, initiated, developed and implemented in different Indigenous settings. These models were: The Umoona Kidney Project for renal disease prevention and management, the QAAMS Program for diabetes management and the Point-of-Care Testing in Aboriginal Hands Program for chronic disease prevention and management. The principal POCT device used was the DCA 2000 (Bayer

Diagnostics, Tarrytown, USA) which measured haemoglobin A1c and urine albumin:creatinine ratio, established indicators of glycaemic control and early renal disease respectively.

Collectively, the results presented in this thesis represent the first and most comprehensive research assessment of the effectiveness of POCT ever conducted in Australia, and make a significant contribution to the previous void of knowledge in the discipline of POCT in this country. Evidence is presented for the first time to confirm that (i) POCT can be conducted by trained operators from a non-laboratory background to a level of analytical quality equivalent to that of a laboratory and which meets internationally-recognised analytical goals, (ii) POCT is a culturally effective mode of health service delivery, gaining wide acceptance by Indigenous POCT operators, Indigenous patients with chronic disease and clinical staff, and (iii) POCT is clinically effective, being useful for chronic disease risk assessment and contributing to improved management of Indigenous patients with diabetes and renal disease. These models have immeasurable potential to be adapted to Indigenous communities and/or rural and remote communities globally.

Finally, the adaptability of the Indigenous POCT models was confirmed in a non-Indigenous rural community setting and is currently being assessed in a Government-funded POCT Trial involving 30 general practices in Australia.

STATEMENT OF ORIGINALITY

This thesis contains material that has been published in peer-reviewed journals and books. I have been the first or principal author of these publications that form the main body of this thesis.

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis being made available to the University Library.

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15 May 2007

Mark DS Shephard Date

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My research work would not have been possible without the continuing support of the following staff from the Australian Government's Department of Health and Ageing and I thank them all sincerely for their assistance and commitment to my work over many years: Marion Dunlop, Jan Streatfield, Jacquie Millard, Wendy Akers, John Bacon, Jonathan Wraith, Pamela McKittrick and Fifine Cahill.

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grassroots' has been pivotal to success of my POCT models and a constant source of inspiration to me.

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SECTION 1: BACKGROUND AND LITERATURE REVIEW

CHAPTER 1: OVERVIEW OF PROGRAM OF RESEARCH

Background

The peer-reviewed publications presented in this thesis describe the program of research that I have conducted over the past 10 years in the field of point-of-care pathology testing (POCT) for the early detection and management of diabetes and renal disease.

POCT is defined in this thesis (see Chapter 2) as:

> 'pathology testing which is performed on behalf of the treating medical practitioner by a trained operator in an on-site clinical setting at the time of patient consultation, allowing the test result of desired analytical quality to be generated and to be used to make an immediate informed decision that contributes to an improved health outcome for the patient.'

My research studies focus primarily on POCT models I have conceived, initiated, developed, implemented and managed within Indigenous medical services across urban, rural and remote Australia. They also describe how these models have been adapted to non-Indigenous community settings, including a rural community hospital and general practice.

My personal contribution to each of these research studies has included:

- undertaking scientific validation of the point-of-care (POC) devices used in these studies,
- being the Program Manager for each of the Indigenous POCT models described,
- being directly responsible for the development and delivery of the education, training and quality management framework for all the POCT models,
- assessing the analytical quality of POCT conducted by non-laboratory POCT operators from participating services against national and international benchmarks,

- analysing and interpreting qualitative and quantitative outcome measures from POCT conducted on patients with diabetes and renal disease,
- writing and submitting funding applications to conduct these studies (with funding support principally sourced from the Australian Government's Pathology Section within the Department of Health and Ageing), and,
- preparing manuscripts for both peer-reviewed publications and for Australian Government reports (required by the grants secured).

The work described in this thesis was initially conceived when my interests within and outside my professional career intersected during the mid 1990s.

From 1977 to the mid 1990s, I worked as a medical scientist in the routine clinical biochemistry laboratory at Flinders Medical Centre. My main areas of scientific work were the development and evaluation of diagnostic methods for pathology tests used for the management of diabetes, renal and cardiovascular disease, and the fields of quality assurance and analytical performance standards (or analytical goals) for pathology tests. I also regularly conducted POC Haemoglobin A1c (HbA1c) pathology testing using the DCA 2000 device (Bayer Diagnostics, Tarrytown, NY, USA) on patients attending the weekly diabetes clinic at Flinders Medical Centre.

Outside of health, I have always held a particular passion for and interest in Australian deserts and Indigenous* culture.

*The Australian Indigenous population comprises both Aboriginal and Torres Strait Islander people. Aboriginal people originally arrived in Australia some 50,000 years ago from Asia and inhabited the bulk of the Australian mainland, including every Australian desert. People from the Torres Strait region in far north Queensland, are of Melanesian origin and comprise approximately 11% of Australia's total Indigenous population (1, 2). Throughout this thesis the words Indigenous and Aboriginal will be used interchangeably.

I travelled extensively across many Aboriginal desert communities during a 10-year period from 1985 to 1995 and authored books on the Simpson Desert and Great Victoria Desert (3, 4). As a result of my travels, I observed first-hand the appalling level of poverty and the significant burden of diabetes

and renal disease (hereafter together referred to collectively as chronic disease) in rural and remote Indigenous Australia. Delivery of mainstream health (and laboratory) services to these communities was very poor, the turnaround of laboratory test results was slow, while of most concern was the extreme difficulty in getting chronic disease patients to return for a follow-up visit to enable their doctor to act on laboratory results and mediate treatment.

Having used POC technology in the diabetes clinic at Flinders Medical Centre, I believed POCT may be useful in the rural and remote Indigenous medical service setting.

In Australia, Indigenous medical services are either managed or controlled by the local Indigenous people with funding provided by federal or state governments, or they are controlled and funded by state or territory governments. The former category, known as Aboriginal Community Controlled Health Services (ACCHS), now represents the principal vehicle for delivering primary healthcare to Aboriginal and Torres Strait Islander people (5, 6). There are more than 125 ACCHS throughout Australia, over 90% of which are located in rural and remote areas. The National Aboriginal Community Controlled Health Organisation (NACCHO) represents the interests and affairs of ACCHS nationally (7). ACCHS vary considerably in size, infrastructure, resources and the number of Indigenous people they serve. Some may be located many hundreds of kilometres from the nearest hospital or laboratory service. Staffing levels vary widely, but most comprise as a minimum a doctor, a clinic nurse and one or more Aboriginal Health Workers (Aboriginal people living and working in the community and trained in basic primary health care). Aboriginal Health Workers now play a pivotal role in the delivery of health care in Indigenous communities and act as a crucial communication bridge between patients and non-Aboriginal medical and nursing staff (8).

Intuitively, I believed POCT could potentially deliver the following advantages in the Indigenous medical service setting:

- the rapid testing process would be convenient and accessible for the patient,
- the immediacy of the pathology test result could facilitate on-site changes in treatment and negate the need for a follow-up visit by the patient,
- the sense of community control and ownership would be fostered by the testing process being conducted *in situ*, and,
- the Aboriginal Health Worker could have a pivotal role as a POCT operator, provide the crucial cultural link between the POC device and the patient, and facilitate acceptance of POCT in the Indigenous community setting.

Aim and Objectives of Research Program

The aim and objectives of this research program are summarised in Table 1.1. In attempting to introduce POCT in the Indigenous health setting, my research aim was:

- To develop POCT models for the early detection and management of chronic disease which were analytically sound in Indigenous hands and culturally and clinically effective in the Indigenous medical service setting.

My overarching research objectives were:

- To scientifically validate the analytical performance of POCT devices to be used in Indigenous medical services.

  Implicit in the use of POCT outside the laboratory would be the need to critically assess analytical performance and to only use devices that met currently acceptable analytical goals. My laboratory background would provide me with this skill set.

- To develop a culturally appropriate education and training framework for teaching Aboriginal Health Workers (and other allied health professionals) to be competent POCT operators in their community setting.

I believed the ability to conduct POCT may provide a sense of empowerment for Aboriginal Health Workers and raise their self-esteem in the community context, and that this would prove an important cultural benefit of POCT. My understanding of Indigenous culture from the decade-long field trips undertaken across desert Aboriginal communities would also provide me with an ability to develop education resources and training methods that would be culturally appropriate.

- To develop a quality management framework for maintaining surveillance of the analytical quality of results generated by the POCT devices used in the Indigenous medical service setting.

  In using POC devices outside the laboratory, it would be critical that POC pathology results were of equivalent standard to those of the laboratory thereby ensuring there was no diminution in the quality of patient care. My laboratory science background would also enable me to adapt and modify laboratory principles for internal quality control and external quality assurance testing to design a culturally appropriate quality management framework.

- To gather evidence from both qualitative and quantitative research outcome measures to assess the cultural and clinical effectiveness of POCT as a mode of health service delivery for Indigenous patients with chronic disease.

- To determine whether the key elements of the Indigenous POCT models (education, training and quality management) were adaptable and transferable to other non-Indigenous primary health care settings (particularly in rural and remote Australia).

At the time I commenced this pioneering work in 1997, POCT as a medico-scientific discipline was very much in its infancy in Australia and its utilisation was mainly confined to ward or clinic testing within the hospital environment supported by the associated laboratory. As evidenced by the results of the literature review undertaken in Chapter 2, POCT had never before been applied or evaluated

in a research sense within the Indigenous primary health care setting. There was no evidence base for the analytical rigour and quality, cultural and clinical effectiveness, or adaptability and sustainability of POCT outside the laboratory in this setting.

Table 1.1. Aim and objectives of this program of research.

AIM	To develop POCT models for the early detection and management of chronic disease which were analytically sound in Indigenous hands and culturally and clinically effective in the Indigenous medical service setting.
OBJECTIVES	To scientifically validate the analytical performance of POCT devices to be used in Indigenous medical services.
	To develop a culturally appropriate education and training framework for teaching Aboriginal Health Workers (and other allied health professionals) to be competent POCT operators in their community setting.
	To develop a quality management framework for maintaining surveillance of the analytical quality of results generated by the POCT devices used in Indigenous medical services.
	To gather evidence from both qualitative and quantitative research outcome measures to assess the cultural and clinically effectiveness of POCT as a mode of health service delivery for Indigenous patients with chronic disease.
	To determine whether the key elements of the Indigenous POCT models (education, training and quality management) were adaptable and transferable to other non-Indigenous primary health care settings (particularly in rural and remote Australia).

Summary of POCT Models Developed for this Program of Research

The remainder of this chapter describes the chronological evolution of the series of POCT models which I developed and managed over the past 10 years. It also describes the linkage between the models and provides the logic behind the progression of the research program. The timeframe, chronic disease focus, POC tests conducted and health care settings in which these POCT models were undertaken are summarised in Table 1.2.

Table 1.2. POCT models developed during this program of research.

Model	Timeframe	Chronic Disease	Focus	POC Tests	Health Setting
Umoona Kidney Project	1997-2000	Renal	Prevention & Management	UACR	Indigenous
Quality Assurance for Aboriginal & Torres Strait Islander Medical Services (QAAMS)	1999-present	Diabetes	Management	HbA1c and UACR	Indigenous
POCT in Aboriginal Hands	2001-2005	Chronic Disease	Prevention & Management	HbA1c, UACR and lipids	Indigenous
Diabetes Management Along the Mallee Track	2002-present	Diabetes	Prevention & Management	HbA1c, UACR and lipids	Non-Indigenous
POCT in General Practice Trial	2005-2007	Diabetes, Renal, Cardiovascular (and Coagulation)	Management	HbA1c, UACR, lipids and INR	Non-Indigenous

* HbA1c = haemoglobin A1c, UACR = urine albumin:creatinine ratio, INR = international normalised ratio

The Umoona Kidney Project

The first opportunity to use POCT in the Indigenous medical service setting was the Umoona Kidney Project, a program for the early detection and management of renal disease that I conceived, initiated, developed, implemented and managed at the request of the inaugural Director of the Umoona Tjutagku Aboriginal Health Service (Ms Waluwe Simpson-Lyttle). The Umoona Tjutagku Health Service is located at Coober Pedy in South Australia's far north, 850 kilometres from Adelaide. Ms Simpson-Lyttle, along with Dr Lindsay Barratt (then Director of the Renal Unit at Flinders Medical Centre) and myself, had formerly worked together as foundation members of the inaugural Aboriginal Health Initiatives Working Party established at Flinders Medical Centre in 1996. Ms Simpson-Lyttle was aware of the growing concern among the 400-strong Umoona community about the number of community elders who were being forced to leave the community to undergo dialysis treatment for end-stage renal disease (ESRD) and therefore invited me to work with the community to address this concern. As the centrepiece of the Umoona Kidney Project, POCT for urine albumin:creatinine ratio (ACR) on the Bayer DCA 2000 device was conducted for the first time in Australia to assess community risk of renal disease and manage patients clinically assessed as being at the highest risk of renal disease.

Prior to its introduction into field use, I undertook the first scientific validation of POC urine ACR measurement on the Bayer DCA 2000 device in Australia which showed that this POC test was analytically sound and suitable for use in a non-laboratory setting. The results of this first Australian evaluation were published in an international peer-reviewed journal (9).

As a key element of this POCT model, I taught Umoona's Aboriginal Health Worker team how to conduct POCT on patients and how to undertake internal quality control testing, with a view to the long-term sustainable use of the device in the community setting. This was the first time in Australia that Aboriginal Health Workers had been educated and trained as POCT operators.

Risk assessment was carried out not only on adults in the Umoona community but also on their children, through a co-operative partnership I brokered between the Renal Units at Flinders Medical Centre and the Womens and Childrens Hospital in Adelaide. Results of the adult risk assessment program were published in two peer-reviewed journals, one national and one international (10, 11). These results represented the first accurate assessment of renal disease risk in a South Australian Aboriginal community. The papers also reported for the first time that, with appropriate education, training and support, Aboriginal Health Workers could conduct quality control testing for POC urine ACR testing to an acceptable analytical standard.

POCT for urine ACR was also used for the first time in Australia for the management of adult patients identified at greatest risk for renal disease. Through a clinical management protocol developed in consultation with the Flinders' renal specialist team, the renal function of a group of 35 high risk patients was monitored across two years. During this time there was a stabilisation of renal function (as assessed by POC urine ACR measurement) and an improvement in blood pressure among the patient group. This key research finding was published in an international peer-reviewed journal (12) and as part of a peer-reviewed chapter I was invited to write (13) in the book *Point of Care Testing*, which is now globally regarded as the definitive text book on the subject of point-of-care testing (14).

The use of POCT was well accepted by the Umoona community. POCT became a focal point for raising community awareness about renal disease and provided the impetus to develop other community health promotion activities, particularly around nutrition. I was co-author (but not first or principal author) of a peer-reviewed paper in an international journal which described the implementation of a nutrition training program for Umoona's Aboriginal Health Worker team (15).

In an attempt to document and promote the pivotal role of the Aboriginal Health Worker as a POCT operator, a peer-reviewed article was published on the Umoona Kidney Project in the *Aboriginal and Islander Health Worker Journal* (16). This journal has been the principal Australian journal for this group of health professionals for the past 30 years. The article was written for this journal to specifically and strategically target this desired audience.

Both the South Australian Government's Department of Human Resources *Renal and Urology Services Implementation Plan 2000-2011* (17) and the Statewide Iga Warta Aboriginal Renal Disease Summit 1999 endorsed the Umoona model for expansion to other Aboriginal communities in rural and remote South Australia.

The Quality Assurance for Aboriginal and Torres Strait Islander Medical Services (QAAMS) Program for Diabetes Management

As a result of my pioneering use of POCT in the Umoona Kidney Project, I was appointed by the Australian Government's Department of Health and Ageing in 1999 as the inaugural Program Manager of a new pilot study that used the Bayer DCA 2000 device to conduct on-site POCT for haemoglobin A1c (HbA1c), an established pathology test for diabetes control, in Aboriginal Community Controlled Health Services (ACCHS). As Program Manager, I conceived, initiated, developed, implemented and managed the subsequent POCT model, the so-named QAAMS Program, an acronym for Quality Assurance for Aboriginal and Torres Strait Islander Medical Services. I have continued to be Program Manager of the QAAMS Program to the present. When the QAAMS Program commenced in July 1999, it had a national focus and involved 42 ACCHS and approximately 2300 Aboriginal patients with established diabetes across Australia.

My primary initial research task was to develop, for the first time, a large-scale structured education and training program for POCT including a set of culturally appropriate resources and a quality

management framework that incorporated both internal quality control (QC) and external quality assurance (QA) testing. The quality assurance arm of the program, which I conceived, initiated and subsequently developed through a collaborative partnership with the RCPA Quality Assurance Programs Pty Ltd (the main providers of laboratory-based quality assurance programs in Australasia), is a world first for the Indigenous health care sector. The key research questions and initial focus of the QAAMS model were:

- With culturally appropriate education and training, could Aboriginal Health Workers, from a broad range of diverse Indigenous medical services across Australia, collectively perform quality assurance testing to a standard that was equivalent to laboratory users of the DCA 2000 POC device, and,
- Could Aboriginal Health Workers achieve or approach national and international laboratory-derived analytical goals for HbA1c testing?

The answers to these research questions were published initially in 2003 and updated in 2006 in *The Clinical Biochemist Reviews* (18, 19); this is the national peer-reviewed journal of the Australasian Association of Clinical Biochemists (AACB) and the AACB is the main professional body representing clinical biochemistry in Australia and New Zealand. With a common framework for education and training, Aboriginal Health Workers maintained very high on-going participation rates and demonstrated consistently sound and continually improving analytical performance for POC HbA1c testing (as assessed by imprecision or reproducibility across over 6100 quality assurance tests).

As key outcomes of the initial pilot, in December 2000, the Federal Health Minister approved and introduced a Medicare rebate for POC HbA1c testing conducted by participating sites in the QAAMS Program, thereby facilitating the long-term sustainability of the program and changing its status from an initial pilot to a mainstream Indigenous health program.

To promote the availability of the QAAMS program and the utility of POCT for diabetes management to the national targeted audience of Aboriginal Health Workers, a peer-reviewed paper on the QAAMS Program was published in 2003 in the *Aboriginal and Islander Health Worker Journal* (20).

The QAAMS Program was now beginning to attract international attention. During 2003, through a collaboration I brokered with the Australian Centre for Diabetes Strategies in Sydney, the Western Pacific Island of Tonga joined the QAAMS Program, with permission of the Australian Government. Tonga participated in the QAAMS Program for three years. Their analytical performance achieved for POC HbA1c testing remained sound, providing preliminary evidence that the QAAMS model could be successfully transferred to Indigenous communities in other countries of the world.

In 2003, following a further submission I prepared for the Australian Government, a new program for POC urine ACR testing on the DCA 2000 was approved by the Government and incorporated into the QAAMS framework as a separate program. I developed and managed the education, training and quality management framework for this new program. The Government initially capped the number of participating Indigenous medical services at 30 (all of whom were existing sites in the QAAMS HbA1c program).

A peer-reviewed article describing the results of the first two years of the QAAMS Urine ACR program was published in an international clinical biochemistry journal (21). The key research findings were that the QAAMS HbA1c model was readily adapted to the new POC urine ACR test and Aboriginal Health Workers could perform the urine ACR test to an acceptable degree of analytical quality. Updated data on analytical quality of POC urine ACR testing was also published in a peer-reviewed paper in *The Clinical Biochemist Reviews* in 2006 (19).

To ensure the sustainability of the QAAMS Urine ACR Program, the Australian Government introduced a Medicare rebate item number for this test in June 2006. The HbA1c and urine ACR rebates now available through the QAAMS Program are the only rebates for specialised POC pathology tests which are able to be claimed under the Australian Government's Medicare system (other than a small group of qualitative tests such as urine dipstick and pregnancy tests). The availability of these rebates represents one of the most significant outcomes of this research program. They have ensured that participating Indigenous medical services can conduct POCT for diabetes management on a cost-neutral basis (with the on-going reagent and consumable costs associated with the program paid for by the rebates), thereby guaranteeing the long-term sustainability of this POCT model.

The QAAMS model now provided the means for Indigenous medical services to perform a blood test (HbA1c) for the monitoring of diabetes control and a urine test (ACR) for assessment of renal function, the main complication of diabetes. Following the securing of a further Government contract in 2006, the QAAMS HbA1c and urine ACR programs have been merged into a single program, the number of QAAMS participants has increased to 80 (for HbA1c) and 60 (for ACR) at the time of writing (March 2007), while the analytical performance base for quality assurance testing continues to meet national and international benchmarks.

Having successfully developed a culturally appropriate education, training and quality management framework for QAAMS (the principal charter of my initial contracts with the Australian Government), I was keen to investigate several further research questions. These included:

- How well had POCT been accepted by Aboriginal Health Workers (in their role as POCT operators), by Aboriginal patients with diabetes (the consumers of the POCT service) and by clinicians (responsible for patient management)?

- Could POCT conducted for the management of patients with established diabetes be clinically effective and contribute to improved diabetes control?

The first research question was answered through a series of qualitative surveys, which I conceived, prepared, implemented and analysed with the help of the Flinders Centre for Biostatistics and Epidemiology, Flinders University. To answer the second question, patient POCT data was sourced, tracked and analysed from two rural Indigenous medical services, at their request. The results of these research investigations were published in *The Clinical Biochemist Reviews* in 2006 (22). This paper documented the widespread acceptance of POCT among all stakeholder groups surveyed by questionnaire, and provided clinical data demonstrating improvements in diabetes control among Indigenous patients, as assessed by statistically significant reductions in HbA1c levels after the introduction of POCT.

The evidence that the QAAMS POCT model has made a significant contribution and improvement to the way diabetes services are delivered in the Aboriginal health sector in Australia has been independently verified and documented in two reviews on the QAAMS Program commissioned by the Australian Government and conducted by the National Aboriginal Community Controlled Health Organisation (NACCHO) and Campbell Research & Consulting Pty Ltd (23, 24).

The Point-of-Care Testing In Aboriginal Hands Program

During 2000 I received many enquiries from Indigenous medical services concerning the availability of a POCT analyser for lipid testing. In 2001, I conceived, initiated, developed, implemented and managed a new POCT model for the early detection and management of chronic disease called the Point-of-Care Testing in Aboriginal Hands (POCAH) Program. This model was introduced into four rural and/or remote Indigenous medical services across South Australia and Western Australia. Each of these services had a different geographic location, physical size, number of Aboriginal Health

Workers and clinical and infrastructure support. In addition to the Bayer DCA 2000, a new POCT device for lipids was introduced in this program for the first time in the Indigenous community setting – the Cholestech LDX lipid analyser (Cholestech Corporation, Hayward, CA, USA). This device performed a full lipid profile (total cholesterol, triglyceride, HDL cholesterol and calculated LDL cholesterol) on a capillary blood sample with results available in approximately 5 minutes.

Prior to its introduction in this program, I undertook the first evaluation of this new device in Australia, the results of which were published in a peer-reviewed national publication (25). The key finding from this study was that the Cholestech LDX exhibited satisfactory analytical performance, and could confidently be used for cardiovascular (and, by association, diabetes) risk assessment in the Aboriginal community setting.

The POCAH program was conducted over a 4-year period from 2001 to 2005. The main research questions examined in this study were:

- Could POCT work effectively across Indigenous medical services with differing sizes and staff resources (health workers and clinical and other support staff)?
- What were the overall chronic disease risk profiles in these different Indigenous communities?
- Could POCT measurements (including lipids) be integrated into the management of patients with chronic disease?
- How well was POCT accepted by doctors, POCT operators and patients with chronic disease?

The key findings from this study were that POCT proved equally effective across a diverse mix of Indigenous medical services, high rates of chronic disease risk between and across communities were identified, POCT was again clinically effective for patient management and there was

widespread acceptance of POCT by all stakeholders. These findings were published in an international peer-reviewed journal (26), with early data from this POCT model also being reported in an invited book chapter (13), and in the *Aboriginal and Islander Health Worker Journal* (27).

The adaptability and versatility of POCT was also confirmed in this program through a series of community initiatives and the utilisation of POCT in a range of diverse locations and situations.

On-going Assessment of Analytical Performance of POCT Devices

During the course of developing and implementing these three POCT models for chronic disease prevention and management in Indigenous medical services, I conducted regular studies comparing POCT and laboratory results on the same patient samples and verified both the accuracy and precision of the POCT devices used in my research program. Published patient comparison studies have been conducted both at Flinders University and in field settings (the latter through collaborative partnerships I have established and fostered with researchers from other hospitals and medical research institutions) (9, 25, 28-30). The first three of these evaluations are included in the published papers in this thesis as I was either first or equal first author on these papers. I have also compared the POCT devices used in my program of research with new POCT devices that have come onto the Australian market during the period of my research studies (31).

Diabetes Management Along the Mallee Track Program

Having verified the analytical quality and the clinical and cultural effectiveness of POCT in the Indigenous health sector, I then addressed the following research question:

- Could the POCT framework for chronic disease detection and management pioneered in the Indigenous community setting be adapted and transferred to the non-Indigenous health setting?

The opportunity to test this hypothesis arose in 2003. I was invited and subsequently contracted by the Mallee Track Health and Community Service (MTH&CS) from the remote country town of Ouyen in Victoria to establish and maintain a specialist POCT service as part of a program entitled *Diabetes Management Along the Mallee Track*. A Rural Chronic Disease Initiatives (RCDI) program grant had been secured by the MTH&CS to undertake this program. The health service wanted to implement a community risk assessment program and establish an integrated, multidisciplinary 'one-stop' service for the management of people with diabetes which involved the local general practice and included POCT for HbA1c, urine ACR and lipids as its centrepiece. Following the delivery of an education and training program by the author, the MTH&CS community nurse acted as the local POCT operator. As well as being responsible for the delivery of specialist POCT services, I developed a patient data management system, designed and implemented patient satisfaction surveys (again with assistance from the Flinders Centre for Bistatistics and Epidemiology) and, at the request of the MTH&CS, wrote the final report on the *Diabetes Management Along the Mallee Track* program for the Australian Government.

The results of the program were published in a peer-reviewed international journal in 2005 (32). Statistically significant improvements in glycaemic control, cholesterol levels and blood pressure were observed among the 54 patients with diabetes following the intoduction of the one-stop management service and POCT. There was widespread support among the community's diabetes patient group for the continued use of POCT as part of their management, while their level of satisfaction with the new diabetes service was high.

At the conclusion of the RCDI funding period, the Australian Government selected the *Diabetes Management Along the Mallee Track* project as one of three demonstration projects from the RCDI program grants for showcasing to all rural and remote health services in Australia through the production of an education resource called *Building Healthy Communities* (33).

Point-of-Care Testing (POCT) in General Practice Trial

Having supported and funded the Umoona Kidney Project and the QAAMS Program since the late 1990s, the Australian Government's Department of Health and Ageing was becoming increasingly aware of the practical application and effectiveness of POCT in the community setting. In 2001, the Government commissioned a report on the role and value of POCT in the general practice environment (34). In 2003/4, the Government recommended that a trial of POCT in general practice be conducted and a Sydney-based consultancy firm was contracted to develop a trial design. The 18-month randomised controlled trial aimed to recruit approximately 60 general practices across urban, rural and remote geographic regions, and approximately 5000 patients who had either established diabetes, hyperlipidaemia or were receiving anticoagulation therapy.

The Government then established a series of Working Parties to determine the standards and guidelines under which POCT would be conducted during the trial. I was an invited member of the Government's Technical and Clinical Working Party of the PoCT Subcommittee, Quality Use of Pathology Committee. In this role, I conducted a literature review and wrote the recommendations for the analytical goals to be achieved by the POCT instruments used for the trial. These recommendations were accepted and approved by the Government, published on the Government's web site and are being utilised in the trial to formally assess the quality of the POCT devices used. Using this review as a basis, I subsequently wrote a paper on analytical goals for POCT devices for diabetes management, which was published in an international peer-reviewed journal (35). This is the first published paper which specifically promulgates analytical goals for POCT in the non-laboratory setting (as opposed to goals derived for laboratory methods and instruments).

In 2004, the Australian Government called for separate tenders to implement the three major components of the trial design, namely overall trial management; management of POCT devices and

delivery of training and an internal quality control program; and management of an external quality assurance program. On behalf of the Flinders University Rural Clinical School, I wrote the successful tender for the management of devices and the delivery of the training and quality control programs. I was appointed POCT Device Manager and my Community Point-of-Care Service unit was charged with the delivery of this tender. I was also a member of the consortia which successfully tendered for the trial management and quality assurance arms of the trial. The POCT instruments recommended for use in the trial by our device tender were the Bayer DCA 2000 for HbA1c and urine ACR testing on patients with diabetes, the Cholestech LDX Lipid analyser for monitoring lipids on patients with hyperlipidaemia and the CoaguChek S analyser (Roche Diagnostics, Sydney, Australia) for measuring the International Normalised Ratio (INR) on patients on warfarin therapy.

From the POCT device perspective, the key research objectives of the trial were:

- to develop an education and training framework appropriate for a general practice environment,
- to assess the analytical quality of POCT in general practice against the goals recommended by the trial (through the results generated by the internal quality control program), and,
- to determine if there was any difference in analytical performance across geographic regions.

The live phase of the Point-of-Care Testing in General Practice Trial commenced in September 2005 and concluded in February 2007. The education and training framework and the preliminary results of the internal quality control testing program have been reported to the Australian Government through a series of Progress Reports which I have written as POCT Device Manager. At the invitation of the journal editor, a brief descriptive summary of the trial aims and objectives was published in the peer-reviewed international publication *Point of Care* in 2006 (36). This journal is the

official publication of the American Association of Clinical Chemistry's (AACC) Critical and Point of Care Division. The results of this arm of the trial remain confidential and will not be published until 2008 at the earliest (which is beyond the time frame of this thesis).

Conclusion

The continuous program of research described in this thesis represents the first and most comprehensive research assessment of the effectiveness of POCT ever conducted in Australia. The significant contribution that my pioneering work has made to the field of POCT, particularly the Indigenous health sector, has been recognised nationally and internationally by Government, my scientific peers and by the wider community.

The Australian Government will have continuously funded my main POCT model (The 'QAAMS' POCT Program for diabetes management) for ten consecutive years at the completion of our current contract. This longevity of funding support for a single project, particularly one conducted in an Indigenous health care setting, is extremely rare. I am now also regularly consulted by the Government's Pathology Section and the Office for Aboriginal and Torres Strait Islander Health on general POCT matters.

In 2004 I was appointed as Chairperson of the Australasian Association of Clinical Biochemists (AACB) Working Party on Point-of-Care Testing and invited to be the AACB's Inaugural Regional Travelling Lecturer (in which I lectured on my POCT models to 19 regional centres across Australia and New Zealand).

Since 2000, I have been an invited speaker at 8 international conferences and meetings (delivering a total of 11 lectures at these events) and 7 national conferences and meetings (delivering 8 lectures).

These meetings have collectively encompassed the professional fields of clinical biochemistry, Indigenous health and diabetes. At the XIX International Congress of Clinical Chemistry IFCC/AACC (International Federation of Clinical Chemistry/American Association of Clinical Chemistry) Annual Meeting, Orlando, Florida, USA, in July 2005, I was not only an invited speaker but also the poster I prepared and presented on the QAAMS Program won the AACC Critical and Point-of-Care Testing Division's Annual Meeting Abstract Award and was also the recipient of the National Academy of Clinical Biochemistry's (NACB) Distinguished Abstract Award.

As mentioned previously, in 2004, I was also invited to write a chapter in the definitive global textbook on POCT entitled *Point-of-Care Testing* (14).

In the wider community I was the recipient of an Australian of the Year Award in 2004, in recognition of the contribution of my POCT work towards assisting Aboriginal communities to improve diabetes management. I was also awarded the Order of Australia Medal (OAM) in the Australian Honours list announced on the Queens Birthday June 2006, for service to public health through medical research (as well as to the environment through conservation organisations, and to aviculture).

CHAPTER 2: LITERATURE REVIEW

METHODOLOGY USED IN THIS LITERATURE REVIEW

The primary aim of this literature review was to identify published papers concerning the use and application of point-of-care pathology testing (POCT) in the Australian Indigenous health care setting.

To do this, a computerised electronic search covering the period 1988 to March 2007 was initially undertaken with Ovid Medline using the search strategy and key words described in Figure 2.1.

Figure 2.1 Summary of search strategy used in this literature review.

Number	Search History
1	((point of care or near patient or bedside or physician office or offsite or alternate or ancillary or decentralised) and testing)
2	((point-of-care or near patient or bedside or physician office or offsite or alternate or ancillary or decentralised) and testing)
3	1 or 2
4	Limit 3 to English language
5	indigenous or exp Health Services, Indigenous/
6	Aborig$
7	4 and 5
8	4 and 6

In total 2338 unique references were identified by this broad search strategy (#3 in Figure 2.1). However apart from published papers which have been either (i) written by the author and presented as part of this thesis or (ii) studies in which the author has collaborated and been a co-author (29, 30), only two papers on POCT and Indigenous health were found – neither of which were relevant to

this thesis. One of these concerned a telemedicine clinic used in Aboriginal communities in Canada (37) and the other related to a registry of stroke patients in South Africa (38).

To widen this primary search, supplementary searches of the Embase and Web of Knowledge (incorporating Science Citation Index, Current Contents and CINAHL) electronic databases were undertaken using the same key words, phrases and timeframe. The Informit database was searched to cover the 'grey' medical and scientific literature with particular reference to Australasia. The website Australian Indigenous Health*InfoNet* (39) was also used to source material specifically on Australian Indigenous health. Recent text books on POCT by Price, Hicks and St John (14) and Kost (40) were also consulted. Two further papers which briefly describe the use of POCT for diabetes management in Australian Indigenous medical services were identified; both of these papers were from participants in one of the main research programs developed by the author (QAAMS) (41, 42).

Thus, outside the research conducted directly or collaboratively by the author, no articles were found in the literature concerning the use and application of POCT in Indigenous health.

However, the literature search did enable the systematic identification of a number of important themes which permit a fuller understanding of the field of POCT. These themes will be discussed and appraised in this literature review, with the aim of identifying current gaps in the literature and placing this program of research in the context of POCT. Papers relating to these themes were consolidated into an EndNote reference library (43). Reference lists from these papers were searched to identify further papers of relevance to these themes. The final EndNote library constructed to support this literature review comprised 729 references.

INTRODUCTION TO POINT-OF-CARE TESTING (POCT)

The origins of POCT can be traced to the very beginnings of diagnostic pathology in the 15th century when urine specimens were tested and inspected at the patient's bedside, at their point of care (44-46). Thus POCT is not strictly a new discipline of medical science but one which has made a significant re-emergence over the past 20 years. There have been many different definitions of POCT proposed by numerous authors and professional groups, a representative sample of which are shown in Table 2.1. In addition, a multitude of acronyms have been used to describe this mode of health service delivery. These include current accepted terms such as point of care testing (with or without hyphenation) and near patient testing (NPT), as well as a number of historical expressions no longer used in the literature such as bedside testing, physician office testing, alternate or off-site testing, ancillary testing, and decentralised testing (47-55).

The variety of definitions and lack of standardisation of a single accepted terminology for this mode of health service delivery reflect the relative infancy of this field. No single definition has been proposed that (i) adequately encompasses the scope of POCT, (ii) can be applied across all applications of POCT, and (iii) reflects the now widely-accepted importance of linking POCT to measurable outcome benefit(s).

For the purpose of this thesis, the author has developed his own definition of POCT as follows: POCT is '*pathology testing which is performed on behalf of the treating medical practitioner by a trained operator in an on-site clinical setting at the time of patient consultation, allowing the test result of desired analytical quality to be generated and to be used to make an immediate informed decision that contributes to an improved health outcome for the patient.*'

The various phrases in this definition can be broken down further to explain POCT more fully. Firstly POCT is a pathology investigation, generally a clinical biochemistry, haematology or microbiology

test. POCT is most commonly, but not exclusively, performed on small portable *in vitro* medical devices that require a small sample volume (generally ranging from 5 to 50 µL of capillary whole blood or urine) to conduct the test, making the sample collection process simple, convenient and less stressful for the patient. The test should only be performed by a POCT operator who has undergone an appropriate level of training and certification in performing the test and conducting quality management procedures on the relevant POCT device; these practices ensure that results of acceptable analytical quality (equivalent to that of the laboratory) are generated for patient care. The POCT operator may be one of a number of healthcare professionals including a doctor, nurse, primary health care worker, diabetes educator, pharmacist, paramedic and even the patient. The clinical settings in which POCT can be conducted are numerous and comprise hospital-based, community-based, and other diverse locations (as shown in Table 2.2). Prior to this program of research, the Australian Aboriginal medical service was a notable absentee from the list of community-based, primary-care locations in which POCT was practiced. The definition of POCT implicitly excludes the test being performed by a trained medical scientist or technical officer in the hospital laboratory. POCT also has both a spatial and temporal relevance (56). By conducting POCT on-site at the time of consultation with the patient, POCT brings pathology testing closer or 'nearer' to the patient and to the doctor. The speed at which the pathology result is available to the doctor, who in turn uses the result to make an immediate informed clinical decision, is a primary objective of POCT. With the development of evidence-based laboratory medicine, it is now widely recognised that an overarching goal of pathology testing, whether it be POCT or laboratory-based testing, is to maximise the health outcome benefit to the patient as a result of the medical practitioner taking appropriate action on the test result (57). However, as will be discussed later in this chapter, the speed of the POCT result alone does not necessarily confer an improved outcome for the patient.

Table 2.1. Representative examples of different definitions of POCT.

Definition of POCT	Reference Source
'Testing at the point of patient care, wherever that medical care is needed'.	Kost (58)
'Those analytical patient testing activities provided within the institution, but performed outside the physical facilities of clinical laboratories …'	College of American Pathologists (59)
'Diagnostic testing conducted close to the site where clinical care is delivered'.	Nicholls (60)
'Any investigation carried out in a clinical setting or the patient's home for which the result is available without reference to the laboratory and perhaps rapidly enough to affect immediate patient management'.	Delaney et al (61)
'Any kind of test performed outside the central hospital laboratory, usually at the patient's bedside'.	Mor (47)
'Testing that is performed close to the patient'	Hicks (62)
'Any type of testing undertaken close to the patient to enable a decision to be made on the care of that patient.'	Price (63)
'A pathology investigation by or on behalf of the treating medical practitioner on-site, at the time of and for use during consultation'.	Guibert (34)
'Testing at or near the site of patient care'.	Kost (40)
'Any test that is performed at the time at which the test result enables a decision to be made and an action taken that leads to an improved health outcome'.	Price and St John (64)
'Testing that is performed near or at the site of a patient with the result leading to a possible change in the care of the patient'.	ISO Standard (65)
'Clinical laboratory testing conducted close to the site of patient care, typically by clinical staff whose primary training is not in the clinical laboratory sciences, and sometimes by patients themselves'.	Pearson (66)

Table 2.2 Examples of health care settings where POCT is used.

Environment	Health Care Setting
Hospital-based	Emergency Department
	Adult Intensive Care Unit
	Neonatal Intensive Care Unit
	Coronary Care Unit
	Operating Theatre
	Ward
	Outpatient Clinic
Community-based	General Practice/ Physician Office
	Pharmacy
	Community Health Clinic
	Aboriginal Medical Service
	Home Care
	Retrieval Unit
	Workplace
	Veterinary Care
	Leisure Facility
	Sports Medicine
	Disaster Management
Other	Military
	Space

THE INCREASED GLOBAL UPTAKE OF POCT

Since the re-emergence of POCT in the late 1980s, the uptake of POCT in the health sector has burgeoned, mainly in the Western developed world. The USA now comprises approximately 60% of the global POCT market share, followed by Europe 20%, Japan 10% and the Asia-Pacific region including Australia 5% (67). In the USA, POCT comprised a fifth of all diagnostic testing in 2000 (68). Globally, the POCT market was estimated to be worth US$3 billion in 1997, $5.4 billion in 2002, $10 billion by 2005 and growing at an estimated 12% per year (61, 67-69). The blood glucose self-monitoring component of the POCT market however dominates these dollar figures, representing 60% of the global market value (67). There are no available data on the current market value of POCT in Australia.

The upsurge of interest in POCT has been driven by several factors. Firstly, there is now greater emphasis on placing the patient at the centre of the health care process. The patient of the 21st century is more knowledgeable and aware of disease conditions and has higher expectations of the health care system in terms of quality and convenience of care. Care of patients with chronic conditions is being devolved away from the hospital to a range of community-based care-giving environments conducive to POCT such as the general practice, pharmacies, one-stop community health clinics, and Indigenous medical services (which is the specific subject of the current research) (45, 70, 71). As will be discussed in this thesis, patient satisfaction with the convenience and accessibility of POCT is generally high because pathology testing and consultation with the doctor occurs in the same visit and obviates the need for a follow-up consultation to obtain pathology results (22, 72, 73). With pathology testing being conducted 'closer to' the patient, POCT facilitates a greater sense of ownership of the pathology testing process and supports improved compliance by the patient (22). Individual patient and community ownership of POCT are particularly important cultural benefits of POCT in the Indigenous health setting.

Secondly, the way in which laboratory services are provided has also changed. The majority of hospital-based pathology testing is now performed on high throughput, batch-orientated analytical systems in large core laboratories, creating a niche for smaller volume, needs-specific POCT to be undertaken by regional satellite laboratories and community clinics (45).

Early critics of POCT argued that the speed of POCT analysis was compromised by lack of quality of the result and reliability of the POCT device (48, 74-79). However, over the last decade, POCT device manufacturers have invested heavily in modern design, new technologies and Good Manufacturing Practice to ensure most modern POCT devices are now analytically sound and 'fit for use' by non-laboratory consumers (80). There have been significant advances in POCT technology including:

- miniaturisation,
- simplicity of device operation,
- reproducibility of manufacturing process for both devices and reagents,
- advances in microfluidics, sensor design, and interfacing standards (connectivity),
- the range of tests that can be performed by POCT, and,
- the ability to conduct specialised analyses on minute sample volumes of the order of 5-50 µL (47, 64, 81).

Some of these aspects will be addressed in more detail in the next section.

ANALYTICAL AND TECHNOLOGICAL ASPECTS OF POCT DEVICES

Introduction

The use of POCT devices for the prevention and management of diabetes and renal disease is a key focus of this research program. This section of the literature review therefore discusses the scope of POCT devices that are currently available and some of the recent innovative analytical and technological advances found in contemporary POCT device manufacture and design.

A recent global compendium of POCT devices lists 90 devices that are currently used in hospital and primary care settings and over 110 devices that test for infectious diseases (82). While this list is the most comprehensive and current in the published literature, these devices are not available in all countries, and some remain under development or await approval by the U.S. Food and Drug Administration (FDA). A list of POCT devices currently used in Australia is unavailable; however the Australasian Association of Clinical Biochemists (AACB) Working Party on POCT (of which the author is a member and former Chair) are currently conducting a national survey to source this information.

POC devices can be classified as *in vitro, in vivo, ex vivo* or minimally invasive (47, 64, 82-85).

In Vitro *POCT Devices (IVD)*

In vitro devices (IVD), where the sample is collected from the patient and analysed externally, are by far the most common type of POCT device (64). *In vitro* devices can be classified by:

- their size/format,
- whether they provide a qualitative, semi-quantitative or quantitative result,
- the type of technology, and
- the analytical principle employed to measure the POC analyte of interest (64, 82).

Most *in vitro* devices range in size from handheld, to small portable bench-top analysers, to mid-sized analysers that can be transported (for example on a hospital trolley) to the site where POCT is conducted. The analytical principle encompasses both the mode by which the analyte is recognised (or sensed) and the resultant signal which is detected (or transduced). Chemosensors utilising a chemical indicator or binding molecule to recognise the analyte are the most widely available sensor type. Biosensors, which use a biological recognition molecule such as an enzyme or antibody, are becoming increasingly popular in the design of POCT devices. A list of selected *in vitro* devices used in Australia and their different device characteristics is shown in Table 2.3. The key devices used in this program of research (the DCA 2000 [Bayer Diagnostics, Tarrytown, NY, USA] and the Cholestech LDX lipid analyser [Cholestech Corporation, Hayward, CA, USA]) are small, portable, single-use *in vitro* devices (that is, only one patient sample can be tested using each cartridge or cassette).

Most *in vitro* POCT devices utilise whole blood for testing whereas corresponding laboratory analysis is generally performed on a different matrix, most often venous plasma. This can lead to potential differences in the accuracy of POCT and laboratory results. The best illustrative example is glucose measurement where the International Federation of Clinical Chemistry (IFCC) recommends that a factor of 1.11 is applied to convert capillary whole blood measurements to an equivalent plasma concentration (due to the lower concentration of water in erythrocytes) (86). Many POCT devices now apply correction factors in their calibration procedures to covert a whole blood measurement to a plasma equivalent value. However, this process assumes the patient has a normal haematocrit. Many trauma, post surgical and oncology patients may have low haematocrits (in the 25-35% range), while neonates and patients with polycythaemia may have high haematocrits (over 55%) (87-89). As an example of how diagnostic companies are addressing this potential source of error, a new glucose meter has recently been released that measures haematocrit and glucose simultaneously and automatically corrects for haematocrit (90).

In vivo, ex vivo *and minimally invasive POCT devices*

In vivo, ex vivo and minimally invasive POCT devices remain largely in the developmental phase but are likely to spawn a new generation of POCT devices and applications in the coming years. With *in vivo* devices, the sensing device is placed directly into the bloodstream enabling continuous monitoring of the analyte under investigation. For *ex vivo* devices, blood is taken from the body passed across an external sensor and then returned to the body in a closed loop. Minimally invasive devices generally utilise a sensor placed sub- or trans-cutaneously. These devices are likely to find widest application in the area of neonatal acute care (for blood gas, electrolyte, glucose and bilirubin measurement for example) where blood conservation is critical (91, 92), or in the area of diabetes management where continuous glucose measurement could assist tighter glycaemic control (64, 82, 85, 93-96).

Advances in Connectivity Standards

Lack of documentation of POCT results was also an often-quoted limitation of POCT in the early to mid 1990s, using the rationale that it is pointless performing a POC test if the result is not incorporated into the patient's clinical file nor acted upon clinically (97, 98). Indeed poor documentation of and/or transcription errors with POCT results could potentially lead to increased risk of medicolegal problems (99).

In the late 1990s, a survey conducted for the American Association of Clinical Chemistry (AACC) in over 500 US hospitals revealed that only 17% of POCT data was transferred electronically while two thirds of the data did not reach the laboratory information system (LIS) (100). By 2000, calls were made in the literature to find an overarching solution to the connectivity problem which was considered a major barrier to the future uptake and application of POCT (100-103).

In February 2000, a group of 49 POCT device vendors, diagnostic test system vendors, healthcare institutions and informatics experts formed the Connectivity Industry Consortium (CIC). The aim of the CIC was to develop a global standard for connectivity which facilitated the seamless linking of POCT devices to clinical information systems regardless of vendor, location or interface (104). The standard addressed bidirectional communication between POCT device and information system, device connection commonality, commercial software interoperability, user security and confidentiality and QC/regulatory compliance (101, 104-107). In 2001 the National Committee for Clinical Laboratory Standards (NCCLS), now known as the Clinical and Laboratory Standards Institute (CSLI), approved the connectivity standard (108). Benefits of the introduction of this connectivity standard have already been reported; they include reduction of error rates, increased operator compliance and decreased POCT management and nursing costs (109). The full benefits of connectivity may not been seen for some years yet but the bipartisan addressing of this key issue by industry has unquestionably advanced the cause of POCT.

Table 2.3. Examples of selected *in vitro* POCT devices in Australia and their characteristics.

POCT Device/Strip	Technology	Usage	Analytical Principle (recognition/detection)	Result	Size/Format	Analytes Measured
Bayer Albustix	Single Strip (dipstick)	Single use	Chemical/visual	Qualitative	Handheld	Urine albumin
Roche Combur-Test	Complex Strip (multi-pad dipstick)	Single use	Chemical/visual	Qualitative	Handheld	10 urine analytes
Roche Trop T	Immunosensor Strip	Single use	Lateral flow immunoassay/optical	Semi quantitative	Handheld	Troponin T
Roche Cardiac Reader	Strip with monitoring device	Single use	Immunoassay/reflectance photometry	Quantitative	Portable	Troponin T, myoglobin, D-dimer
Roche CoaguChek S	Strip with monitoring device	Single use	Impedance of magnetic particle motion/ reflectance photometry	Quantitative	Handheld	INR
Bayer DCA 2000	Cartridge with monitoring device	Single use	Latex agglutination inhibition/turbidimetry	Quantitative	Portable	HbA1c
Cholestech LDX	Cassette with monitoring device	Single use	Enzymatic/ reflectance photometry	Quantitative	Portable	Lipids and glucose
Abbott i-STAT	Cartridge with monitoring device	Single use	Electrochemistry	Quantitative	Handheld	Blood gas and electrolytes
Bayer RapidPoint 400	Reagent pack with benchtop monitoring device	Multi use	Electrochemistry	Quantitative	Transportable	Blood gas and electrolytes

ESTABLISHING AND MANAGING A POCT SERVICE

Introduction

One of the primary aims of this research program was to develop, implement and manage POCT models for the prevention and management of diabetes and renal disease in the Australian Indigenous health care setting. The purpose of this section of the literature review was to identify what are the key principles and current best practice standards for establishing and managing a POCT service and to assure that the models implemented in this research program were closely aligned with these principles and standards.

There is an often misguided perception among health professionals without a sound understanding of the field of POCT that one simply needs to buy a POCT device from a vendor "off the shelf", take it to the location where it is to be used, turn it on and start testing. The reality is that there are many aspects to consider when setting up a POCT service and there needs to be a logical and systematic approach to the organisation and management of POCT.

Standards and Guidelines for the Conduct of POCT

The International Organisation for Standardisation (ISO), a worldwide federation of national standards bodies, has recently published a standards document (ISO 222870), detailing requirements for quality and competence for POCT (65). This document states that these standards can be applied not only to the hospital setting but also to the clinic or health care organisation providing ambulatory care. However the standards are written in a highly technical fashion and require constant cross-referencing to a second set of standards (ISO 15189) which provides requirements for quality and competence in medical laboratories; this makes the POCT standard difficult to understand, interpret and implement in a practical sense by non-laboratory trained health professionals and in non-laboratory POCT environments.

Multiple guidelines on how to establish and maintain a POCT service (both generally and for specific tests) have been published by professional societies and expert panels representing many countries and/or regions of the world (Table 2.4).

Most of these guidelines share common principles that can be applied logically and systematically when establishing and maintaining a POCT service (84, 110-112). These principles are listed in Figure 2.2 and summarised briefly in Table 2.5. However, like the ISO Standard, most of the guidelines are focussed on hospital and laboratory based POCT applications.

There are no standards or guidelines written exclusively for conducting POCT in a non-hospital, community-based setting, including the Australian Indigenous medical service. Interim standards and guidelines have been developed for the performance of POCT in general practice in Australia as part of a major Government-funded trial of POCT currently being undertaken in this sector (36, 113). However, these standards and guidelines have not been introduced into routine general practice and the decision to do so rests on the outcomes of the trial, which will not be reported upon nor assessed by the Australian Government until 2008.

In wider practice, the key principles recommended for establishing and maintaining a POCT service must be tailored and adapted to meet local needs and specific POCT settings (114, 115). Working examples of how to set up and manage POCT services used in both acute and chronic clinical settings in the Australian rural community environment have recently been published (116, 117). The support and knowledge of the local laboratory or specialist POCT provider (such as the unit directed by the author, where scientific staff all originate from a strong laboratory background) is critical in setting up a POCT service because many of the principles address specific analytical and laboratory concepts which are outside the domain of the non-laboratory health professional (111, 118).

Device Selection, Training and Analytical Quality Management – Key Elements of Establishing and Managing a POCT Service

Device selection, training of POCT operators and performance of analytical quality management procedures (internal quality control and external quality assurance testing) are factors which have been identified as crucial but often neglected elements of a POCT service (101, 111, 119). If these elements are not addressed appropriately as part of an overall organisational and risk management strategy, then there is increased likelihood that errors will occur in the conduct of POCT. For example, Pearson stated the major sources of error in conducting POCT include poor selection and maintenance of POCT devices, incorrect storage of consumables, untrained operators performing POCT, and errors associated with the total analytical testing cycle including pre analytical, analytical and post analytical processes (66). Meier and Jones identified operator incompetence, non-adherence to test procedures and the use of uncontrolled reagents and equipment by operators as the three main sources of POCT error (120). Demers listed the 10 most cited deficiencies in POCT as failure to: follow manufacturer's instructions explicitly; perform quality control testing; document quality control activities and take appropriate corrective action of quality control outliers; perform external quality assurance testing; document personnel training and competency; provide continuing education for POCT operators; and have a procedure manual for testing and result reporting (121). A recent NCCLS guideline which utilises a source-of-error matrix (including categories for device capabilities, training and applicable quality monitoring) identified more than 60 potential sources of error in the total POCT testing process (122). Jones and Meier described the need for a 'culture of safety' for POCT by focussing on 'procedural consistency, operator competency, quality control and result integrity, monitoring patient identification, specimen adequacy, and report accuracy' (123).

As will be described in the published papers in the next chapter, issues of device selection, training and quality management have been foundation elements of the POCT models developed and described in this research program. Key factors that need to be addressed in device selection and

the training of POCT operators are summarised in Table 2.5. The development of models for the monitoring of analytical quality of POCT through both internal quality control and external quality assurance testing has formed a significant component of this research program and these practices are therefore briefly reviewed below.

Internal Quality Control Testing for POCT

Traditional laboratory QC involves the testing of samples which have a known (or target) analyte concentration, assigned by the manufacturer of the material (124). Samples are most commonly lyophilised human blood, urine products or liquid solutions. Two or three levels of QC samples are usually provided by the manufacturer, which enables analytical performance to be assessed within and outside the reference interval for that analyte. The QC sample undergoes the same analytical processes as the patient sample, including sample preparation, sensor recognition and signal detection and readout, but this process is not able to assess pre-analytical steps (notably patient sample collection) and post-analytical reporting steps in the total patient testing process (125, 126). Results of QC testing are compared against the target for the QC sample, and established acceptable limits of performance above and below the target, immediately after the result is available. Many simple and complex 'rules' have been developed for accepting and rejecting laboratory QC results, the most widely accepted being those promulgated by American clinical biochemist James Westgard (127). Westgard rules have been incorporated into many POCT devices that have the capacity to electronically capture QC results (80).

Imprecision for QC testing, calculated statistically as the coefficient of variation (CV%) from the formula CV% = (SD [standard deviation]/mean)*100, is widely used as a measure of analytical performance and the CV% can be compared to defined analytical goals for the particular analyte to objectively assess whether the analytical system has remained stable across time and whether observed performance meets analytical expectations (128-132).

In relation to the practice of QC testing for POCT, two key questions have been widely debated in the literature; namely: "Are traditional laboratory statistical QC procedures relevant to POCT?" and "At what frequency should QC testing be used for POCT?"

For multi-use cartridge-based POCT devices, where all sensors and reagents are contained within a cartridge pack which can be used to test a specified number of samples or last for a specified period of time, there is general consensus that traditional statistical QC procedures can be applied in this setting (64, 133). These devices, most commonly used in critical care settings, feature a degree of automation in their QC process whereby the measurement of a liquid QC sample can be programmed at specified time intervals. QC results can be electronically downloaded *in situ* and assessed according to Westgard rules. If QC results are unacceptable, then operators can be locked out of being able to conduct further testing until corrective action has been taken. Systems using automated QC also have the advantage that they can often be managed remotely by the POCT Coordinator, thereby saving time and resources (134).

However, for single-use or unit-use POCT devices (such as those used in this research program), only one sample test can be performed on each cartridge or strip which is then discarded. It is now widely acknowledged that traditional QC practices are not entirely appropriate for this mode of device (124, 126, 133, 135, 136). As Ehrmeyer states "the principles of traditional, statistical QC need to be customised and adapted for the unit-use test system" (126).

To address the need for a different approach to QC testing, the NCCLS recently published an approved guideline for quality management of unit-use POCT (122). This guideline recommends that a combination of different methods of control be used maintain analytical surveillance of POCT device operation and result quality. These methods include:

- periodic internal QC testing,
- external QA testing,
- electronic QC testing (which assesses only the electronic measurement circuitry of a POCT device using a surrogate material [such as a reference cassette, coloured filter, coloured solution or bar code] to generate an electric signal that would normally be produced by a sensor responding to an analyte in a patient sample),
- acceptance testing (which involves performing internal QC testing when there is a change in the test system, for example when a new lot number of reagent is used for the first time or when a new POCT operator commences POCT in the organisation),
- split patient sample testing (which involves the periodic duplicate testing of the same patient sample by both the POCT method and by the local laboratory method that is traceable to a recognised standard),
- clinical surveillance (whereby patient POCT results are correlated with the clinical status of the patient). This technique is particularly useful in identifying gross errors in POCT measurement where reported results do not match the patient's clinical condition, and,
- preventative maintenance (122).

The guideline also recommends that internal QC testing should be conducted with a minimum frequency of no longer than 0.1 ($1/10^{th}$) of the reagent stability as stated by the manufacturer. Thus if a lot of reagents has a stability of 10 months, then QC testing should be performed at a minimum once a month. In practice, an optimal balance must be obtained between the frequency of QC testing and the number of patients tested to ensure that QC testing does not become too time consuming for POCT operators and too costly (137). This is particularly relevant to sites conducting a low volume of patient tests. Prior to this research program, there have been no published papers documenting QC practices and procedures for POCT in the Australian Indigenous health care setting.

External Quality Assurance Testing for POCT

External quality assurance (QA), also referred to as external proficiency testing (EPT), involves testing samples that are prepared and distributed to participating sites by an external source, most commonly a national QA provider (for national programs) or a local hospital laboratory (for regional/local programs). For QA testing, samples with analyte concentrations covering a wide measuring range can be produced, with target values specified by the provider or laboratory. In contrast to QC testing, the operator has no knowledge of the true value of the QA sample when it is tested. Results are returned to a central location (QA office or laboratory) and a report is prepared which identifies the range of results obtained by all participants for the testing of that particular sample. The report is then sent to each participating organisation. In this way, QA enables a comparison of the analytical performance between participating sites. An assessment of both imprecision and inaccuracy is possible for quantitative biochemical markers through QA testing.

Examples of national external quality assurance schemes for POCT include: the drugs of abuse program in the USA (through the College of American Pathologists [CAP]), the cholesterol and urinalysis programs in the United Kingdom (through the UK National External Quality Assurance Scheme [UKNEQAS] and the Wales External Quality Assessment Scheme [WEQAS] respectively), and, the QAAMS (Quality Assurance for Aboriginal and Torres Strait Islander Medical Service), General Practice and Near Patient Testing Programs in Australia (the last two having being developed by the author as part of this research program and in collaboration with the RCPA Quality Assurance Programs Pty Ltd) (18, 19, 21, 138-141).

Locally run QA schemes generally use the split sample testing approach in which a sample is aliquoted multiple times (according to the number of participants) and distributed for external testing. In contrast to national schemes where lyophilised samples and reconstitution fluid are generally supplied to participants separated by long distances, fresh appropriately preserved whole blood or

urine from patients can be used as a sample matrix for local schemes. An example of a cost effective local QA scheme for POC HbA1c testing involving 23 sites in the county of Uppsala in Sweden has recently been published (142). Split sampling using whole blood from diabetes patients was used over a three-year period to verify the analytical performance of the POCT device.

Table 2.6 below provides a brief summary of the differences between QC and QA testing.

Summary

In summarising this section of the thesis on establishing and managing a POCT service, there were no published papers found by this literature search on:

- Models for the organisation and management of a POCT service in the Australian Indigenous health care setting,
- Methods for the culturally appropriate training of Aboriginal Health Workers as POCT operators (and, as a corollary, whether Aboriginal Health Workers could indeed be successfully trained as POCT operators), and
- Local or national models for the surveillance of analytical quality (through internal quality control or external quality assurance testing) of POCT devices in an Indigenous health care setting.

Table 2.4. Examples of professional bodies that have published guidelines on establishing and maintaining a POCT service.

Country/Region	Professional Body	Reference Source
United Kingdom	Association of Clinical Biochemists	(143, 144)
	Joint Working Group on External Quality Assessment	(145, 146)
	Joint Working Group on Quality Assurance	(146)
Europe	European Committee for Clinical Laboratory Standards	(147)
	Dutch Association of Clinical Chemistry	(148)
	German Society for Clinical Chemistry	(149)
New Zealand and Canada	New Zealand Institute of Medical Laboratory Scientists and the Canadian Society of Laboratory Technologists	(150, 151)
USA	International Federation of Clinical Chemistry	(152)
	National Academy of Clinical Biochemistry	(153)
	National Committee for Clinical Laboratory Standards (NCCLS), now known as the Clinical and Laboratory Standards Institute (CLSI)	(154), (155), (122)
Australia	Australasian Association of Clinical Biochemists (AACB)	(156, 157)

Figure 2.2 Key principles for establishing and managing a POCT service.

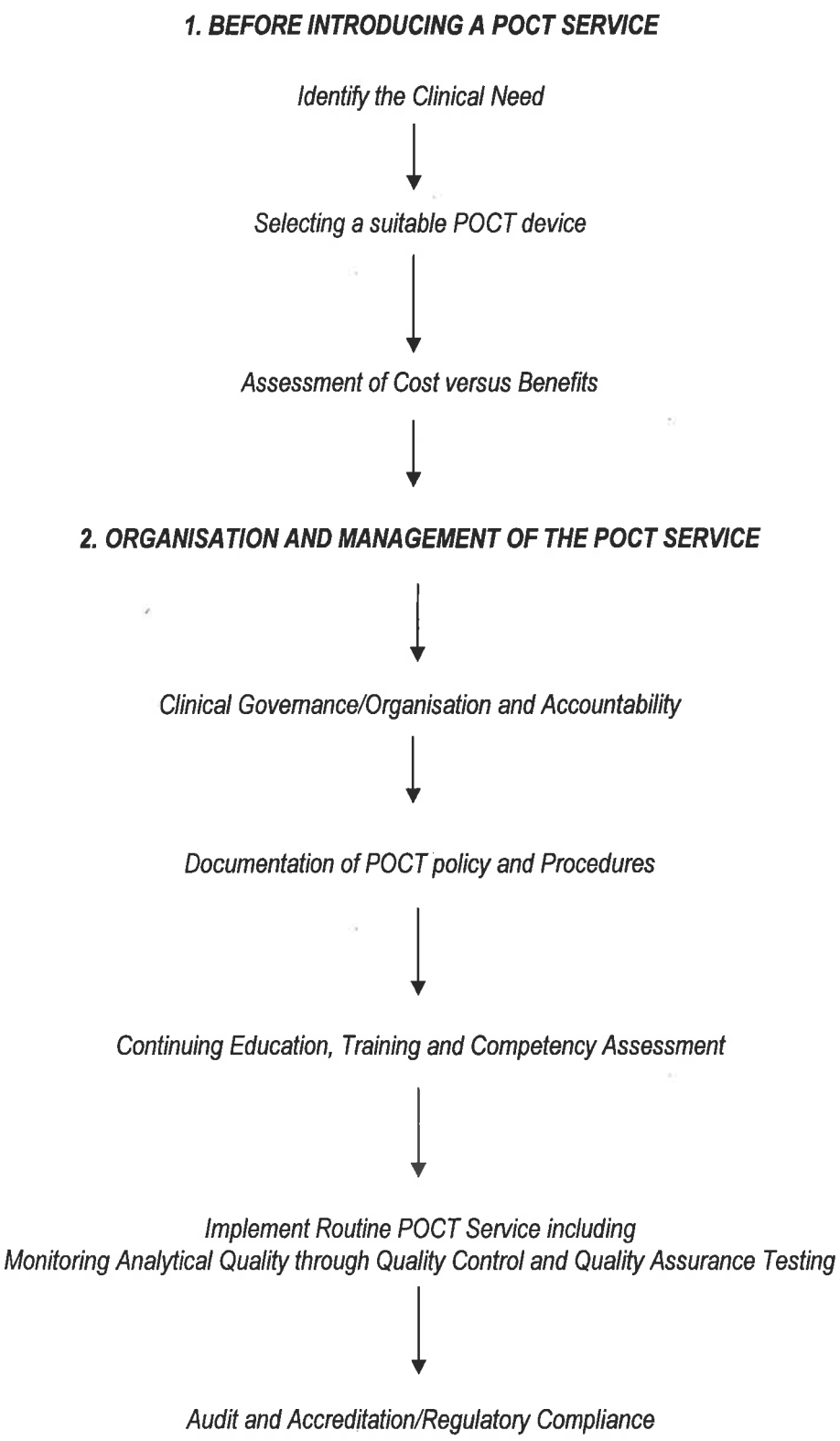

Table 2.5. Brief descriptive summary of key principles in establishing and organising a POCT service. (Table continues to page 55).

Principle	Summary of Principle
BEFORE INTRODUCING A POCT SERVICE Identify the clinical need	➢ POCT should be introduced to address a defined clinical need, with the ultimate goal of providing optimal quality of care for the patient. ➢ POCT should provide at least an equivalent, if not better, clinical service than is currently available through the laboratory, or provide access to a service that currently does not exist but for which there is an identified clinical need (65).
Selecting a suitable POCT device	➢ Survey the range of currently available POCT devices that can perform the required tests. This can be done by peer-reviewed literature search; consultation with laboratory, professional colleagues and/or vendor(s); or reference to evaluation reports by government agencies (158). ➢ Define the analytical expectations of the POCT instrument (particularly in relation to precision and accuracy). As an overarching principle, the POCT device must be able to achieve the same or at least equivalent level of analytical performance compared to that of the equivalent laboratory instrument when it is used for the same clinical purpose. Source data on current analytical performance standards (analytical goals) for the analyte (128-132). ➢ Source information on other aspects of analytical performance. These include (where appropriate) associated test menu, measuring range, linearity, common interferences, calibration requirements, availability and suitability of internal quality control (QC) and external quality assurance (QA) materials, maintenance of the POC equipment, level of vendor support for servicing and/or repair, and reference intervals, clinical decision levels and panic values. ➢ Validate the POCT device prior to its introduction to ensure that it meets analytical expectations (159-161). Ideally validation should take place at the intended site of use by the (trained) operator who would be expected to routinely use the device, with the support of the laboratory or the specialist

Principle	Summary of Principle
	POCT service provider and the vendor. If this is not possible, then the technology should be validated by the supporting laboratory or specialist POCT service provider. ➢ Assess the impact of the introduction of POCT on the site's organisation and infrastructure. These include (i) physical (non-analytical) attributes of the POCT device - sample type and volume, size and portability of the device, power source (battery, AC or both), degree of device automation and connectivity, and turnaround time for result, (ii) expectations of the staff - user-friendliness of device, number of manual steps, complexity and labour intensiveness of device operation, and reagent preparation time, (iii) projected future workloads and/or patterns of testing – there needs to be an acceptable level of POCT activity over a defined time period to ensure maintenance of POCT operator skills, (iv) spatial requirements - adequate space needed for patient preparation and sample collection, POCT equipment, ancillary equipment eg centrifuges and fridges, and storage of reagent, quality testing kits and consumables. Fridge space may be a crucial element to consider, particularly in rural and remote settings, (v) health and safety – a safe working environment for both patients and staff is needed for POCT; one that has adequate lighting, power, temperature control, plumbing, waste disposal and infection control.
Assessment of cost vs benefit	➢ An assessment of the costs of introducing the POCT system - and weighing up this cost up against the defined clinical, patient, operational and/or service delivery benefits of introducing such a system - is an implicit part of the decision-making process for the adoption of POCT (84, 162). ➢ Both capital and variable costs need to be taken into account when determining the total costs of implementing POCT (111, 163).
ORGANISATION AND MANAGEMENT Clinical Governance	➢ Clinical governance for POCT should provide a quality system that has as its objectives (i) the optimisation of patient care through practising evidence-based medicine and ensuring the clinical effectiveness of POCT is maximised, (ii) the establishment of a well-defined organisation and accountability structure for POCT and (iii) the minimisation of patient risk through the delivery of a quality POCT service (66, 68, 118).

Principle	Summary of Principle
Organisation and Accountability	In an 'ideal' POCT setting, there needs to be a clearly defined organisational structure with lines of accountability for each and every facet of the POCT service. ➢ The POCT Director (usually the most senior clinical staff member available) has overarching responsibility for clinical governance (110). ➢ Under the POCT Director, a POCT Co-ordinator (experienced in the practice of POCT and with a strong laboratory background) should oversee and manage the POCT service (65, 66, 110). ➢ The POCT Director and Co-ordinator should be supported by a multidisciplinary committee (POCT Management Committee or Coordination Committeee) (65, 111, 164). This structure encourages a whole-of-system approach to POCT and ensures all stakeholders feel part of delivering an effective POCT service (66). Stakeholders will vary according to the nature and location of the specific POCT service being implemented but may include health professionals such as other clinical staff, other laboratory scientists, nurses, nurse educators, diabetes educators, IT personnel, pharmacists, finance and planning officers, risk managers (64, 66) and a patient or consumer representative. ➢ A POCT Site Supervisor (usually a senior nurse) may act as a link between the POCT Coordinator/POCT Management Committee and the POCT Operator, who represents the person in the organisation who performs POCT at 'the bench level' (165). It should be emphasised that his 'ideal' organisational hierarchy may be impractical or impossible to implement in small services or in rural and remote services with limited staff and should be tailored to local needs.
Documentation of POCT Policy and Procedures	➢ A Quality Manual (in hard copy and/or electronic form) should be kept as an accessible and logically organised primary source for describing POCT policy and procedures for delivering a quality POCT service. ➢ The Quality Manual should be used as the benchmark against which the quality of the POCT service can be continually reviewed and assessed.

Principle	Summary of Principle
Continuing Education, Training and Competency Assessment	➢ POCT should only be carried out by staff who have undergone appropriate initial training and competency certification, who have their competency levels regularly assessed, and who participate in regular retraining and recertification sessions (65, 122, 166). ➢ POCT training should be organised by the POCT Coordinator under the direction of the POCT Management Committee and delivered by the POCT Coordinator. ➢ A training manual should be provided for all candidate POCT Operators. The content of the training manual will be determined by the nature of the POCT service being implemented and the needs of the organisation undertaking POCT; however, particularly in a non-hospital setting, candidate POCT Operators are unlikely to have had access to any previous formal training in laboratory or analytical concepts (including quality control and quality assurance). ➢ Training should cover both the theory and practice of conducting POCT. ➢ At the completion of formal training, trainee competency should be determined by written and practical assessment. ➢ Successful trainees should receive a competency certificate, with a fixed expiry date, at the completion of training. ➢ Post training surveillance of competency should be undertaken by regular review of quality control and quality assurance testing results. ➢ Competency should be formally reviewed regularly through retraining and education updates. ➢ A register of all persons receiving initial and renewed competency certificates should be prepared and maintained (165).
Implement Routine POCT Service including Monitoring Analytical Quality	Routine POCT should proceed, paying particular attention to: ➢ Addressing all aspects of the total testing process including pre-analytical (patient preparation and specimen collection), analytical and post analytical (result turnaround time, reporting, interpretation and actioning) factors.

Principle	Summary of Principle
	➢ Monitoring analytical quality through established practices such as internal quality control and external quality assurance testing procedures; these quality management procedures should be considered mandatory components of a POCT service. Quality materials, procedures and frequency of testing will vary depending on the type of POCT device used and whether the service participates in local or national quality assurance programs.
Audit and accreditation/regulatory compliance	➢ It is important to continually audit and document the performance of the POCT system both internally and, where required, externally through accreditation by a regulatory agency. Where findings are below expectations or benchmarks, then continuous quality improvement measures should be implemented. Currently in Australia, there are no specific government regulations or accreditation requirements for POC devices and POCT testing (167), other than a provisional accreditation framework being trialled in the Australian Government's POCT in General Practice Trial (34, 36, 113, 168).

Table 2.6. Summary of main differences between QC and QA testing procedures.

Parameter	**Quality Control**	**Quality Assurance**
Assessment	Internal, immediate assessment of analytical performance specifically for POCT site conducting the test	External, delayed assessment of analytical performance with results compared to peers (other participating POCT sites)
Samples tested	Usually two or three levels	Multiple levels
Target Values	Known at time of testing	Not known at time of testing
Analytical Performance Indictor measured	Precision	Precision and Accuracy

CRITICAL APPRAISAL OF THE EVIDENCE BASE FOR THE EFFECTIVENESS OF POINT-OF-CARE TESTING IN DIFFERENT CLINICAL APPLICATIONS

Introduction

One of the aims of this research program was to assess the effectiveness of POCT in the Australian Indigenous health care setting. The purpose of this section of the literature review was to critically appraise how the current evidence for the effectiveness of POCT has been studied in other clinical settings and to assess whether these approaches could be applicable to the Indigenous health care setting. The literature review focusses initially on the hospital in-patient setting (the most widely studied setting for the effectiveness of POCT), followed by the primary care setting (as there is now considerable current interest in this setting with health care being increasingly devolved to the community). Finally the evidence base for the effectiveness of POCT for diabetes and renal disease management in both primary and secondary settings is critically assessed, as this is the POCT application of most relevance to this research program.

The growth of POCT during the 1990s occurred in parallel with the development of evidence-based medicine and evidence-based laboratory medicine (57, 169-172). The measurement of outcomes is now viewed as an integral part of developing and maintaining an evidence base to support the use of pathology tests, including POCT. Outcome measures in the literature reviewed as part of this thesis have been categorised under the following broad headings: clinical outcomes (where a defined benefit to the patient can be measured), operational outcomes (where there is a benefit for the delivery of care) and economic outcomes (where benefits to the patient, healthcare provider or society overall can be demonstrated) (45, 56, 63, 83, 169, 173, 174).

Mortality and morbidity are critical clinical outcomes by which to judge the overall effectiveness of POCT. However, these are difficult to measure because (i) it may take a long time for these endpoints to be reached and (ii) there are many elements of long term clinical care that impact on

mortality and morbidity outcomes making it difficult to determine the specific contribution made by the pathology test alone (172). For these reasons, a variety of short-term, readily measured 'surrogate' outcome markers have been used to assess the effectiveness of POCT (169, 172). Examples of these surrogate markers include clinical outcomes such as more rapid stabilisation of an acute condition or more rapid and sustained optimisation of therapy for chronic diseases; operational outcomes such as reduced surgery time and reduced patient waiting time; and economic outcomes such as reduced use of medical products. In many instances, outcome measures can have benefits which overlap more than one category; for example reduced length of stay can have both operational and economic benefits and reduction in disease complication rates can have both clinical and economic benefits. These and other surrogate outcome measures will be described in detail in the following sections of this thesis.

Most of the early POCT literature focussed on either (i) the speed (or faster turnaround time) of the POCT result without relating speed to an outcome measure or (ii) the evaluation of a new POCT device and/or application of POCT without conducting an outcomes assessment of the clinical, operational or economic benefits (62, 175). The lack of outcome-based studies on POCT led to repeated calls in the literature for more research to be performed in this area and guidelines on how to conduct such research in both primary care and hospital settings were proposed by several authors (61, 176-179). Rainey and Scott (178, 179) recommended that, to obtain maximum benefit from a POCT outcome study, the following was required:

- a prospective randomised controlled study design should be implemented where possible,
- a surrogate outcome measure that is easily measured and can be assessed within a short time frame should be selected,
- confounding sources of variability should be minimised, and
- site-specific factors that may affect results should be identified.

As shown in the following sections, improved studies of POCT outcomes can now be found in the more recent literature.

POCT Outcome Studies In the Hospital In-Patient Setting

The most common and widely published application for POCT is the acute care hospital in-patient setting, where POCT is used widely in the emergency department, critical care units (including adult and neonatal intensive care and coronary care) and the operating theatre.

Even though acute care hospital-based POCT is not the principal focus of this thesis, a representative sample of papers from this area have been selected for review because they report on the effectiveness of a variety of POC tests, across a range of acute hospital settings, and using different outcome measures. They also illustrate the diversity of study designs employed and results found. The study methodology and key findings of these papers is summarised in Table 2.7.

Study designs included randomised controlled trials (180-185), cohort studies (186-189), and pre and post studies (190-193). Many of the studies examined POCT in a complex health setting where other elements of the total clinical care process (notably time delays in waiting for the availability of beds and other non POCT tests and medical procedures) were rate limiting steps in measuring outcome benefits (183, 189, 191, 192). Others measured POCT outcomes in patients who were admitted but not discharged from the emergency department (193). The small sample size of some studies, including one randomised controlled trial, limited the generalisability of the benefits found (180, 187). In another study, improvements in technology and equipment across the lifetime of the study confounded the differences in outcome measure observed between the historical and test cohort (188).

Results reported for specific outcome measures were variable, as summarised in Table 2.8. Some studies reported positive benefits following the introduction of POCT, while other studies contradicted those findings even for the same test conducted in the same hospital location.

Length of stay (LOS) was examined as an outcome measure in four emergency department (ED) studies (179, 183, 185, 192). Murray *et al* observed a reduction in LOS in ED patients having POC electrolyte and blood gas tests; however this difference was only observed in patients who were discharged from the hospital ED and not in those admitted (185). In contrast Kendall *et al* found no difference in LOS in ED patients undergoing the same tests (183); however Kendall *et al* noted other elements of clinical practice, particularly availability of inpatient beds, needed to be changed to take advantage of the faster results by POCT. Similarly, Parvin *et al* found no difference in LOS between POC or laboratory electrolyte, urea and glucose measurement (192), although the applicability of their findings were limited because the turnaround of laboratory results was significantly enhanced in this study by the very close proximity of the laboratory to the emergency department and the use of a rapid pneumatic tube for specimen transport to the laboratory (179, 192).

Zarich *et al* found a reduced LOS in patients with and without acute coronary syndrome (ACS) who had POC troponin T (cTnT) tests performed in addition to standard cardiac tests compared to standard tests only (184). Singer *et al* also found a reduced length of stay in ED patients with chest pain receiving POC troponin I (cTnI) testing who were subsequently admitted to hospital; although the impact of POCT was not examined in those discharged (193). In contrast, Collison *et al* found no difference in overall LOS among all patients admitted to coronary care with chest pain and suspected ACS who received cTnT POC or laboratory testing as part of a broad cardiac management strategy. However, a reduction in non-coronary care unit stay and overall hospital stay was observed in patients considered at low risk of ACS and ruled out of further intensive investigation by a negative cTnT POCT result (181).

Chen *et al* observed a reduced LOS in patients who had access to an intraoperative parathyroid hormone (iPTH) assay as part of parathyroid surgery compared to those patients who did not have access to this POC test. However the number of patients for whom iPTH was available was small (over 5-times less than the number of control patients), making the generalisability of the findings limited (186).

Total patient waiting time was examined as an outcome measure by the ED studies of Nicholls *et al* and Van Heyningen *et al* (189, 191). Nicholls *et al* found decreased patient waiting time for patients needing renal testing but not in patients requiring coagulation studies until systematic changes in patient management strategies were made. Van Heyningen *et al* found no difference in patient waiting time for POCT versus laboratory electrolyte results; but their finding was confounded by reduced bed availability and delays associated with clinical investigations other than POCT.

Collectively the studies of Kendall *et al*, Parvin *et al*, Nicholls *et al* and Van Heyningen *et al* emphasise that the capacity of POCT to deliver a positive outcome benefit is contingent on the POCT result being acted upon in a timely and efficient clinical manner and the effective integration of POCT with all other aspects of patient care (62, 83, 174). Kilgore *et al* also highlighted an important distinction between analytical turnaround time of the POCT result and therapeutic turnaround time, which is the time taken between the decision to test (by POCT) and the initiation of therapeutic intervention by the clinician (194). Improved outcomes can only occur when POCT and therapeutic intervention operate in concert and the confidence and willingness of clinical staff to respond to and make management decisions based on POCT is the ultimate driver for the implementation of POCT (62).

Becker reported a significantly reduced time to achieve an optimal therapeutic state of systemic anticoagulation in patients receiving an activated partial prothrombin time (APPTT) by POCT rather

than the laboratory; nonetheless the study was conducted on a very small number of patients (as a sub-study of a larger investigation) and the generalisability of its findings are therefore limited (180).

Reduced intra- and post-operative complication rates in patients having access to iPTH assays were also found in studies by Irwin *et al* and Chen *et al* but both studies were limited by the small numbers of patients investigated (186, 187).

Rossi *et al* found reduced mortality rates in a current, but not historical, cohort of paediatric intensive care patients undergoing POCT lactate testing during cardiac surgery (188); however improvements in technology and equipment used in cardiac surgery over the study period may have contributed to the reduced mortality. In contrast, no reduction in mortality following POCT was reported in the ED studies of Kendall *et al* and Collison *et al* (181, 183).

Increased clinical and patient satisfaction was reported by Nicholls *et al* but only in a qualitative sense with no detailed results of clinical or patient satisfaction surveys being presented (191). Clinical and patient satisfaction remains a valid POCT outcome measure despite being poorly addressed in the literature.

The studies of Zarich *et al* and Chen *et al* and the randomised controlled trial conducted by Despostis *et al* show POCT can result in cost savings associated with reduced length of hospital stay and more efficient use of resources, facilities, clinical and nursing time (182, 184, 186). Nonetheless, the issue of cost effectiveness of POCT is highly contentious and remains widely debated in the literature. On a purely cost per test basis, POCT is often cited as being more expensive than laboratory services. This is largely because laboratories have the advantage of economy of scale by performing large numbers of a particular test in a single analytical run, whereas POCT is mainly conducted with a single-use testing cartridge (195-200). Other authors have stated that the ease of availability of POCT can lead to an over-utilisation of tests performed and an

increased cost of care (60, 83). The longer-term economic benefits from POCT which may accrue as a result of the delay in the onset of complications and the wider societal benefits through improved quality of life and greater longevity remain extremely difficult to measure (174). As Freedman states: 'Few studies to date have taken a holistic view of the economic benefit of POCT. There is an urgent need for research comparing the cost of the entire episode of care in patients with POCT versus the same care in patients without POCT' (118). Each clinical situation must assess the cost-benefits of POCT in its own unique circumstance (79).

Table 2.7. Selected POCT outcome studies in the acute care in-patient hospital setting. (Table continues to page 68).

Outcome Category Assessed	POCT Outcome Measure(s)	Location of Study	Study Design	POC Test	Author	Summary of Methodology and Key Findings
Operational	LOS	Emergency Dept (ED)	RCT	Electrolytes, blood gas and metabolites	Murray (185)	180 patients randomly allocated to having either ED POCT or laboratory tests. Patients randomized to POCT (n = 93) had a median stay of 3 hrs 28 min (IQR 2:28 to 5:30), while those allocated to laboratory testing (n = 87) had a median stay of 4 hrs 22 min (IQR 3:04 to 5:47). This difference in LOS was statistically significant (p = 0.02). However, when all patients who were discharged or admitted where compared, the reduced LOS was only significant among discharged patients (n=135). Median LOS in the discharged patients was 3.05 (IQR 2.22 to 4.08) in the POCT group and 4.17 (IQR 3.0 to 5.41) in the control group, p <0.001. Median LOS in the admitted group was 6.07 (IQR 3.5 to 8.5) in the POCT group and 4.46 (IQR 3.2 to 6.1) in the control group, p=0.25, ns).
Clinical and Operational	Change of treatment in which timing was considered critical to clinical outcome LOS Mortality rate	ED	RCT	Electrolytes, blood gas, PCV and haemoglobin	Kendall (183)	1728 patients were randomly allocated to having either ED POCT or laboratory tests. Changes in management in which timing was considered to be critical occurred in 59 out of 859 patients having POCT (6.9%, 95%CI 5.3% to 8.8%). Decisions were made 74 minutes earlier (95%CI 68 min to 80 min, p <0.0001) when POCT was used for haematology tests compared to laboratory testing, 86 minutes earlier (95%CI 80 min to 92 min, p <0.0001) for biochemical tests, and 21 minutes earlier (95%CI -3 min to 44 min, p = 0.09, ns) for analyses of arterial blood gases. Importantly, there were no differences between the groups in the amount of time spent in ED, length of stay in hospital, admission rates, or mortality.
Operational	LOS	ED	Pre and Post	Electrolytes, urea & gluc by i-STAT	Parvin (192)	4985 patients seen in ED. During two 5-week and 3-week control periods (before), tests were performed by laboratory on 2918 patients. During 5-week experimental period (after), tests were performed by POCT in ED on 2067 patients.

Outcome Category Assessed	POCT Outcome Measure(s)	Location of Study	Study Design	POC Test	Author	Summary of Methodology and Key Findings
						There was no difference in LOS (median time between triage and either admission/discharge) between experimental and control groups (209 vs 201 mins respectively, p >0.05). Stratifying patients by presenting condition or discharge/admission status did not result in difference in LOS.
Operational and Economic	LOS Hospital charges Hospital admissions	ED	RCT	TnT	Zarich (184)	856 consecutive patients with suspected MI were randomised to a control group having standard tests (ECG and CKMB) or TnT group (having standard tests plus TnT) performed at 3 and 12 hrs after presentation. Significant reductions in hospital LOS were seen in TnT patients both with (3.6 vs 4.7 days; p = 0.01) [n=654] and without (1.2 vs 1.6 days; p = 0.03) [n=202] acute coronary syndromes compared with controls. Total hospital charges were reduced in a similar fashion in TnT patients with and without acute coronary syndromes ($15,004 vs $19,202; p = 0.01, and $4,487 vs $6,187; p = 0.17, respectively) compared with controls. TnT patients without acute coronary syndromes had fewer hospital admissions (25% vs 31%; p = 0.04), whereas TnT patients with acute coronary syndromes had shorter telemetry and coronary care unit lengths of stay (3.5 vs 4.5 days; p = 0.03) compared with controls.
Operational	LOS	ED	Pre and Post	TnI	Singer (193)	336 consecutive patients with chest pain seen in ED and subsequently admitted over a one month period. During the first 2-week period (before), only laboratory testing of TnI was performed. During the second 2-week period (after), treating nurses performed POCT TnI, as well as laboratory testing. There were 232 patients before and 134 after introduction of POCT. ED length of stay (time from patient triage until patient left ED for the admitting floor) was significantly reduced after introduction of POCT (5.2 hours [95%CI 4.6 to 5.8 hours] versus 7.1 hours [95%CI 6.6 to 7.7 hours]; mean difference 1.9 hours [95%CI 1.1 to 2.7 hours]).

Outcome Category Assessed	POCT Outcome Measure(s)	Location of Study	Study Design	POC Test	Author	Summary of Methodology and Key Findings
						The time until the admission was called in to bed control was also significantly reduced after introducing POCT (2.7 hours [95%CI 2.4 to 3.1 hours] versus 4.7 hours [95%CI 4.3 to 5.0 hours]; mean difference 1.9 hours [95%CI 1.4 to 2.5 hours]).
Operational	LOS Mortality rate	Coronary Care unit (CCU)	RCT	TnT	Collison (181)	263 consecutive admissions to CCU with chest pain and suspected acute coronary syndrome were randomized to measurement of TnT by POCT or by the lab only as part of a protocol-driven management strategy including clinical features, ECG and other cardiac markers. Outcome measures included mortality and length of stay in all patients and those considered at low risk and triaged for early discharge. Overall there was no difference in length of stay or mortality in all patient (overall hospital LOS 202 hrs for POCT versus 218 hrs for lab; 6-month mortality 4/131 POCT vs 1/132 lab). However, in those considered at low risk (n = 64) there was a significant reduction in median length of non-CCU stay (79.5 hrs POCT vs 145.3 hrs lab) and overall hospital stay (149.9 hrs POCT vs 209.3 hrs lab) in those randomized to POCT ($p<0.05$).
Clinical, Operational and Economic	LOS Total hospital charges	Operating theatre	Cohort Study	PTH	Chen (186)	The length of hospital stay and total hospital costs were compared in two groups: Group 1 comprised 33 patients with hyperparathyroidism who underwent minimally invasive parathyroidectomy with the support of iPTH between March and Nov 1998, while Group 2 consisted of 184 consecutive patients who underwent bilateral parathyroid surgery by the same physician between 1990 and 1996. Group 1 with iPTH had a significantly shorter LOS than Group 2 (0.3 ± 0.2 vs 1.8 ± 0.1 days respectively, $p<0.001$). Group 1 with iPTH had a significantly lower total hospital costs than Group 2 (US\$3174 $\pm$ \$386 vs \$6328 $\pm$ \$292 respectively, $p<0.001$).
Clinical	Surgical success	Operating Theatre	Cohort study	PTH	Irwin (187)	Two groups of patients had re-operative parathyroidectomy for failed surgery or recurrent disease. In group 1 (n=31), intraoperative PTH (iPTH) assays were performed to assist localisation and confirm excision, whereas in group 2 (n=17) this intraoperative PTH adjunct was not available. In group 1, iPTH assisted in localising and confirming complete excision of parathyroid glands in all but

Outcome Category Assessed	POCT Outcome Measure(s)	Location of Study	Study Design	POC Test	Author	Summary of Methodology and Key Findings
						2 cases (94% success rate). In group 2 without access to iPTH, there were four surgical failures (76% success rate). Thus with intraoperative PTH available, the need for re-operative parathyroidectomy reduced from 94% to 76%.
Operational and Clinical	Total patient waiting time Patient satisfaction	ED	Pre and Post	Coagulation and renal tests	Nicholls (191)	216 patients requiring testing for coagulation (prothrombin time/activated partial thromboplastin time) and/or renal function (urea, creatinine, sodium, and potassium) before elective invasive cardiac and radiological procedures were studied over 7 months. Overall patient management and workflow were examined in phase 1. POCT was implemented in phase 2 but laboratory results were used for patient management. In phase 3, POCT results were used for therapeutic decisions. Phase 4 optimised workflow around the availability of POCT. In phase 1, 44% of laboratory results were not available before the scheduled time for procedure (n = 135). Mean (SD) waiting times (arrival to procedure) were 188 (± 54) min for patients who needed renal testing (phase 2; n = 14) and 171 (±76) min for those needing coagulation testing (n = 24). POCT decreased patient wait times for patients needing renal testing (phases 3 and 4 combined, 141 (± 52 min); n = 18; p = 0.02). However, for patients needing coagulation testing, wait times improved only when systematic changes were made in workflow (phase 4, 109 ± 41 min; n = 12; p = 0.01).
Operational	Total patient waiting time	ED	Cohort	Electrolytes	Van Heyningen (189)	Total patient waiting time for POCT results available in ED (n=131 patients) was compared to waiting times resulting from either a porter to carry patient samples to lab (n=191 patients) or the use of a rapid pneumatic tube to transport samples to lab (n=192 patients). There was no difference in total patient waiting time for POCT results available in ED (median 219 mins) compared to waiting times resulting from transport to the laboratory by the porter (median 212 mins) or the pneumatic tube (median 258 mins); p value not stated.
Clinical	Stabilisation of acute condition	CCU	RCT	Coagulation	Becker (180)	33 heparin-treated patients with active thromboembolic disease were randomised to activated partial prothrombin time testing (APTT) by bedside POCT or by the laboratory. (This randomised controlled trial was a sub-study within a broader study on comparative TAT of APTT measurements by POCT and lab on 120 patients).

Outcome Category Assessed	POCT Outcome Measure(s)	Location of Study	Study Design	POC Test	Author	Summary of Methodology and Key Findings
						The time to achieve an optimal therapeutic state of systemic anticoagulation was 8.2 hours for POCT and 18.1 hours for the lab ($p < 0.005$). The time from APTT determination to a management decision regarding heparin titration adjustments was 14.5 minutes and 3 hours for POCT and lab testing, respectively ($p < 0.001$).
Clinical	Mortality rate	Paediatric cardiac intensive care unit	Cohort study	Lactate	Rossi (188)	Mortality rates in 1656 paediatric patients undergoing cardiac surgery from 1995 to 2001 (historical cohort) were compared with 710 patients undergoing the same surgery from 2001 to 2003 (test cohort). In the latter group, blood lactate measurements were performed serially for 24 hrs after surgery with results being linked to goal directed medical therapy (GDMT). The authors state improvements in technology and equipment used in cardiac surgery had occurred over the study period. Mortality was lower for the test cohort (1.8 vs 3.7%, $p = 0.02$). A reduction in mortality between test and historical cohorts was noted in neonates (3.4 vs 12%, $p = 0.02$), but not in older patients. Patients in the test cohort undergoing higher risk operations had a significant reduction in mortality when compared to the historical cohort (3 vs 9%, $p = 0.006$). No difference was noted in patients undergoing lower risk operations.
Clinical, Operational and Economic	Intra and post operative complications Operating time Blood product usage	Operating Theatre	RCT	Coagulation	Despostis (182)	254 patients requiring cardiopulmonary bypass (CPB) surgery were randomised to a control group receiving fixed anticoagulation protocol following bypass or an intervention group receiving anticoagulation and protamine therapy based on an intraoperative POC haemostasis testing system. Intervention group had shorter operating time, half as many patients required peri-operative blood products (fresh frozen plasma, platelets and cryoprecipitate) and had less chest drainage in the first 4 hours after surgery. Annual cost savings in reduced blood product usage were estimated at $267,700 (at mid 1990s prices).

LOS = length of stay; RCT = randomised controlled trial; TnT = troponin T; TnI = troponin I; IQR = interquartile range; ECG = electrocardiogram; CKMB = creatine kinase from heart muscle; TAT = turnaround time

Table 2.8. Summary of reported outcome measures, illustrating variability in results.

Outcome Measure	Test	Acute In-Patient Hospital Setting	POCT Benefit Found	POCT Benefit Not Found
Length of Stay	Electrolytes	Emergency	Murray (185)	Kendall (183) Parvin (192)
	TnT TnI	Emergency	Zarich (184) Singer (193)	
	TnT	Coronary care		Collison (181)
	PTH	Operating Theatre	Chen (186) Irwin (187)	
Patient Waiting Time	Renal and Coag	Emergency	Nicholls (renal) (191)	Nicholls (Coag) (191) Van Heyningen (189)
Rapid Stabilisation of Acute Condition	Coag	Coronary care	Becker (180)	
Mortality	Lactate	Paediatric ICU	Rossi (188)	
	Electrolytes	Emergency		Kendall (183)
	TnT	Coronary care		Collison (181)

POCT Outcome Studies In the Primary Care Setting

As mentioned earlier in this literature review, care of patients (particularly with chronic conditions) is now being devolved away from the hospital to a range of primary care or community-based care giving environments conducive to POCT. Primary care represents the first point of contact for individuals, families and the community with the health care system and includes all care that occurs until referral to secondary and tertiary care providers (201). Interest in the application of POCT in primary care settings has continued to increase since the year 2000 (202).

The main health settings in which primary care POCT is conducted are general practice, pharmacies, and community health centres. In Australia, Aboriginal medical services (the majority of which are managed and controlled by an Aboriginal Board of Directors representing the community) constitute an important community-based primary care setting for Indigenous people (5) (and will be discussed in more detail later in this chapter). However, as stated previously, no articles on POCT in Aboriginal medical services were found in this literature review other than those published as part of this thesis by the author, those that relate to the research program described in this thesis (41, 42), or those in which the author has been a collaborative author or partner (29, 30).

In the late 1990s, Hobbs *et al* conducted a detailed systematic review of POCT in primary care for the National Health Services' Health Technology Assessment (HTA) Program in the United Kingdom (UK) (177). The major findings of this detailed review were summarised by Delaney *et al* two years later (61).

This HTA study identified just over 100 published papers covering POC biochemical, haematological and microbiological tests used in primary care including tests for diabetes, haematuria, home pregnancy, cardiac enzymes and allergy, anticoagulation, anaemia, deep vein thrombosis, streptococcal throat, Chlamydia, urinary tract and HIV infections, as well as markers of general

inflammation/infection (microbiological) (61, 177). The quality of these papers was poor due to the lack of reference standards and inappropriate statistical analyses being used. No randomised controlled trials were sourced.

Only 32 papers, describing 209 comparisons, passed quality filters for detailed appraisal in the systematic review. The large number of comparisons relative to the small number of papers arose because (i) some studies assessed more than one POC test, (ii) others measured the same POC test against more than one comparator and (iii) some investigated different aspects of the same POC tests (177).

Over 70% of the studies assessed in detail related solely to the analytical performance of these tests, without addressing an outcome measure. Some measured the same POC test but used different reference standards, while others used only a small number of patient samples for comparison, limiting the generalisability of the findings. Less than 10% of the studies reported both test performance and an outcome measure; however these studies were described by the authors as "extremely poor, seeming to be inadequately planned add ons" to test evaluations, while the quality of outcome measures was "poor, with almost no objective measurement" (61). Patient satisfaction was highlighted as an outcome measure that was poorly addressed by the reviewed literature.

Regarding cost benefits of POCT, the systematic review identified 18 papers containing health economic data. However, the quality of these papers was considered very poor, with most being either feasibility studies rather than outcome trials or reporting simple direct costs only (177).

Delaney *et al* summarised the evidence for the effectiveness of POCT in primary care in the late 1990s thus: 'Almost no reports were found of unbiased assessment of the effect of near patient tests in primary care on patient outcomes, organisational outcomes, or cost (61).' The lack of quality

evidence for the effectiveness of POCT in the primary care setting at this time led to the publishing of standards required for evaluations to be undertaken in this setting (176). As will be described shortly, some improvements have been seen in primary care outcome-based studies in the recent literature.

POCT in general practice in Australia was the subject of an extensive recent literature review by Guibert *et al* in 2001 (34, 173). This review was commissioned by the Australian Government's Department of Health and Ageing in response to a significant lack of information on POCT in this setting in Australia. The review aimed to examine the role and value of POCT in general practice by reviewing current literature, sourcing the opinions of key stakeholders in this field (eg consumers, GPs and pathologists) and providing recommendations to the Government on policy and directions for future research for POCT in this setting. The POCT tests reviewed were glucose, lipids, potassium, haemoglobin, human chorionic gonadotropin (HCG), *Helicobacter pylori*, Streptococcus A, micro-urine (dipstick urinalysis and urine microscopy), international normalised ratio (INR), haemoglobin A1c (HbA1c), microalbumin, C-reactive protein (CRP) and substances of abuse (with the latter five being only superficially addressed). However the effectiveness of these tests was not discussed in any detail in this review, other than to note the evidence for the clinical and economic benefits of using POCT in general practice was 'patchy and generally not high level by NHMRC criteria'. In relation to the survey of stakeholders, the authors acknowledged that their study was not truly representative of national opinion as there was a decided 'urban Victorian bias'.

Nevertheless, this timely review documented a number of key recommendations regarding how POCT should be conducted in general practice in Australia, many of which have been subsequently incorporated into the interim standards and guidelines developed for the POCT in General Practice Trial which is currently being conducted in Australia (and which will be discussed later in this research program).

Pharmacy-based POCT is likely to be a growth area for the field of POCT during the next decade (203, 204). In the UK, over 6 million people visit the pharmacist every day and almost three quarters of all pharmacists currently conduct basic POCT (albeit mainly pregnancy testing). A small but expanding potential market exists for the use of pharmacy-based POCT for cholesterol and glucose screening, diabetes and lipid management, and monitoring of anticoagulation therapy, particularly in the USA, UK, Europe and Australasia (204) .

The current evidence base for the effectiveness of POCT in pharmacies is poor for a number of reasons (203, 204). Firstly, the number of studies documenting outcome measures is very limited. Secondly, most study designs focus on pharmacist-led interventions in which the introduction of POCT is but one of a broad number of changes made to patient management, making it difficult to attribute observed patient benefits to POCT alone (203, 204). Thirdly, as will be discussed specifically in the following section on diabetes and renal disease, almost all published studies either (i) do not document the POCT device used in the study or (ii) use laboratory and not POCT-generated results in their assessment of outcomes (205-213). Thus it is likely that many of these reported studies may not in fact represent POCT applications at all. This significant flaw in the literature reflects the inability of authors in this field to make the important distinction between pharmacist-led management interventions at the point of patient care and conducting pathology testing using POC medical devices at the time of patient consultation.

Although acute primary care POCT and POCT for coagulation monitoring are not the principal focus of this research program, a representative sample of papers from this area is briefly reviewed in Table 2.9; as for hospital-based POCT, these papers have been selected because they:

- report on the effectiveness of POCT in different primary care settings, for example general practice and community clinics,

- use different outcome measures, for example rate of antibiotic prescription for the acute marker CRP and time in therapeutic target range for the INR coagulation marker,
- illustrate the diversity of study designs, which include randomised controlled trials (214-216), randomised crossover studies (217, 218) and cohort studies (219), with each study design using sample sizes ranging from very small to large, and
- illustrate some positive outcome benefits from the introduction of POCT in the primary care setting although, as for the hospital setting, the overall quality of the reviewed studies was variable and their results were in some cases contradictory.

Antibiotic prescription rate was examined as an outcome measure in three well-designed studies involving POCT for CRP. Dahler-Ericksen *et al* did not find any difference in overall antibiotic prescription rate between general practitioners (GPs) using or not using POC CRP testing, although they did observe that patients with elevated CRPs greater than 50 mg/L measured by POCT did commence antibiotic treatment earlier (217). In contrast, Takemura *et al* and Bjerrum *et al* did find a reduction in antibiotic prescription in the POCT group (216, 219). However, Bjerrum *et al's* cohort study did not specify which POCT CRP method was used in this study and they could not conclude with certainty that the positive benefit found was not due to the causal relationship of the GP making the decision to prescribe antibiotics and then adjusting the diagnosis to fit the decision to treat.

Regarding cost effectiveness, Dahler-Ericksen *et al* reported net total cost savings despite POCT CRP being more expensive than the laboratory. Takemura *et al* reported a reduction in costs of antibiotics within the POCT group but this was offset by the more frequent prescription of a newer antiviral medication which pushed the total overall costs slightly higher in the POCT group (215).

The Takemura *et al* studies also highlight a recurrent issue identified in this section of the literature review. The authors state that 'this study was carried out ... in a primary care setting'. However the papers then assert that the patients selected for this study visited 'the General/Internal Medicine

Clinic of Nishi-Ohmiya Hospital (a regional/community 150-bed hospital treating approximately 500 outpatients per day)'. Whether this hospital outpatient clinic is a true primary care setting is contentious. As the systematic review of Delaney *et al* states: 'many papers were unclear about whether patients were recruited from outpatient departments or from primary care. Some primary care clinics seemed to be secondary-care based or outreach clinics' (61).

Percentage of time in the therapeutic range was examined as an outcome marker in two well-designed outcome studies by Fitzmaurice *et al* and Shiach *et al* (218, 220). Fitzmaurice *et al* reported a statistically significant increase in the percentage of time POCT intervention patients spent in the therapeutic range. In contrast Shiach *et al* reported no significant difference between intervention and control groups with this outcome measure, although this was a low powered study due to its small sample size. In both studies, the actual percentage differences found between the groups were small (7% or less) and were unlikely to be clinically significant. These studies highlight an important distinction between clinically significant and statistically significant differences in observed results.

Shiach *et al* reported greater patient satisfaction with community POCT monitoring but, apart from the statement that 98% of patients expressed a preference for the community clinic, no specific data is presented to justify this claim (218).

Outcome measures relating specifically to the use of POC tests for diabetes and renal disease (in both primary and secondary care settings) will be appraised in more detail in a subsequent section of this chapter due to their specific relevance to the this program of research.

Table 2.9. Selected POCT outcome studies in primary care settings (excluding diabetes and renal disease). (Table continues to page 78).

Outcome Category Assessed	Clinical Setting	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test	Author	Summary of Methodology and Key Findings
Clinical, Operational and Economic	Acute	Rate of antibiotic prescription Time to initiate antibiotic treatment Total operational costs	General Practice	Randomised crossover study	CRP	Dahler-Ericksen (217)	29 general practices (GP) and 1853 patients from a Danish county. GP randomised to two groups (i) using POCT for CRP [n=919] and (ii) mailing blood to lab for CRP [n=934]. Crossover at 3 months, for a further 4 months. Cost savings of $111,160 per year for county overall, due mainly to reduction in use of laboratory services by GPs. Net savings achieved despite CRP POCT being more expensive than lab CRP. Patients with CRP>50mg/L had antibiotic treatment started earlier when measured by POCT in GP ($p = 0.02$). However, there was no difference in antibiotic prescription rates between intervention and control groups (31.8% vs 32.6%, $p = 0.82$). Authors argued that improved education and better clinical guidelines may result in more appropriate use of antibiotics.
Operational	Acute	Antibiotic prescription rate	Regional community clinic	RCT	CRP	Takemura (216)	305 patients presenting with fever of less than 8 days duration and suspected of having infection. 147 patients underwent CRP and WBC testing before physician consultation (advance testing) and 154 patients did not receive these POC tests before consultation (control). (Patients with raised CRP and WBC were more likely to have a bacterial infection and require antibiotics). A significant reduction of 38% in prescription of antibiotics to acutely febrile patients was achieved in the group receiving advanced POCT (50% of patients receiving antibiotics compared to 88% in control group, $p < 0.001$). Comment: 9% of patients in the POCT group received antiviral medication compared to 4% in the control group ($p = 0.08$, ns).

Outcome Category Assessed	Clinical Setting	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test	Author	Summary of Methodology and Key Findings
Operational	Acute	Antibiotic prescription rate	General Practice	Cohort	CRP	Bjerrum (219)	1444 patients with suspected acute sinusitis where assessed over a three week period in late 2001/early 2002. A rapid CRP test was used by 281 (77% of GPs) to rule in or out antibiotic prescription for those patients suspected of bacterial vs viral sinusitis respectively. 86 (23% of GPs) did not use the POCT. The rate of antibiotic prescription was 59% (95%CI 56-62%) in the group of GPs using the CRP test compared to 78% (95%CI 73 to 82%) in those GPs that did not use the POCT (p not stated).
Economic	Acute	Total costs	Regional community clinic	RCT	CRP	Takemura (215)	Same patient group as in Takemura (216). A 30% reduction in total costs of oral and parenteral antibiotics was achieved with advance testing group compared to the control group (yen105,830 vs. yen151,102, p not stated). However, the savings were largely offset by more frequent prescription of newer, expensive antiviral medications. Overall, total operational costs were slightly higher in the POCT group (yen1,028,827 vs. yen984,105, p <0.001).
Clinical	Chronic	Time in therapeutic range	General Practice	RCT	INR	Fitzmaurice (214)	367 patients recruited from 12 general practices (9 intervention and 3 control) in Birmingham, UK. There were two control populations: patients randomly allocated as controls in the intervention practices (intrapractice controls) and all patients in control practices (interpractice controls). Intervention practice patients were randomized to intervention (nurse-led practice-based POCT anticoagulation clinic with CDSS) or control (hospital clinic) groups. 367 patients were recruited (122 intervention patients, 102 intrapractice control patients, and 143 interpractice control patients). Time spent in the international normalized ratio range showed significant improvement for patients in the intervention group compared to the control group (69% vs 62%, p = 0.008). There was no significant difference in mortality rates or serious adverse events.

Outcome Category Assessed	Clinical Setting	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test	Author	Summary of Methodology and Key Findings
Clinical	Chronic	Time in therapeutic range	Community clinic	Randomised crossover study	INR	Shiach (218)	46 patients were randomized into two groups. At each visit, capillary blood was taken for the CoaguChek POCT device and venous blood for the laboratory coagulometer. In Group 1, for 6 months, dosage was based on the POCT result and for the second 6 months on the lab result. In Group 2, the order was reversed. The time spent within the target therapeutic range was 60.9% and 63.4% in the two time periods using POCT and 59.3% and 64.3% using the lab device (p = 0.2, ns). There was no significant difference in mean INR between devices (2.48 POCT vs 2.50 lab, p = 0.08). Comment: The authors conclude that patient questionnaires show greater satisfaction with community POCT monitoring but, apart from the statement that 98% of patients expressed a preference for the community clinic, no specific data is presented to justify this claim.

RCT = randomised controlled trial; CRP = C-reactive protein; INR = international normalised ratio

Table 2.10. Summary of reported outcome measures, illustrating variability in results.

Outcome Measure	Test	Primary Care Setting	POCT Benefit Found	POCT Benefit Not Found
Rate of antibiotic prescription	CRP	General Practice	Bjerrum (219)	Dahler-Eriksen (217)
		Community Clinic	Takemura (216)	
Cost benefit	CRP	General Practice	Dahler-Eriksen (217)	
		Community Clinic		Takemura (215)
Time in therapeutic range	Coag	General Practice	Fitzmaurice (214)	
		Community Clinic		Shiach (218)

POINT-OF-CARE TESTING FOR DIABETES AND RENAL DISEASE PREVENTION AND MANAGEMENT

This section of the literature review is presented in more detail because the application of POCT for the prevention and management of diabetes and renal disease represents the main focus of the author's research.

The Prevalence Of Diabetes

Globally

Significant changes in human behaviour, lifestyle and the environment particularly over the past 20 years have seen a rapid escalation in the prevalence of diabetes worldwide, with predictions that diabetes will reach epidemic proportions during the early part of this century (221-224). The global prevalence of diabetes exceeded 150 million adults in the year 2000, but this figure is predicted to rise to 220 million by 2010 and to 300 million by 2025 (224). Zimmet *et al* states: 'the prevention of diabetes and its micro- and macro-vascular complications should be an essential component of future public health strategies for all nations' (224).

Type 1 (or insulin dependent) diabetes, in which there is a complete lack of insulin production due to the auto-immune mediated destruction of pancreatic beta-cell islets, comprises approximately 10% of all cases of diabetes globally, with the majority but not all of cases presenting in childhood. Type 2 (or non-insulin dependent) diabetes is characterised by insulin resistance and/or abnormal insulin secretion and accounts for the balance of cases which generally occur in patients greater than 40 years of age (224). However of particular concern is the increasing incidence of type 2 diabetes in younger people, associated primarily with accelerating rates of childhood obesity in western societies (222).

Australia

Recently, the Australian Diabetes, Obesity and Lifestyle (AusDiab) Study was commissioned by the Federal Government to conduct a national study of diabetes prevalence in this country (225). The study measured blood glucose levels and glucose tolerance in 11,247 participants randomly selected from 42 regions across Australia. The study's key findings included: (i) the number of Australian adults with diabetes had increased three-fold since 1981, (ii) the national prevalence of diabetes among adults aged 25 years and over in the year 2000 was 7.5% (amounting to 940,000 people), (iii) the prevalence of impaired glucose metabolism was 16.3% and, (iv) for every known case of diabetes, there was estimated to be one undiagnosed case.

Indigenous Australia

Within Australia's Indigenous Aboriginal and Torres Strait Islander population, which numbers approximately 460,000 people and accounts for 2.4% of Australia's total population, rates of type 2 diabetes are significantly higher than those reported for the AusDiab study (226). The overall prevalence of type 2 diabetes among Australia's Indigenous people varies between 10-30% and is generally 3-4 times higher at any age than the general population, with an earlier age of onset. Indigenous Australians also experience 12-17 times more deaths due to diabetes than non-Indigenous Australians (227-229). In response to the significant burden of diabetes experienced by Australia's Indigenous people, the Federal Government's National Diabetes Strategy and Implementation Plan 1998 recommended that, to optimise the quality and accessibility of diabetes prevention and care for Indigenous Australians, the clinical utility of providing Indigenous health services with a point-of-care DCA 2000 analyser (Bayer Australia) to perform HbA1c POCT should be examined. This decision led to the development and establishment of the national Quality Assurance for Aboriginal and Torres Strait Islander Medical Services (QAAMS) Program which forms a significant component of this research program.

The Prevalence Of Renal Disease

Globally

Like diabetes, the burden of renal disease is continuing to rise globally for both patients and healthcare services. There has been a two-fold increase in the number of patients undergoing treatment for end-stage renal disease (ESRD) in the USA, Europe and Australia over the past decade, with diabetes being the primary cause of ESRD (230, 231).

Australia

The AusDiab Kidney study found that 16% of the 11,247 participants studied had at least one indicator of kidney damage, with the markers of damage being proteinuria, haematuria or reduced glomerular filtration rate (GFR) (231). In Australia, the treatment of renal disease has been estimated to account for 5.7% of the total health care budget (231).

Indigenous Australia

In Indigenous Australians, recent data from the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA), covering the period 1997-2001, indicated overall age-standardised rates of ESRD were 645 per million, almost 9-times the rate of 75 per million for non-Indigenous Australians (232). In many remote regions and in northern Australia, ESRD rates in Indigenous people reached epidemic proportions across this same period (1471 per million in the Northern Territory and 906 per million in Western Australia) (233-236). Rates of ESRD in Indigenous Australians also doubled every 4 years from 1985 to 1996 (235). The reasons for the significant burden of Indigenous renal disease are complex, inter-related and multifactorial, and include low birth weight, post streptococcal glomerulonephritis in childhood, obesity, alcohol, hypertension and repeated acute bacterial infections. However diabetes is without doubt the primary cause of ESRD in Indigenous Australians,

with 47% of all cases of ESRD in Indigenous people being directly attributed to diabetes compared to 17% for non-Indigenous Australians (234, 236, 237).

Overview Of POC Tests For Diabetes and Renal Disease and Their Clinical Utility

The main biochemical tests used in the prevention and management of diabetes and renal disease management, for which POCT devices are available, are haemoglobin A1c (HbA1c), microalbumin, lipids, glucose, electrolytes and creatinine, ketones and lactate (222). The first three tests will be specifically discussed as these are most relevant to this thesis, with a brief summary of glucose also provided.

Haemoglobin A1c

What is HbA1c?

Haemoglobin A1c (HbA1c) is formed by the attachment of glucose specifically to the N-terminal valine of the beta chain of haemoglobin. HbA1c is also often referred to loosely in the literature as glycated haemoglobin or glycohaemoglobin but these terms refer more generally to the attachment of glucose to haemoglobin at a range of sites including not only N-terminal valine but also side chain lysine groups of the two alpha and beta chains of adult haemoglobin A (238, 239).

Clinical Use of HbA1c

HbA1c has now become the universally accepted 'gold standard' pathology test for monitoring glycaemic control in patients with established diabetes. HbA1c provides a long-term measure of glycaemic control over the preceding 3-4 months (reflective of the progressive glycation of haemoglobin during the mean life span of red blood cells) (240).

The clinical utility of HbA1c was firmly established in two landmark randomised controlled trials conducted during the 1990s; namely, the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS). The methodology and key findings of these

studies is summarised in Table 2.11 (241-247). Both studies highlighted the importance of tightly controlled glycaemia, as assessed by HbA1c, in reducing long-term microvascular complications of diabetes.

HbA1c targets have also been proposed to guide clinical management. Since 1997, the American Diabetes Association (ADA) recommended a target HbA1c of less than 7% for optimal glycaemic control, whereas an HbA1c of greater than 8% indicated the need for more intensive clinical therapy (248, 249). An HbA1c of 7% currently remains as the optimal glycaemic goal for Indigenous Australians with diabetes (228, 250). However, the most recent ADA guidelines for standards of medical care in diabetes recommend the optimal HbA1c target for individual patients should be as close as possible to a normal HbA1c of less than 6%, without significant hypoglycaemia (251, 252).

Current ADA and Australian guidelines recommend that HbA1c should be performed 6-monthly in patients who have stable glycaemia and are meeting treatment goals, and 3-monthly in patients who are not meeting glycaemic goals or whose therapy has changed (251). More frequent monitoring of HbA1c is recommended for all Indigenous Australians with diabetes due to the high percentage of patients with poor control, with 3 to 4-monthly HbA1c testing being the default frequency (228, 250).

As Jeffcoate states: 'The place of HbA1c in diabetes management has become firmly accepted, established, even entrenched over the past 25 years' to the point where 'HbA1c assays play central roles in patient management, clinical guidance and audit, and clinical trial design' (253).

Limitations of the HbA1c test

Nonetheless, in critically appraising the clinical utility of the HbA1c test, there remain a number of issues which confound its effectiveness (253). There is significant analytical variability associated with laboratory (and POCT) methods for measuring HbA1c which has resulted in concerted efforts by the International Federation of Clinical Chemistry (IFCC) to introduce a reference system for the

global standardisation of HbA1c methods (239, 254-260). This system, which will involve the introduction of a new set of units for reporting of HbA1c values, is close to completion but not yet in place in routine pathology practice.

While HbA1c generally reflects mean glucose over the past 3-4 months, red cell turnover is exponential rather than linear and hence HbA1c concentration is weighted to recent glycaemia with 50% being formed in the most recent 30 days, 25% in the previous month and 25% in months three and four (261, 262). In addition, any condition which enhances erythrocyte destruction or reduces red cell survival such as haemolytic anaemia, hypersplenism or liver cirrhosis can cause falsely low HbA1c results to be reported (240).

In patients with end-stage renal failure, urea may dissociate to form cyanate which in turn condenses with the N-terminal amino groups of haemoglobin to form carbamylated haemoglobin. This carbamylated haemoglobin may co-migrate with HbA1c in charge-dependent methods causing falsely elevated HbA1c concentrations in renal patients (263).

Exact correlations between HbA1c and various components of glycaemia (fasting, post prandial and overall) remain uncertain while variable estimates of within- and between-subject biological variation make it difficult to extrapolate with certainty the predictive role of HbA1c across the general population (253, 262, 264-267). HbA1c values may also appear to be falsely near normal in a patient with extremely poor control who has recurrent alternating episodes of both severe hypoglycaemia and hyperglycaemia (252).

Structural variants of haemoglobin, including those found in haemoglobinopathies of both homozygous (HbSS, HbACC, HbAEE) and heterozygous (HbAS, HbAC and HbAE) origins as well as patients with persistently increased foetal haemoglobin (HbF), can cause spurious falsely low or falsely high HbA1c results, depending on the method used (252, 268, 269).

The association between glycaemic control and risk of microvascular complications in both type 1 and 2 diabetes has been firmly established and recent evidence from long-term follow-up of patients in the DCCT study suggests intensive therapy reduces the risk of cardiovascular disease in type 1 diabetes (243). However the evidence that monitoring of HbA1c can predict or prevent macrovascular diabetic complications (coronary artery disease, cerebrovascular disease or peripheral arterial disease) in patients with type 2 diabetes remains uncertain and controversial (238, 253).

Finally, while the clinical utility of HbA1c is firmly established in the management of diabetes, both ADA and National Health and Medical Research Council (NHMRC) Australian guidelines currently preclude the use of HbA1c as a screening test for the diagnosis of diabetes due to the its low sensitivity (251, 270). Nonetheless there is some recent evidence to support the further investigation of HbA1c as a potential diagnostic test, particularly in the rural and remote Australian Indigenous community setting where access to laboratory testing is difficult and the oral glucose tolerance test is impractical and inconvenient to perform (271).

Despite these limitations, HbA1c remains unchallenged as the most widely used and commonly accepted marker of glycaemic control in patients with established diabetes.

Table 2.11. Study Methodology and Key Findings of the DCCT and UKPDS Clinical Trials.

Study	No. of Patients	Diabetes Type	Methodology and Key Findings
DCCT	1441	Type 1	1441 patients with type 1 diabetes were randomly assigned to receive either intensive or conventional treatment. Intensive therapy involved the administration of insulin at least three times daily by injection from an external pump, with dosage guided by self-monitoring of blood glucose at least four times per day. Conventional therapy comprised one or two daily injections of insulin and daily blood or urine glucose self-monitoring and did not involve daily adjustments of insulin dose. After 6.5 years, the intensively treated group had a mean HbA1c of 7.2% compared to the conventionally treated group mean of 9.1% ($p < 0.001$). The risks of developing microvascular complications of diabetes, namely retinopathy, microalbuminuria and neuropathy, reduced by 76%, 39% and 60% respectively in the intensively treated group (241). These reductions in risk of progressive retinopathy and nephropathy resulting from intensive therapy in patients with type 1 diabetes have been sustained for a further 4 and 8 years following the cessation of the original DCCT trial (242, 244).
UKPDS	3867	Type 2	3867 patients with type 2 diabetes were randomly allocated to intensive treatment with a sulphonylurea drug or insulin, or conventionally treated with dietary advice alone. The aim of the intensively treated group was to achieve a fasting plasma glucose concentration of less than 6 mmol/L, while the aim of the group treated conventionally was to achieve the best fasting plasma glucose possible with diet alone. After 10 years, the intensively treated group had a mean HbA1c of 7.0% compared to conventionally treated group mean of 7.9% ($p < 0.0001$). The risks of developing retinopathy and microalbuminuria were reduced by 21% and 34% respectively (246).

Microalbumin

What is Microalbumin?

Microalbumin refers to the presence of subclinical amounts of albumin in the urine which exceed normal excretion but are undetected by conventional urine dipsticks. As will be discussed shortly, microalbuminuria is now a recognised early phase of diabetic nephropathy and indicates initial structural damage to the kidney causing loss of selective glomerular permeability (230, 272).

Microalbumin in urine has been measured either as (i) urine albumin excretion per day, (ii) urine albumin excretion (AER) in a timed (4hr or overnight) urine sample or (iii) the urine albumin:creatinine ratio (ACR) on a spot urine sample, as outlined in Table 2.12.

The 24-hour urine albumin excretion is considered the 'gold standard' for urine microalbumin measurement; however this specimen type is generally impractical to collect in an outpatient setting and is subject to timing and collection inaccuracies (238). The timed overnight urine requires the measurement of urine volume to calculate excretion, exhibits greater biological variation than the urine ACR measurement and is also subject to timing inaccuracies (273). Urine ACR correlates well with the 24 hour albumin excretion, is simple and convenient for the patient to collect, and the measurement of urine creatinine corrects for variation in concentration of the urine (251, 273). The 2006 American Diabetes Association (ADA) guidelines on the standards of medical care for diabetes state that the analysis of the urine ACR is 'strongly recommended by most authorities' (251).

The first morning urine is the preferred specimen for urine ACR measurement because the wide diurnal variation in albumin excretion is minimised and it is more likely that a false positive urine ACR result could occur with a random spot sample (274).

Table 2.12. Different measures of urine microalbumin.

Category of albuminuria	Source	Urine ACR (mg/mmol)	Timed Albumin Excretion Rate (AER) (µg/min)	24 hr Albumin Excretion (mg/24 hrs)
Normal	Diabetes Australia and RACGP (275)	< 2.5 mg/mmol M; <3.5mg/mmol F	<20 µg/min	n/a
	American Diabetes Association (251)	<3.4 mg/mmol (< 30 µg/mg)	<20 µg/min	<30 µg/min
Microalbuminuria	Diabetes Australia and RACGP (275)	2.6 to 25 mg/mmol M; 3.6 to 35 mg/mmol F	20-200 µg/min	n/a
	American Diabetes Association (251)	3.4 to 34 mg/mmol; (30-299 µg/mg)	20-199 µg/min	30-299 µg/min
Macroalbuminuria	Diabetes Australia and RACGP (275)	> 25 mg/mmol M; >35 mg/mmol F	>200 µg/min	n/a
	American Diabetes Association (251)	≥ 34 mg/mmol (≥300µg/mg)	≥ 200 µg/min	≥ 300 µg/min

Clinical Utility of Microalbumin

As mentioned previously, microalbuminuria is a recognised early phase of diabetic nephropathy and the measurement of microalbumin has become an important test in both the prevention and management of renal disease in patients with (and without) diabetes (230, 272).

Microalbuminuria is a predictor of the progression of renal disease to clinical albuminuria (also known as macroalbuminuria, overt proteinuria or overt nephropathy) and ESRD in type 1 and type 2 diabetes (and in non-diabetic kidney disease) (234). Without treatment, 80% of patients with type 1 diabetes and microalbuminuria progress to overt nephropathy with 50% of these developing ESRD within 10 years. In untreated type 2 diabetes patients, 20-40% progress to overt nephropathy and 20% of these develop ESRD within 20 years (274). In addition, there is a strong correlation between the degree of albuminuria at baseline and both the magnitude of decrease and rate of decline in renal function over time (238).

Microalbuminuria is also a predictor for risk of cardiovascular morbidity and mortality in patients with either type 1 or type 2 diabetes (and non-diabetic patients with hypertension) (234, 238, 272, 274, 276).

The importance of detecting microalbuminuria in patients with diabetes lies in the fact that the progression of renal disease can be delayed or prevented through early treatment with antihypertensive agents that target the renin-angiotensin system such as angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) (238, 272, 277).

Current best practice clinical guidelines recommended by the ADA state that patients with type 1 diabetes of greater than 5 years duration should have an annual test for microalbuminuria, while patients with type 2 diabetes should be tested for microalbuminuria at onset of diagnosis of diabetes and thereafter annually (251). An initial urine ACR in the microalbuminuric range should be repeated on at least two occasions over 3-6 months, with two out of the three results in the microalbuminuric range before a diagnosis can be confirmed (251, 274). This recommendation has been made not only because of the wide biological variability in albumin excretion as discussed previously but also because other confounding factors such as exercise within 24 hours, fever, infection, congestive heart failure, pyuria, haematuria, marked hypertension or hyperglycaemia can also cause a false positive urine ACR result (278).

Once microalbuminuria is confirmed, most guidelines recommend continued surveillance of patients to assess the response to therapy and progression of disease (251). For Indigenous Australians, recent recommendations state that urine ACR should be measured 6-monthly for diabetes patients with microalbuminuria and every 3-6 months for diabetes patients with microalbuminuria undergoing therapy (279).

Limitations of the Urine ACR test

In critically appraising the utility of the urine ACR test, there are several areas of concern. Firstly there is no international consensus on the units for urine ACR measurement. While most countries report urine ACR in units of mg albumin/mmol creatinine, the ADA still quotes µg/mg creatinine in its recommendations.

A single specimen of choice needs to be adopted globally for both screening for and monitoring of microalbuminuria. It is the author's view that the first morning sample should be recognised universally as the preferred specimen, but current ADA recommendations allow for a random spot urine sample or 'uniformity in timing for different collections in the same individual' (274).

Cut-offs for classification of albuminuria categories need to be standardised globally. Australian recommendations specify gender-specific cut-offs while the ADA has a single cut-off criteria with no gender difference (Table 2.12). A recent paper documents increased urine ACR levels with age and suggests that age- as well as gender-specific cut-offs should be reported (280).

The time frame for confirmation of the diagnosis of microalbuminuria following a single raised urine ACR is variable. For example the ADA allows 3-6 months for verification of microalbuminuria, but earlier guidelines recommended by the America National Kidney Foundation and the New South Wales Department of Health state that repeat testing for urine ACR should be conducted within 3 months and 6 weeks respectively for confirmation of microalbuminuria (281, 282).

As mentioned previously, false positive urine ACR measurements can occur due to a range of factors including urinary tract infections. Conversely a false negative urine ACR result can occur when a patient has gross proteinuria, due to the flooding of available antibody by an abundance of albumin (antigen excess). For these reasons, a urine dipstick test should always be performed prior

to conducting the urine ACR test to ensure the patient sample is suitable for analysis. Urine ACR testing is effectively ruled out if nitrites or leucocytes (indicating urinary tract infection) or excessive proteinuria (2+ or greater protein) is detected by the dipstick.

Recently, the reporting of a previously unknown non-immunoreactive form of urine albumin in diabetes patients separated by size exclusion HPLC has raised concerns about the accuracy of urine albumin measurements and a Working Group of the IFCC has been formed to address the issue of global standardisation of urine albumin (283-286).

From a clinical perspective, it should be noted that some patients with type 1 and type 2 diabetes can have a decreased glomerular filtration rate (GFR) in the absence of increased urine albumin excretion (251, 287, 288). For this reason, serum creatinine should be measured at least annually for the estimation of GFR in all patients with diabetes regardless of their urine microalbumin status (251). As a result of a recent recommendation by the Australasian Creatinine Consensus Working Party, most Australian laboratories now report an estimated or 'eGFR' based on the person's age, sex, race and serum creatinine (289). eGFR does not require body surface area measurements required by the previously and widely used Cockcroft-Gault formula (290, 291).

Despite these limitations, the urine ACR test is now widely accepted as a marker of early and progressive renal disease in patients with diabetes.

Lipids

The lipid profile of tests, namely total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, and triglyceride, are commonly measured as part of the prevention and management of patients at high risk of cardiovascular disease (CVD). The Australian Lipid Management Guidelines 2001, produced by the National Heart Foundation of Australia and the

Cardiac Society of Australia and New Zealand, list both patients with diabetes mellitus and people of Aboriginal and Torres Strait Islander descent as such high risk groups (292). Other high risk groups include patients with known coronary heart disease (CHD), those with either familial hypercholesterolaemia or combined hyperlipidaemia, and people with levels of total cholesterol > 6.0 mmol/L or LDL cholesterol > 4.0 mmol/L plus any two or more risk factors from the following: HDL cholesterol < 1.0 mmol/L, age ≥ 45 years, significant family history, hypertension, overweight or obesity, smoking, impaired glucose metabolism, microalbuminuria and/or renal impairment (292).

As for microalbuminuria, the importance of measuring lipids stems from the fact that lipid profiles can be significantly altered and improved through both diet and lifestyle intervention and the use of lipid lowering pharmacological agents, notably the HMG (hydroxymethylglutaryl) CoA reductase or 'statin' class of drugs (251). In patients with type 2 diabetes, who often have the combination of low HDL cholesterol and high triglyceride levels, treatment with statins has been shown to significantly reduce both the coronary and cerebrovascular events (293-296).

Testing for lipids is recommended annually for all patients with diabetes (251). For management of diabetes patients on lipid lowering medication, recommended treatment goals vary between professional groups, but current Australian guidelines (275, 292) state targets of:

- Total cholesterol < 4.0 mmol/L
- LDL cholesterol < 2.5 mmol/L
- HDL cholesterol > 1.0 mmol/L
- Triglyceride < 2.0 mmol/L.

For Indigenous Australians, screening for lipids is also recommended annually for all adults over 18 years of age with or without diabetes (228, 297). Due to their high number of co-existing risk factors for cardiovascular disease, statin treatment is now recommended in all Indigenous Australians with

either a total cholesterol > 6.5 mmol/L, total cholesterol > 5.5 mmol/L and HDL cholesterol < 1.0 mmol/L, or total cholesterol > 4.0 mol/L and pre-existing coronary heart disease (298). The same treatment goals listed above are recommended for Indigenous Australians with either diabetes and/or existing cardiovascular disease (228, 298).

Lipids should ideally be measured on a fasting venous blood sample (minimum 8 hours overnight fast), as the triglyceride concentration can be falsely raised by recent dietary intake if a non-fasting sample is analysed. An inaccurate triglyceride will also affect the LDL cholesterol result when LDL cholesterol is calculated from the Friedewald formula (LDL cholesterol = total cholesterol – HDL cholesterol – [triglyceride/2.2]) (299). The Friedewald formula provides an adequate surrogate measurement of LDL cholesterol when the sample has a triglyceride of 4.5 mmol/L or less and the sample is free of chylomicrons.

POCT devices generally measure blood lipids on a capillary whole blood sample; detailed instructions in how to correctly collect a capillary lipid sample is a crucial component of POCT training for this test as poor collection technique and the mixing of interstitial fluids with the capillary blood can lead to poor quality POCT lipid results.

Glucose

Glucose measurement is an integral test for screening, diagnosis and management of diabetes.

Diabetes Australia lists the following groups as being at high risk for type 2 diabetes: (i) Aboriginal and Torres Strait islander people over 35 years of age, (ii) people over 45 years of age with a one or more of the following risk factors: obesity, hypertension or family history of diabetes (first degree relative), (iii) all people over 55 years of age, (iv) people with impaired glucose metabolism, (v)

women with a history of gestational diabetes, and (vi) all people with clinical cardiovascular disease (275).

A diagnosis of diabetes can be made if one of the following criteria is satisfied:

- the fasting laboratory plasma glucose is ≥ 7.0 mmol/L,
- a random (non-fasting) laboratory plasma glucose is ≥ 11.0 mmol/L in a person with symptoms of diabetes, or
- the 2 hour laboratory plasma glucose is ≥ 11.0 mmol/L as part of an oral glucose tolerance test using a 75g glucose load (251, 275).

A repeat laboratory test should be performed on a separate day to confirm the diagnosis in all asymptomatic individuals whose results are suggestive of the diagnosis of diabetes (251, 275).

Current Australian guidelines recommend that capillary whole blood testing on POC glucose meters should not be used for the diagnosis of diabetes, due to the difference in results between whole blood and plasma glucose and the largely historical concerns regarding the diversity, reliability, accuracy and reproducibility of POC glucose devices (270). Nonetheless, many POC blood glucose devices are now able to report a plasma equivalent value and, particularly in rural and remote Indigenous communities, a random capillary whole blood POC glucose measurement may be useful as part of a general diabetes risk assessment that incorporates other risk factors including blood pressure, body mass index, urine testing, family and personal history, smoking and alcohol status (32). A random capillary whole blood glucose of ≥ 11.0 mmol/L suggests that the patient is likely to have diabetes and the patient should have follow-up confirmatory laboratory tests as outlined above (270).

Blood glucose self monitoring (BGSM) also plays a role in the management of type 1 and type 2 diabetes although, as will briefly be discussed later in this section, the evidence base for the effectiveness of BGSM is not strong.

Critical Appraisal Of POC Devices For HbA1c, Microalbumin and Lipid Testing

This section of the literature review was undertaken to determine which POCT devices are available for conducting HbA1c, urine microalbumin and lipids, and to assess how the analytical performance of these devices compared.

As mentioned under Organisation and Management, a POCT method should be validated against a well-established laboratory method before it is introduced into routine service. Ideally validation should take place at the intended site of use by the (trained) operator who would be expected to routinely use the device, with the support of the laboratory, the specialist POCT service provider and the vendor. If this is not possible, then the technology should be validated in a laboratory setting by the supporting laboratory or specialist POCT service provider.

A minimum analytical assessment, consistent with that routinely conducted by laboratories and recommended by professional societies/expert groups, should include the determination of accuracy and precision of the test system (300-303). Accuracy is the closeness of agreement between the value (measured by POCT) and the true value of the analyte (measured by an established laboratory method which is traceable to a recognised reference method). Precision is the closeness of agreement between replicate measurements of the same analyte on the same sample (and is often referred to as the reproducibility or repeatability of these measurements). Coefficient of variation (CV%) is the statistical measure of imprecision and is calculated, as mentioned previously, from the formula CV% = SD/mean *100 (302).

To assess whether observed analytical performance is acceptable in the laboratory setting, there is now an internationally recognised, multi-tiered hierarchical approach to setting and defining desirable analytical performance standards (hereafter referred to as analytical goals) based on clinical outcome studies, biological variation, opinions of professional groups, data from proficiency testing programs and the general literature (129, 130, 132, 159). Fraser states that, as an overarching principle, the POCT device should be able to achieve the same or at least equivalent level of analytical performance compared to that of the equivalent laboratory instrument when it is used for the same clinical purpose (128, 131). However, this literature review found no published papers which specifically investigated or defined analytical goals for POCT for diabetes and renal disease (or any other POCT application), apart from an article published by the author and presented in Chapter 4 of this thesis (35).

Haemoglobin A1c

Devices Available

This literature search identified seven devices capable of conducting HbA1c testing at the point of patient care (255, 304). The specifications of these devices are summarised in Table 2.13. Four of these devices - the DCA 2000, Micromat 11, A1c Now and Nycocard Reader - are true POCT devices being small, readily portable, and consisting of either a device with a single-use cartridge or a single use device. (The Micromat 11 is identical to the following devices marketed under different names and by different companies: the Cholestech GDX, Provalis Glycomat and Provalis Haemaquant/Glycosol). The remaining three devices - Diastat, PDQ and D10 - are designed mainly for laboratory use but can be transported (on a trolley) to a hospital diabetes clinic and used on-site; these devices are technically sophisticated and can perform tests in a batch mode. Based on current data provided by the RCPA Quality Assurance Programs Pty Ltd, the DCA 2000 is the POCT device most widely used by Australiasian laboratories participating in the Glycohaemoglobin QAP (Table 2.13).

Comparative Analytical Performance of POCT HbA1c Devices

The literature review found three evaluation reports by government agencies (305-307), three papers that compared two or more POCT devices (308-310), 10 papers that evaluated the DCA 2000 only (including one co-authored by the author (30)), one that reported on the performance of the A1c Now device (311) and two on the Glycosol system (312, 313). Two further papers written by the author on POCT HbA1c device evaluations are presented in Chapter 3 (28, 31).

In 2003 the US government agency known as the ECRI (formerly the Emergency Care Research Institute) conducted a comparative evaluation of 5 POCT HbA1c devices – the DCA 2000, Diastat, Micromat 11, A1c Now and Nycocard Reader - focussing on accuracy, precision and ease of use (305). The results of this evaluation are summarised in Table 2.14. The DCA 2000 device scored the highest overall rating for the three parameters evaluated. The DCA 2000 was also selected as the preferred device for use in the POCT environment (as well as the laboratory setting where it shared the preferred device rating with the Diastat).

The UK government's Medical Devices Agency (MDA) conducted two evaluations in 2002/3, the first specifically on the DCA 2000 and the second comparing three POCT devices – the A1c Now, the Nycocard Reader and a device identical to the Micromat (called the Haemaquant Glycosol analyser) (306, 307). As with the ECRI report, the DCA 2000 received the highest overall rating for accuracy, precision and ease of use (Table 2.14). Whilst these evaluations were comprehensive, a major limitation was the lack of quantitative data provided on accuracy. Linear regression and Bland Altman plots were presented for accuracy assessment, but quantitative data on regression equations or mean differences between POCT and comparator methods were not reported.

The results of the multi-device studies of St John *et al*, Greaves *et al* and Hawkins, which have all been published since 2003, are summarised in Table 2.15 (308-310). The well-designed study of St

John *et al* obtained data on accuracy, precision and user friendliness using both laboratory technicians and nurses as POCT operators. The authors concluded that only the DCA 2000 could be recommended for HbA1c testing outside the laboratory, with this device being the only one capable of achieving a between-batch imprecision of less than 5%. The analytical performance achieved by nursing staff was similar to laboratory technicians for all devices, except the Nycocard where performance was poorer (310). The DCA 2000 was rated by nurses as the most user friendly device. Greaves *et al* compared the DCA 2000, D10 and PDQ devices against each other, but did not use an independent comparative laboratory method. While the mean difference between all three analysers was <0.1%, the authors concluded the PDQ device was the preferred instrument for use in their hospital-linked paediatric diabetes clinic because it had the fastest turnaround time and exhibited the best imprecision (308). Hawkins concluded the DCA 2000 and Diastat devices produced the best performance, with total imprecision < 3% and close agreement with the comparator laboratory method and each other (309).

The results of single device evaluations undertaken on the DCA 2000 (10), the A1c Now (one) and the Glycosol (two) are summarised in Table 2.16.

Overall, the DCA 2000 device received widespread support in the published literature for its analytical performance and user-friendliness; while the Nycocard rated poorly for both parameters in most studies. However, it is difficult to synthesise firm conclusions on comparative performance between these studies because of the following limitations:

- Only the study of St John *et al* (and a paper published by the author (28)) assessed analytical performance in the hands of the non-laboratory trained POCT operator,
- All studies reported different measures of imprecision and used different sample matrices for the assessment of this performance indicator. For example, across the studies identified, imprecision was reported as within-run, between-run, between-batch, between-

day and total imprecision. Sample matrices on which imprecision studies were conducted included patient, quality control and external quality assurance samples. In addition, the number of repeated measures of imprecision varied from 6-26.

- As far as accuracy was concerned, every study used a different laboratory comparator method while, in the case of Greaves *et al*, the three POCT devices were compared to each other. There was no consistency in the number of patient samples used for the method comparisons. Some papers reported linear regression equations and correlation coefficients as their measure of accuracy, some reported the mean bias (and limits of agreement), while few reported both.
- Different papers judged acceptable performance against different analytical goals. For example, in the two major governmental agency studies, the ECRI considered acceptable imprecision to be <4% (conforming to NGSP method certification requirements), while the MDA used <5% to represent acceptable performance. This observation highlights the need for analytical goals specific for the use of POCT in the non-laboratory setting to be developed (which was a focus of this research program (35)).
- Apart from the very recent study of St John *et al* and the papers written by author (Chapter 3), none of the studies validate the use of POC HbA1c devices under Australian conditions.

These issues are also common to studies reporting analytical performance for POC urine albumin and lipid measurement, as discussed below.

Table 2.13. Device specifications for HbA1c POCT devices.

Device Name	DCA 2000	Micromat 11*	A1c Now	Nycocard Reader	Diastat	PDQ	D10
Manufacturer	Bayer	Bio-Rad	Metrika	Axis Shield	Bio-Rad	Primus	Bio-Rad
Primary site of use	POCT or lab	POCT	POCT	POCT	Lab, but can have POCT application	Lab, but can have POCT application	Lab, but can have POCT application
Technology	Device with single use cartridge	Device with single use cassette	Single use device	Reader, reagent kit and single use card	Device and reagents, multiuse, 15 samples in batch	Device and reagents, multiuse, 30 samples in batch	Device and reagents, multiuse, 10 samples in batch
Method Principle	Immunoassay (latex agglutination inhibition)	Boronate affinity chromatogaphy	Immunochromatography	Boronate affinity chromatography	Cation exchange LPLC	Boronate affinity chromatogaphy	Cation exchange HPLC
Sample size (µL)	1	10	10	5	20	10	5
Time to result (mins)	6	5	8	5	10	2	3
Ability to walk away once sample loaded	Yes	No	Yes	No	Yes	Yes	Yes
Connectivity	Possible	Possible	Poor	Possible	Possible	Yes	Yes
Year first marketed	1992	2002	2002	2000	n/a	2003/4	2003/4
Device registered in 2006 RCPA QAP Glycohaemoglobin Program (current number)	Yes (69)	Yes (1)	No	No	No	Yes (10)	Yes (5)
Measurement Range	2.5-14%	3-18%	3-15%	3-18%	n/a	Approx 3-33%	na
NGSP certified	Yes	Yes	Yes	Yes	Yes	Yes	Yes
HbA1c variant interference**	HbF>10%**	None**	HbS, HbC, HbF**	None**	HbF**	None	None

*The Micromat 11 is identical to the following devices marketed under different names and by different companies: the Cholestech GDX, Provalis Glycomat and Provalis Haemaquant/Glycosol;

LPLC = low pressure liquid chromatography; HPLC = high pressure liquid chromatography; HbA1c variant interference reported by manufacturer** (as listed in the ECRI report [335]).

Table 2.14. Summary of findings from Governmental Agency evaluations.

A. Overall descriptive rating from ECRI study.

Rating	For use in Hospital environment	For use in POCT environment
Preferred	DCA 2000, Diastat	DCA 2000
Acceptable	Micromat 11, A1c Now	Micromat 11, A1c Now
Acceptable with conditions	Nycocard	Nycocard

B. Summary of HbA1c POCT devices, as assessed by three performance indicators, in both ECRI and MDA studies.

Category	Study	DCA 2000	Micromat 11 (ECRI)/ Glycosol (MDA)	A1c Now	Nycocard	Diastat
Accuracy*	ECRI	Good; 88% of results within 5% of reference value	Good; 60% of results within 5% of reference value	Fair; 53% of results within 5% of reference value	Poor; 21% of results within 5% of reference value	Good; 70% of results within 5% of reference value
	MDA	Very good; no quantitative data	Very good; no quantitative data	Satisfactory; small negative bias; no quantitative data	Good; small positive bias; No quantitative data	Not evaluated
Precision**	ECRI	Excellent; CV 2.5-3.6%	Fair; CV 4.4-5.3%	Fair; 5.2-6.5%	Good, CV 2.8-4.4%	Excellent; 2.2-3.4%
	MDA	BD CV 2.4-2.7%; BB CV 2.8%	BD CV 3.2-8.5%; BB CV 6.7%	BD CV 4.5-12.0%; BB CV 7.0%	BD CV 3.3-8.9%; BB CV 2.5%	Not evaluated
Ease of use	ECRI	Excellent	Fair	Good	Good	Good
	MDA	Good	Good, but strict time limits	Generally good	Initially daunting, multiple steps	Not evaluated

ECRI= is a non-profit health services research agency and a collaborating centre of the World Health Organisation; it is also designated as an Evidence-based Practice Centre by the US Agency for Healthcare Research and Quality focussing on healthcare technology.

MDA = The Medical Devices Agency (MDA) was an agency of the government of the United Kingdom which specialised in the evaluation of medical devices available on the UK market. The MDA has now merged with the Medicines Control Agency to form the Medicines and Healthcare Products Regulatory Agency (MHRA) for the UK government.

Accuracy*: ECRI = 20 blood samples in duplicate, how many were within 5% of the value obtained by the laboratory NGSP certified (but not specified) reference method; MDA = 50 blood samples compared to laboratory reference method (Menarini HPLC), but no quantitative data given.

Precision**: ECRI = 3 bloods tested 3 times on each of 5 days by both lab technician (all 3 bloods) and 3 volunteers (tested two highest levels); MDA = 50 patient samples in duplicate (SD calculated, not CV); 2 levels of one or two QCs of single lot tested daily for 20 days (between-day[BD]); single patient HbA1c 7.4% tested 6 times each across 3 batches of reagent (between-batch [BB]).

Table 2.15. Summary of general papers that compared two or more HbA1c POCT devices.

Parameter	DCA 2000	Cholestech GDX	A1c Now	Nycocard	PDQ	D 10	Diastat
Study 1. St John (310)							
Evaluation performed by	Nurse and lab	Nurse and lab	Nurse and lab	Nurse and lab			
Patients in method comparison	114	114	114	114			
Accuracy (mean bias; LOA)	0.16 (-0.63 to 0.96)	-0.31 (-1.73 to 1.11)	0.01 (-1.01 to 1.03)	0.39 (-0.98 to 1.76)			
Precision (Between batch CV, 2 QC, n=20)	Nurse 3.7-4.8%	Nurse 7.2-8.1%	Nurse 6.5-8.4%	Nurse 8.4-13.1%			
	Lab 3.3-4.9%	Not done	Lab 6.6-7.7%	Lab 5.8-10.8%			
Comparator lab method	Primus HPLC	Primus HPLC	Primus HPLC	Primus HPLC			
Study 2. Greaves (308)							
Evaluation performed by	Lab				Lab	Lab	
Patients in method comparison	228				228	228	
Accuracy (mean bias between devices)	<0.1				<0.1	<0.1	
Precision (Between-run CV, 2 QC, n=20)	2.4-2.8%				1.6-2.8%	3.4-3.5%	
Comparator lab method	None				None	None	
Study 3. Hawkins (309)							
Evaluation performed by	Lab			Lab			Lab
Patients in method comparison	114			114			114
Accuracy (mean bias, LOA)	0.20 (0.12-0.27)			0.40 (0.28-0.52)			0.17 (0.07-0.27)
Precision (Total CV, 2 patients twice per day for 6 days; & 2 QC)	2.6-2.9%			8.5-8.6%			1.6-2.2%
Comparator	Roche Tinaquant			Roche Tinaquant			Roche Tinaquant

Table 2.16. Summary of papers reporting on a single POCT HbA1c device.

Device	Author	Evaluation Performed by/in	Accuracy*								Precision**				
			No. of Patients	Slope	Intercept	r	Mean Diff	LOA	p	Comparative Method	Type	Material	HbA1c conc (%)	CV%	No. of replicates
A1c Now	Klonoff (311)	Part 1. Patients	297	0.988	0.168	0.93	na	-0.9 to 1.06	0.50	HPLC	Not studied				
		Part 1. Nurse	297	0.965	0.4	0.94	na	-0.81 to 1.1	0.21	HPLC					
		Part 2. Patients	30	0.95	0.28	0.95	0.07	-0.78 to 0.92	0.85	HPLC					
DCA 2000	Shemesh (29)	na	39 Indig	na	na	0.96	-0.1	-1.1 to 0.8	> 0.05	HPLC	Not studied				
	Shemesh (30)	na	117 Indig	na	na	na	-0.02	-0.65 to 0.61	0.947	HPLC	Not studied				
	Arsie (314)	na	171	0.911	0.462	0.923	na	na	< 0.0001	HPLC	WR	3 Patients	5.0-9.5	**3.2-3.9**	10
	Metteucci (315)	Lab	161	0.89	0.56	0.95	0.3	na	< 0.001	HPLC	WR BR	2 Patients 2 Patients	na na	**1.1,1.0** **2.3,4.2**	na na
	Fonfrede (316)	na	300	na	na	na	8 > 1% higher; 6 <1% lower	na	na	HPLC	BR	2 QC	5.5 9.7	**2.5-2.8** **3.5-4.6**	Weekly for 6m
	Guerci (317)	na	1016 across 5 sites	1.01	-0.233	0.95	-0.116	-1.23 to 0.998	na	HPLC	Not studied				
	Carter (318)	Community workers	43 (1994) 14 (1995)	na	na	0.968	na	na	na	HPLC	WR BR BR	2 Patients 2 QC 1994 2 QC 1995	na 4,7,9.7 4,8,10.9	**3.0,2.8** **3.2,4.1** **3.2,2.8**	na na na
	John (319)	na	na	0.70	1.18	0.90	na	na	na	HPLC	WR WB	2 Patients 2 Patients	4.3,12.1	**1.9,3.1** **2.2,2.2**	15 15 over 3d
	Pope (320)	Lab Paediatric clinic Obstetric clinic GP outpatient	48 19 24 15	na	na	na	-0.69 -0.93 -0.29 -0.77	-1.4 to 0.04 -1.93 to 0.07 -1.09 to -0.51 -1.3 to -0.24	na	HPLC	BR	2 QC	5.2, 13.0	**1.6,2.4**	6
	Marrero (321)	Lab	207	0.98	1.12	0.97	na	na	na	Cation exchange	WR BR	3 QC 3 QC	4.9-11.6 4.9-11.6	**1.7-3.5** **2.1-2.3**	26
Glycosol	Gebrekidan (312)	Diabetes clinic	100	na	na	0.96	na	na	na	HPLC	Not studied				
	Stevenson (313)	na	62	0.80 1.12	0.85 -0.23	0.983 0.98	na	na	na	HPLC 1 HPLC 2	BD	3 QC	4.5-11.0	**2.0-4.5**	10

Footnote to Table 2.16

***Accuracy**: expressed either as (i) a linear regression equation (y [POCT] = slope x[lab] ± intercept; r=correlation coefficient, the closer to 1.00 the more highly correlated the two data sets (ie POCT and lab results) (160) or (ii) Mean Diff = mean difference between POCT and lab results, with lower and upper limits of agreement (LOA), using the Bland Atman plot (161); $p < 0.05$ indicates there is a significant difference between the mean of POCT and lab results.

****Precision**: Type WR = within run imprecision; BR = between run imprecision; WB = within batch imprecision; CV% is the statistical measure of imprecision and is calculated from the formula CV% = SD/mean *100; no. of replicates = no. of repeated measurements performed to assess imprecision.

Total analytical error can be calculated from the formula Total Error (TE) = Bias + 1.65*precision (159).

na = information not available in paper.

Indig = Indigenous Australian patients recruited for study.

Urine Microalbumin

Devices Available

This literature review identified four POCT devices that measure urine microalbumin quantitatively. The DCA 2000 measures urine albumin and creatinine and reports the urine ACR, while the remaining three - the Nycocard, HemoCue and Quik-Read - report urine albumin only (304, 322). The specifications of these devices are summarised in Table 2.17. The DCA 2000 is the only POCT device used by laboratories participating in the RCPA Quality Assurance Programs Basic Urine Chemistry QAP (with 9 devices registered in 2006).

Comparative Analytical Performance of POCT Microalbumin Devices

This literature review found one evaluation report by a government agency (322), five papers that evaluated the DCA 2000 (30, 323-326) and one that investigated the analytical performance of the HemoCue urine albumin device (327). A paper written by the author on an evaluation of the Bayer DCA 2000 urine ACR method (the first conducted in Australia) is presented in Chapter 3 (9).

The UK government's Medical Devices Agency (MDA) undertook an evaluation of all four POCT devices in 2004 (322). The authors concluded that the DCA 2000 and the QuikRead were the most precise devices, achieving CV%s of less than 7% for all modes of imprecision evaluated. (Imprecision was assessed in three ways; total CV% using a single commercial quality control material assayed on all devices (2 separate runs for 20 days), SD using duplicate analysis of 40 patient samples, and between-day CV% using each supplier's quality control material [number of repeats varying from 21 to 37]). The DCA 2000 was judged to have exhibited the best accuracy in a 40-patient method comparison versus the reference laboratory method (Bayer ADVIA 16500). The Nycocard and HemoCue devices exhibited concentration dependent negative biases in this comparison. However, as for HbA1c, a major limitation of this MDA report was the lack of quantitative data provided on accuracy.

The results of the single device evaluations undertaken on the DCA 2000 and HemoCue are summarised in Table 2.18. Overall, the DCA 2000 performed well in the five reported studies although, as for HbA1c, differences in the reported measures and sample matrices used for precision studies, different laboratory comparator methods for urine albumin, different number of patients studied in method comparisons and lack of consistency in reported accuracy measures limited the generalisability of these findings.

One study by Shemesh *et al*, in which the author of this thesis was a co-author, and another evaluation conducted by the author and presented in Chapter 3 represents the only studies of the DCA 2000 undertaken under Australian conditions (9, 30).

The HemoCue performed well for urine albumin measurement in the only paper found in this literature search, but a drawback of this device is that its upper measuring range only extends to 150 mg/L. Given that the upper cut-off for microalbuminuria is 300 mg/L, the device provides no quantitative measure of urine albumin in the upper half of the microalbuminuric range, limiting its use for management. No individual papers were found on the other two devices evaluated by the MDA.

Table 2.17. Device specifications for urine microalbumin POCT devices.

Device Name	**DCA 2000**	**HemoCue Urine Albumin**	**Nycocard Reader**	**QuikRead**
Manufacturer	Bayer	HemoCue	Axis Shield	Orion Diagnostica
Measure of Microalbumin; units	Urine albumin:creatinine ratio (ACR); mg/mmol	Urine albumin; mg/L	Urine albumin; mg/L	Urine albumin; mg/L
Technology	Device with single use cartridge	Device with single use microcuvettes	Reader and reagent kit	Device with single use cuvette and reagents
Method Principle	Urine albumin: immunoturdimetric Urine creatinine: colorimetric	Immunoturbidimetric	Immunocolorimetric	Immunoturbidimetric
Sample size (µL)	40	15	50	20
Time to result (mins)	7	2	4	3
Calibration reference material	Urine albumin: CRM 470 Urine creatinine: NIST SRM 914a	Urine albumin: CRM 470	Urine albumin: CRM 470	Urine albumin: CRM 470
Connectivity	Possible	Possible	Possible	na
Year first marketed	1998	2003	2000	2002
Measurement Range	Urine albumin: 5-300 mg/L Urine creatinine: 1.3-44.2 mmol/L	Urine albumin: 10-150 mg/L	Urine albumin: 5-200 mg/L	Urine albumin: 5-150 mg/L
Antigen excess	>2000 mg/L urine albumin	>2000 mg/L urine albumin	Not affected by excess urine albumin	Not specified
Interferences	Urine glucose >139 mmol/L	Urine glucose >110 mmol/L	Urine glucose >50 mmol/L	Urine glucose >50 mmol/L

CRM = certified reference material; NIST = National Institute of Standards and Technology; SRM = standard reference material

Table 2.18. Summary of papers reporting on a single POCT Urine Microalbumin device.

Device	Author	Eval'n by/in	Test	Accuracy								Precision				
				No. of Patients	Slope	Intercept	r	Mean Diff	LOA	p	Comparative Method	Type	Material	Conc*	CV%	No. of repeats
DCA 2000	Shemesh (30)	Field	Alb Creat ACR	78 100 76	na	na	na	3.05 -0.19 0.28	0-8 to 14 -1.29 to 0.9 -0.38 to 0.94	na	Immunoneph Kinetic Jaffe	Not studied				
	Khawali (323)	Lab	Alb Creat ACR	55	na	na	0.98	na	na	na	Immunoturb Kinetic Jaffe	Not studied				
	Collins (324)	Trained diabetes nurse	Alb Creat ACR	133 152 132	1.09 1.04 1.06	-2.9 na -0.29	0.997 0.997 0.993	-3.2 -0.33 -0.10	-4.8 to 1.6 -0.4 to 0.25 -0.31 to 0.12	na	Immunoturb Kinetic Jaffe	WR BR	2 QC, 3 Patients 2QC	Alb 6-192 Creat 6-32 Alb 34,197 Creat 9,32	**1.9-7.1** **1.6-3.7** **3.0,4.3** **2.1,3.7**	10 15
	Parsons (325)	Lab	Alb Creat ACR	96 96 96	1.02 1.06 0.97	1.4 0.13 0.13	na	na	na	na	Immunoassay Kinetic Jaffe	WR	2 QC, 2 Patients 2 QC	Alb 6-266 Creat 8-31 ACR 0.4-30 Alb 30,190 Creat 8,31 ACR 3.8-6.1	**2.6-7.3** **1.8-1.9** **1.8-8.0** **0.4-4.8** **0.4-2.1** **2.3-5.4**	15 20
	Poulsen (326)	3 nurses	Alb Creat ACR	195	na	na	0.987	na	na	na	Immunoturb	Not studied				
HemoCue	Von Schenk (327)	Lab	Alb	137 137	1.06 1.08	-7.2 -3.1	0.94 0.94	na na	na na	na na	Immunoturb Immunoneph	WR BR	8 Patients 2 QC	Alb 28-105 Alb 12,65	**4.3-13.8** **18.2,6.1**	24 24

Accuracy: expressed either as (i) a linear regression equation (y [POCT] = slope x[lab] ± intercept; r=correlation coefficient, the closer to 1.00 the more highly correlated the two data sets (ie POCT and lab results) (160) or (ii) Mean Diff = mean difference between POCT and lab results, with lower and upper limits of agreement (LOA), using the Bland Atman plot (161); p <0.05 indicates there is a significant difference between the mean of POCT and lab results.

Precision: Type WR = within run imprecision; BR = between run imprecision; CV% is the statistical measure of imprecision and is calculated from the formula CV% = SD/mean 100; no. of repeats = no. of repeated measurements performed to assess imprecision.

Immunoneph = immunonephelometric method; Immunoturb = Immunoturbidimetric method; Conc* Alb mg/L; Creat mmol/L; ACR mg/mmol.

Lipids

Devices Available

This literature search found two POCT devices capable of measuring the full lipid profile of tests, namely the Cholestech LDX and the CardioChek PA. The specifications of these devices are summarised in Table 2.19. The Vitros DT60 (marketed by Ortho Clinical-Diagnsotics, USA), and the Reflotron and the Accutrend (Roche Diagnostics, Basel, Switzerland) POCT devices conduct individual lipid tests but not the complete lipid profile using a single cassette/strip. As such, these devices will not be discussed further in this thesis.

Comparative Analytical Performance of POCT Lipid Devices

The literature review found two evaluation reports by government agencies (one on the Cholestech LDX and one on the CardioChek PA device) (328, 329), two additional papers on the Cholestech LDX (29, 330) and one paper comparing both devices (331). A paper written by the author evaluating the Cholestech LDX analyser for the first time in Australia is presented in Chapter 3 (25).

The Medical Services Advisory Committee (MSAC) conducted a detailed assessment of the Cholestech LDX device on behalf of the Australian Government's Department of Health and Ageing in 2001 (328). Using a literature search they identified 19 studies on the accuracy and precision of the Cholestech LDX, seven of which were published papers (332-338) with the remainder being technical reports, company bulletins or conference abstracts. Data from these studies on accuracy, precision and total error (159) for total cholesterol, HDL cholesterol and triglyceride were pooled to determine an overall estimate of these performance indicators. The pooled estimates were compared to the analytical goals set by the National Cholesterol Education Program (NCEP) for laboratory measurement of lipids (339). (Analytical goals for lipid measurement, including the NCEP goals will be discussed in detail in a paper published by the author and presented in Chapter 4 of this thesis).

The key findings of the MSAC report are summarised as follows:

- The pooled estimates for imprecision and bias on the Cholestech LDX did not always fall within the desired goals; however the pooled estimate of total error for each test did meet the goals (Table 2.20).
- In a sub-study of the main evaluation, in which data from seven studies was pooled, the authors concluded there was no difference between lipid cholesterol concentrations measured on venous or capillary whole blood (pooled bias 0.35%).
- There was insufficient evidence to determine whether the Cholestech LDX would meet NCEP goals when used in a non-laboratory clinical setting, due to the small number of studies in which this was investigated. The report recommended that POCT lipid testing should be restricted to settings where there is adequate training, quality assurance and accreditation.

The UK government's Centre for Evidence-based Purchasing (CEP) undertook an evaluation of the CardioChek device in 2005 (329). They conducted a method comparison between the CardioChek device and laboratory methods (Vitros 950 [Ortho Clinical-Diagnostics] for cholesterol and triglycerides and IL 600 [Instrument Laboratory, USA] for HDL cholesterol) using 106 patient samples. They also measured imprecision by repeated analyses (n=22 on each of two CardioCheks) of three patient samples with different lipid concentrations. This study found the CardioChek exhibited a statistically significant overall mean bias of 0.23 mmol/L for total cholesterol which was inversely related to concentration, and a statistically significant mean bias of 0.11 mmol/L for triglyceride which was concentration dependent. The small bias recorded for HDL cholesterol was not statistically significant, nor concentration dependent. Imprecision (total CV%) averaged 8.2%, 23.6% and 23.4% for total cholesterol, HDL cholesterol and triglyceride respectively, which were all well outside the NCEP goals.

The results of other recent device evaluations undertaken on the Cholestech LDX (since the MSAC study) and the CardioChek are summarised in Table 2.21. The Cholestech LDX study of Shemesh *et al* was conducted among Australian Indigenous participants in a remote community (30). The Stein *et al* evaluation of the Cholestech involved older patients (mean age 75 years) with hyperlipidaemia (330). Panz *et al* tested both POCT devices using patients from a South African lipid clinic who had mainly familial hypercholesterolaemia and were from different cultural backgrounds (331). These different patient groups, representing varying ages and races, limit the applicability of the study findings, as does the fact that the studies used different sample types and different POCT operators (Table 2.21).

Both Shemesh *et al* and Stein *et al* reported no bias for total cholesterol measurement on the Cholestech LDX (mean difference <0.02 mmol/L), yet Panz *et al* found a positive bias for this analyte particularly at concentrations up to 7.5 mmol/L. Shemesh *et al* reported a significant inverse concentration dependent bias with HDL cholesterol measurement but Stein *et al* found the bias was positively correlated with HDL concentration. Panz *et al* reported an overall negative bias for HDL cholesterol but did not state whether this was concentration dependent. All three authors found an overall positive bias with triglyceride measurement with the Cholestech device. In relation to the CardioChek PA, the findings of Panz *et al* conflict with the CEP study because Panz *et al* reported a positive bias for HDL cholesterol and much improved imprecision (albeit on quality control samples rather than patient samples).

Overall, the analytical studies on POCT lipid devices have produced conflicting evidence on their performance characteristics, due to the diversity of study designs and results found. However, most studies have reached similar conclusions; namely that POCT lipid testing has a role in general community risk assessment but whether the analytical quality of these devices is sufficient for use in the management of patients with hyperlipidaemia has yet to be confirmed.

Table 2.19. Device specifications for POCT devices measuring full lipid profiles.

Device Name	**Cholestech LDX**	**CardioChek PA**
Manufacturer	Cholestech Corporation	Polymer Technology Systems
Technology	Device with single use cassette	Device with reagent strip
Method Principle	Enzymatic with reflectance photometry	Enzymatic with reflectance photometry
Sample size (µL)	35µL	40µL
Time to result (mins)	4-5 mins	2 mins
Calibration reference material	Cassettes pre-calibrated	Code chip
Connectivity	No	No
Year first marketed	Approx 1994	Approx 2004
Measurement Range	Chol 2.6 to 12.9 mmol/L HDL Chol 0.4 to 2.6 mmol/L Trig 0.5 to 7.3 mmol/L	Chol 1.3 to 10.4 mmol/L HDL Chol 0.4 to 2.6 mmol/L Trig 0.3 to 5.65 mmol/L
Power source	AC	AC or battery (300 tests)

Table 2.20. Comparative analytical performance of the Cholestech LDX, as assessed by the Medical Services Advisory Committee (MSAC) (328).

Analyte	Imprecision (CV%)		Bias (%)		TE (%)	
	Cholestech LDX	NCEP goal	Cholestech LDX	NCEP goal	Cholestech LDX	NCEP goal
Cholesterol	3.4	3	2.1	3	8.6	8.9
HDL cholesterol	5.1	4	1.5	5	11.7	12.8
Triglyceride	4.1	5	5.2	5	13.3	14.8

Table 2.21. Summary of papers reporting on analytical performance of POCT lipid devices.

Device	Author	Evaluation Performed by/in	Lipid	Accuracy								Precision				
				No. of Patients	Slope	Intercept	r	Mean Diff	LOA	p	Comparative Method	Type	Material	Lipid conc (mmol/L)	CV%	No. of replicates
Cholestech LDX	Shemesh (30)	Field using VWB	Chol	74 Indig	na	na	na	0.003	-0.68 to 0.69	na	CDC certified	Not studied				
			HDL-C	73 Indig	na	na	na	0.10	-0.10 to 0.30	na	CDC certified					
			Trig	71 Indig	na	na	na	0.06	-0.18 to 0.30	na	CDC certified					
	Stein (330)	Trained nurse using CWB	Chol	63	0.84	0.463	0.88	0.016	na	0.492	Non-CDC certified	Not studied				
			HDL-C	63	1.29	-0.133	0.96	0.015	na	0.026	Non-CDC certified					
			Trig	63	0.98	0.33	0.97	0.296	na	< 0.001	Non-CDC certified					
	Panz (331)	Lab using VWB	Chol	100	na	na	0.914	0.218	na	na	Non-CDC certified	WR	2 QC	4.4,6.5	**5.0,4.5**	7
			HDL-C	100	na	na	0.872	-0.113	na	na	Non-CDC certified	WR	2 QC	0.91,1.9	**1.1,3.2**	7
			Trig	100	na	na	0.983	0.086	na	na	Non-CDC certified	WR	2 QC	1.7,2.9	**1.8,2.1**	7
CardioChek PA	Panz (331)	Lab using VWB	Chol	100	na	na	0.832	0.096	na	na	Non-CDC certified	WR	2 QC	4.5,6.3	**2.5,2.4**	7
			HDL-C	100	na	na	0.724	0.160	na	na	Non-CDC certified	WR	2 QC	2.5,2.6	**3.9,0.1**	7
			Trig	100	na	na	0.934	-0.094	na	na	Non-CDC certified	WR	2 QC	1.6,2.7	**5.2,5.6**	7

HDL-C = HDL cholesterol; Indig = Indigenous Australian participants; VWB = venous whole blood; CWB = capillary or fingerprick whole blood; CDC = Center for Disease Control, Atlanta, GA, USA.
Accuracy: expressed either as (i) a linear regression equation (y [POCT] = slope x[lab] ± intercept; r=correlation coefficient, the closer to 1.00 the more highly correlated the two data sets (ie POCT and lab results) (160) or (ii) Mean Diff = mean difference between POCT and lab results, with lower and upper limits of agreement (LOA), using the Bland Atman plot (161); $p < 0.05$ indicates there is a significant difference between the mean of POCT and lab result. Precision: WR = within run imprecision.

Critical Appraisal Of The Evidence Base For The Effectiveness Of POCT For The Management Of Diabetes and Renal Disease In The Ambulatory Care Setting

Haemoglobin A1c

Excluding papers published by the author and presented in Chapter 6, this literature search identified seven papers conducted in a number of ambulatory settings which report on different outcome measures for POC HbA1c testing. The methodology and key findings of these studies are summarised chronologically in Table 2.22. Five of the seven studies used the Bayer DCA 2000 as the POCT device.

Study designs included two randomised controlled trials (340, 341), one quasi-randomised controlled trial (342), one pre and post study (341) as a sub-study of a larger randomised controlled trial, two retrospective cohort studies (343, 344), one retrospective audit (42) and one early observational study (320).

Ambulatory settings comprised primary care and secondary care diabetes clinics, and a specialist diabetes clinic integrated into a primary care setting. The latter was an Australian Indigenous medical service in rural Victoria, which is a participant in one of the main research programs developed by the author (QAAMS) (42).

The results reported in these seven papers support the assertion that POC HbA1c testing at the time of consultation can both optimise clinical care and improve glycaemic control (as measured by a reduction in HbA1c). As shown in Table 2.23, five of the seven studies concluded that POC HbA1c testing positively influenced clinical management, while another five reported statistically significant reductions in HbA1c over time following the introduction of POCT. (Further studies conducted by the author and presented in Chapters 6 and 7 also report improved glycaemic control with POCT (13, 22, 26, 32)).

However, the validity of the findings presented in these seven papers is limited by the following factors. All of the studies were conducted over a relatively short time frame of one year or less. Almost half of the studies presented involved specific cultural groups (African Americans [2] and Australian Aboriginal people [1] (42, 341, 342)), thereby potentially restricting the applicability of the study results to the general population. The small sample size (30 or less) in two studies also limits the generalisability of the findings of these studies (42, 320).

The study by Pope *et al* is the earliest report of POCT HbA1c in the literature which concluded that POCT influenced clinical management, without supporting data (320). The major aim of this paper was to report on the analytical performance of the POCT device which was used in four different clinical settings on a larger patient sample base (n=106). The reporting of an outcome measure was of secondary concern and represents a good example of an 'inadequately planned add on', as described earlier by Delaney *et al* (61).

In the often-cited study of Thaler *et al*, the only reference to the HbA1c method used stated: 'HbA1c was determined by a Boehringer Mannheim turbidimetric immunoinhibition assay' (341). This assay is performed on a laboratory analyser and is not available by a POCT method – thus it is unclear whether an in-clinic POC device was in fact used in this study or whether all HbA1c tests were performed in the laboratory, with the turnaround for analyses occurring more rapidly than normal (for the rapid group) or being available in a conventional time frame (24 hrs) in the control group. Thus this study most likely assessed the impact of the availability of results at the point of care rather than having the result conducted on-site by a specific POC device.

The power and validity of the Ferenczi *et al* study (343) is limited by several factors. Firstly, there were only small numbers of patients (n=22) in the control group. Secondly, the paper does not specify whether the three laboratories, where samples from the control group were tested, used the same or different analytical methods. If the latter, there would be greater between-method variability and bias in HbA1c

results, which could affect the mean (and SD) of the HbA1c values reported in this group. Thirdly, the study was retrospective.

In the Simmons study conducted in the Australian Indigenous setting (42), the authors attribute the observed improvement in glycaemic control to a significant increase in insulin use and self monitoring of blood glucose but make no reference to the contribution of POCT to this improved outcome.

The studies of Caligero *et al* and Grieve *et al* were both well designed (340, 344). Grieve's study was conducted as a Health Technology Assessment (HTA) Program for the National Health Service in the United Kingdom. Their study documents additional clinical and operational outcome benefits of POCT including increased patient satisfaction and reduced hospital visits, while also reporting equivalent costs between POCT and laboratory HbA1c services. No other papers that reported on the economic outcomes of POC HbA1c testing were found in this literature review.

It should be noted that this literature search did identify several other well-designed studies that integrated laboratory-based HbA1c testing into diabetes care programs for Indigenous Australians (345-348); however only the study of Simmons used POC HbA1c testing (42).

In addition to the papers assessed thus far, a further nine papers were sourced which described pharmacist-led interventions that documented improved glycaemic control (as assessed by reduction in HbA1c) in both the primary and secondary care settings (205-213). However, none of these studies (i) specifically stated that the HbA1c tests were performed by a POCT device or (ii) identified when the HbA1c result was provided to the patient (that is, at the point of care during consultation or reported back to the patient at a later date). While this subset of papers highlights that the community-based pharmacist can have an integral role in improving diabetes management, the studies almost certainly did not involve POCT; as such, they will not be discussed further in this thesis.

Both the American Association of Clinical Chemists (AACC) and the National Academy of Clinical Biochemistry (NACB) have recently published recommendations on diabetes care that endorse the use of POCT HbA1c testing for diabetes management (251, 349). Nonetheless, as Winter states, more large scale randomised controlled studies are needed to further verify the clinical effectiveness of POCT for HbA1c (252).

Table 2.22. Outcome studies for POC HbA1c testing for diabetes management in ambulatory care settings. (Table continues to page 124).

Outcome Category Assessed	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test, and Device	Author	Summary of Methodology and Key Findings
Clinical	Influence on clinical management decisions	Primary and secondary care diabetes clinics	Observational	HbA1c, DCA 2000	Pope (320)	18 patients with type 2 diabetes randomly selected from obstetric and general practice diabetes clinics for assessment of clinical utility of POCT HbA1c. In 9 (50%) patients, knowledge of the HbA1c result influenced management decisions made at time of consultation eg initiated insulin therapy in patients with gestational diabetes and prescribed oral hypoglycaemic drugs when increased HbA1c was found by POC.
Clinical	Influence on clinical management decisions, Glycaemic control	Diabetes outpatient clinic (secondary care)	RCT, and pre and post	HbA1c	Thaler (341)	1138 urban, economically disadvantaged African Americans with type 2 diabetes were randomised to receiving their HbA1c result rapidly at the point of care (rapid group, n=575) or delayed by 24 hrs (control group, n=563). Adjustment of therapy was considered appropriate if therapy was intensified in patients with HbA1c >7% or not intensified if HbA1c was ≤7%. Overall, rapid availability of HbA1c resulted in more appropriate management compared to the control group (79% vs 71%, p = 0.003). This improvement resulted mainly from a reduction in inappropriate intensification in therapy for patients with HbA1c ≤7% from 22% to 10% (p <0.0001). For patients with HbA1c >7% a slight, but not significant, increase in intensification was observed (67% vs 63%, p = 0.33). A post hoc analysis, which was not part of the original RCT design, was conducted on 574 patients who had subsequent HbA1c tests performed 2 to 7 months after the baseline testing. Patients in the control group had a mean initial HbA1c of 7.2% and a follow-up HbA1c of 8.0% ie a rise of 0.8% (p <0.0001). Patients receiving rapid results had a mean initial HbA1c of 7.5% and a follow-up HbA1c of 7.9%, ie a rise of 0.4% (p = 0.0005). Thus follow-up HbA1c values rose in both groups.

Outcome Category Assessed	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test, and Device	Author	Summary of Methodology and Key Findings
Clinical and Operational	Glycaemic control Number of contacts between visits	Academic hospital diabetes centre (secondary care)	RCT	HbA1c, DCA 2000	Caligero (340)	201 patients with type 1 (56%) or type 2 (44%) diabetes were randomised to receiving immediate feedback on their HbA1c result (following on-site POCT) or receiving their result from the laboratory according to standard practice (control group). HbA1c levels were measured in both groups after 6 and 12 months. To avoid bias in the treatment of patients, physicians were informed of the nature of the study but not aware that that data on outcomes were being collected. In the group receiving immediate feedback, HbA1c levels decreased significantly by 0.57% (SD±1.44) [from 8.67 to 8.1%] at 6 months (p = 0.001) and by 0.40% (±1.65) [from 8.67 to 8.27%] at 12 months (p = 0.013). In the control group, HbA1c levels did not change significantly, decreasing by 0.11% (±0.79) [from 8.49 to 8.38] at 6 months and by 0.19% (±1.16) [from 8.49 to 8.30%] at 12 months (both decreases were reported by the authors as not significant, although specific p values were not stated). The difference between the groups was statistically significant at 6 months (p = 0.029) but not at 12 months (p = 0.346). The changes in HbA1c levels were similar for type 1 and type 2 patients at both time points. There was no difference between the POCT and control groups in either the number of episodes of severe hypoglycaemia and visits to the emergency department. The availability of immediate POCT result did not decrease the number of contacts (phone or letter) with the heath care providers between clinic visits. The authors postulate that this may have been due to the need to report other laboratory data. As described previously for inpatient hospital setting, factors other than POCT may limit the effectiveness of POCT.

Outcome Category Assessed	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test, and Device	Author	Summary of Methodology and Key Findings
Clinical, Operational, & Economic	Glycaemic control Patient satisfaction Influence on clinical management decisions Frequency of hospital visits Cost of Healthcare services	2 hospital based diabetes clinics (secondary care)	Retrospective cohort study Self administered questionnaire Controlled Trial (not randomised) Self administered questionnaire Resource use data	HbA1c, DCA 2000	Grieve (344)	A range of different outcome measures were assessed when comparing POCT for HbA1c in two hospital diabetes clinics (hospitals 1 and 2) with central laboratory HbA1c testing at hospital 1. Testing at hospital 1 was provided by nurses, while testing at hospital 2 was provided by lab personnel. Results of POCT HbA1c were available prior to doctor consultation, while results of lab HbA1c testing took 5-7 days. 1000 patients having HbA1c measured by laboratory POCT at hospital 2 (n=500) or the laboratory at hospital 1 (n=500) across 1995 and 1996 were included in the study. The mean HbA1c was significantly lower in the patients having their HbA1c measured by POCT vs laboratory, after controlling for case-mix (8.26%±0.144 vs 8.61%±0.156, p <0.001). However the authors note that their study design was unable to control for all confounding factors such as differences in clinical protocols and experience of the managing physicians at the two hospitals. Patients (n=595 and 280) who received their HbA1c result by POCT (either by lab or nurse-based POCT at hospitals 1 and 2 respectively) were significantly more satisfied (p <0.004 and p <0.001) with the test information compared to those who received their result later from the laboratory at hospital 1. A subset of 599 patients were alternatively allocated to HbA1c POCT measured by nurses (n=302) or by the lab (n=297) at hospital 1. The number of management changes related to insulin or oral therapy and diet were recorded. Overall, patients in the POCT group were more likely to have management changes than the control group (Odds ratio [OR] 1.52, 95%CI 1.02-2.26). When patients were split into those with good control (HbA1c <7.5%) and poor control (HbA1c ≥7.5%), the patients with poor control were more likely to have management changes if they were in the POCT group rather than the control group (OR 1.72, CI 1.12-2.21). For patients with good control the number of management changes did not differ between testing methods (OR 0.92, CI 0.35-2.24).

Outcome Category Assessed	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test, and Device	Author	Summary of Methodology and Key Findings
						Patients using the lab POCT service at hospital 2 had significantly fewer hospital visits per annum than those using the lab service at hospital 1 (1.81 visits per patient per year [SD 1.20]) vs 2.28 visits per patient per year [SD 1.01]). However, it was not possible to conclude this difference was a direct result of POCT or due to other factors such as the need to visit hospital 1 more frequently to collect results or differences in clinical practices between the two hospitals. The mean visit costs were £3.80 higher for lab POCT and £12.60 higher for nurse POCT than the laboratory, due to the higher number of POC tests performed and the higher capital costs of the POCT devices. However, the mean difference in annual costs between POCT and the lab was not significant because, as mentioned above, the mean number of visits per patient per year was lower for lab POCT.
Clinical	Influence on clinical management decisions Glycaemic control	Private endocrinology practice	Retrospective cohort	HbA1c, Diastation exchange LPLC	Ferenczi (343)	Study participants were 115 patients with type 2 diabetes over the age of 65 who were referred to a private endocrinology practice between early 1997 and 1998. Patients were classified into two groups; group A had immediate HbA1c results available during visit (n=93), while group B (n=22) had HbA1c tested by one of three laboratories with results available 2-3 days later. In group A using POCT, therapeutic interventions occurred in 40% of visits (145/362), while in group B changes of therapy occurred in 24% of visits (19/80), p = 0.006. In both groups, HbA1c was measured at the first visit and 12 months later. In group A, mean HbA1c levels decreased by 1.03% (±0.3) from 9.5% to 8.47%. In group B, mean levels fell by 0.33% (±0.83) from 8.3% to 7.97%. However the decline in HbA1c was not significantly different between the two groups (no p value was provided).

Outcome Category Assessed	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test, and Device	Author	Summary of Methodology and Key Findings
Clinical	Influence on clinical management decisions Glycaemic control	Primary care clinic	Quasi randomised	HbA1c, DCA 2000	Miller (342)	597 patients with type 2 diabetes, 79% female, 96% African American, of older age (mean 61 years). Patients (n=317) were assigned to having POCT HbA1c if baseline visit fell on even numbered day and routine HbA1c lab testing (visit on odd day). POCT group had more frequent intensification of therapy when HbA1c was ≥7% than control group at their baseline visit (51% vs 32% of patients, p = 0.01). HbA1c was measured in 275 patients (POCT n=141 and lab n=134) at two follow-up visits 2-4 months apart. In the POCT group, the mean HbA1c levels decreased modestly but significantly by 0.3% from 8.4% to 8.1% (p=0.04). In the control group, mean levels fell by 0.1% from 8.1% to 8.0% (p=0.31, not significant). The authors make the observation that 70% of patients in the POCT group and 73% of patients in the control group remained inadequately controlled (HbA1c ≥7%). Comment: Glycaemic control in both groups was only followed prospectively for a very short time period of 4-6 months, which severely limits the impact of the findings. The authors note the study population was African-American and the findings may not be generalisable to other ethnic or cultural groups.
Clinical	Glycaemic control	Specialist diabetes clinic integrated into primary care Aboriginal Community Controlled Health Service	Retrospective audit	HbA1c, DCA 2000	Simmons (42)	30 Aboriginal patients with type 1 or 2 diabetes had HbA1c measured by POCT at baseline and at (a median of) 10 months after commencing POCT. POCT was part of a new weekly integrated specialist diabetes clinic conducted in a primary care Australian Aboriginal health service. Mean HbA1c of group decreased from 10.4% (±2.2) at baseline to 7.9% (±1.9) at 10 months (p <0.001).

RCT = randomised controlled trial

Table 2.23. Comparison of studies documenting the effectiveness of POC HbA1c testing.

Reference	Study design	No. of patients	Was Study Population Indigenous?	Duration of study, months	Statistically significant decline in HbA1c with POCT
Pope (320)	Observational	18	No	Not reported	Not reported
Thaler (341)	RCT/ pre and post	1138/574	Yes	2-7	No; HbA1c rose by 0.4%
Cagliero (340)	RCT	201	No	6 & 12	Yes; HbA1c fell by 0.57% & 0.4%
Grieve (344)	Cohort, retrospective	1000	No	Not reported	Not reported
Ferenczi (343)	Cohort, retrospective	115	No	12	Yes; HbA1c fell by 1.03%
Miller (342)	Quasi-RCT	597	Yes	4-6	Yes; HbA1c fell by 0.3%
Simmons (42)	Audit	30	Yes	10	Yes; HbA1c fell by 2.5%

Urine Microalbumin

This literature search found no papers that reported on the effectiveness of POCT for urine microalbumin in either primary or secondary care settings, apart from articles published by the author and presented in Chapter 7 which showed POCT urine ACR testing was culturally and clinical effective in both community risk assessment and the stabilisation of renal function in Indigenous patients at high risk of renal disease (10-12, 16). As mentioned in Chapter 1, these studies arose following calls in the literature in 1996 for the use of urine ACR testing in Indigenous community-based screening programs for the early detection of renal disease (235, 350); they provided the impetus for the initial program of research described in this thesis, namely the Umoona Kidney Project (11, 12).

While no POCT studies have been reported other than those presented in this thesis, it should be noted that laboratory urine ACR measurements have been widely used in studies of the prevalence, natural history and the multidimensional nature of renal disease in Indigenous Australians (235, 350-364).

The urine ACR test was also selected for the monitoring of microalbumin in diabetes patients recruited for the Australian primary care PoCT in General Practice Trial (36). However the results of the outcome assessments from this Trial will not be available until late 2007/2008.

Lipids

This literature search identified four papers that reported the effectiveness of POCT lipid measurements in ambulatory care settings; two in community pharmacies (365, 366), one in general practice (73) and one involving pharmacist-led home visits (367). The methodology and key findings of these studies are summarised in Table 2.24. Study designs included two randomised controlled trials (366, 367) and two observational studies (73, 365). None of the studies focussed exclusively on patients with diabetes; two involved varying proportions of patients with this disease (11% and 44%) (73, 365, 366), the other two

studies made no specific reference to patients with diabetes. All except Cohen *et al* (73) used POCT as part of multidimensional patient management plans.

Outcome benefits reported in these studies included improved clinical and patient satisfaction (73), improvements in the management process for cardiovascular risk (CVD) (366), improved compliance and achievement of therapeutic targets (365) and reduction in CVD risk (367).

The randomised controlled trial of Tsuyuki *et al* (366) was a well-designed study although the authors acknowledge it was undertaken by a highly selected group of pharmacists, which may have limited the generalisability of the findings. The lack of a control group in the Bluml *et al* study (365) and the fact that only 69% of patients completed the study limits the conclusions that can be drawn from this work. The high proportion of Asian participants may also limit the applicability of the study results to the general population. Peterson *et al* (367) noted that their Australian randomized controlled trial was confounded by the analytical sensitivity of the POCT device (Accutrend) which had a lower limit of measuring range of 3.88 mmol/L. Twenty three and 24 patients across both the intervention and control groups had cholesterol levels below this limit at baseline and at 6 months respectively.

Table 2.24. Outcome studies for POC lipid testing for diabetes management in ambulatory care settings. (Table continues to page 129).

Outcome Category Assessed	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test	Author	Summary of Methodology and Key Findings
Clinical, Operational, Economic	Clinical appropriateness of POCT GPr and patient satisfaction	GP	Observational	Chol, using Reflotron, Vision and Kodak	Cohen (73)	13 GPrs (from Category 5 accredited practices in Victoria, Australia) and 206 patients conducting and having POC cholesterol testing respectively completed quantitative satisfaction surveys about POCT. Of the 206 patients, 11% had diabetes. POCT cholesterol testing was appropriately used by GPrs and recommended management guidelines for lowering cholesterol were followed. GPrs and their patients reported a strong preference for POCT in all attitudinal scales of convenience, issues of patient care, professional factors and cost. For GPrs, the highest positive attitudinal scores (mean >4.4 out of a maximum score of 5) related to the convenience of having results available at consultation, the opportunity to discuss results immediately and the contribution of POCT to preventative and overall patient care. For patients, highest positive attitudinal scores related to the convenience and reduced stress in having results available at consultation, the opportunity to discuss results immediately, and their satisfaction with the GP performing the tests and understanding their needs. A descriptive account of the main cost differences between POCT and laboratory cholesterol measurements was provided but this was not a full economic analysis.
Operational	Improvement in process of managing CVD risk	Community pharmacies	RCT	Chol, using Accutrend	Tsuyuki (366)	675 patients at high risk for cardiovascular events (including 44% with diabetes mellitus) attending 54 community pharmacies from 1998-2000 were included in the study. Patients were randomised to either (i) pharmacist intervention, receiving education and a brochure on risk factors, POCT for cholesterol, referral to their physician, and regular follow-up for 16 weeks or (ii) usual care with patients receiving the brochure and general advice only, with minimal follow-up. The primary end point was a composite measure representing improvement in the process of cholesterol risk management which included (i) performance of a fasting cholesterol panel by the primary care physician or (ii) addition or increase in dose of cholesterol-lowering medication.

Outcome Category Assessed	Example of POCT Outcome Measure	Location of Study	Type of Study	POC Test	Author	Summary of Methodology and Key Findings
						Overall, the primary end point was reached in 57% of intervention patients vs 31% in usual care (odds ratio, 3.0; 95% confidence interval, 2.2-4.1; p <.001). In the subgroup of patients with diabetes, the primary end point was reached in 62% of intervention patients vs 25% in usual care (odds ratio, 4.8; 95% confidence interval, 2.9-8.0; p = 0.01).
Clinical	Achievement of therapeutic targets Compliance	Community pharmacies	Observational	Full lipid profile	Bluml (365)	597 patients attending 26 community pharmacies from 1996 to 1999 were initially enrolled in the study. 397 (69%) completed the study; of these 85% were Asian and were either newly diagnosed with dyslipidaemia or already receiving lipid lowering medications but were poorly controlled. The paper does not state how many patients had diabetes. Patients visited the pharmacist every 3 months and then quarterly thereafter for 2 years. They were given advice by the pharmacist on therapy, treatment plans and goal setting (using NCEP goals). POCT lipids were measured at baseline, mid-study and after 2 years (mean 24.6 months). 62.5% of the 397 patients who completed the entire study patients reached and were maintained at their NCEP lipid goal by the end of the project. Overall, there was a 13% decrease in Chol from baseline, 10% decrease in TG, 22% decrease in LDLC and 14% increase in HDLC. Compliance rate at the end of the study was 90.1%.
Clinical	Reduction in CVD risk	Pharmacist led home care	RCT	Chol	Peterson (367)	81 patients with a cardiovascular-related diagnosis and discharged from hospital, between April and October 2001, on lipid-lowering drug therapy were studied. They were randomized to (i) monthly home visits by a pharmacist, who provided education on diet and lifestyle and monitored the patient's response to therapy using POCT Chol levels for 6 months or (ii) a control group who received standard medical care over 6 months. Chol in the intervention group showed a statistically significant reduction from 4.8 mmol/L (SD 0.7) to 4.4 mmol/L (SD 0.6) after 6 months, P <0.005), whereas there was no change within the control group (4.8 mmol/L (SD 0.9) to 4.6 mmol/L (SD 0.8), p = 0.26). At follow-up, 44% of the intervention group and 24% of the control group had Chol levels below 4.0 mmol/L (p = 0.06).

GP = General Practice; GPr = General Practitioner; GPrs = General practitioners; CVD = cardiovascular disease; Chol = total cholesterol; TG = triglyceride; HDLC = HDL cholesterol and LDLC = LDL cholesterol; NCEP = National Cholesterol Education Program

Glucose

The evidence base for the effectiveness of POCT glucose measurement will be summarised briefly. Self monitoring of blood glucose (SMBG) is generally accepted as a crucial component of the management of patients with type 1 diabetes to minimise the risks of hypo- and hyper-glycaemic episodes (222). Intensively treated patients with type 1 diabetes who undertook self monitoring of blood glucose at least four times a day had reduced risk of developing microvascular complications of diabetes in the DCCT study (241).

The benefits of SMBG in patients with type 2 diabetes are contentious and widely debated in the literature (368). Coster *et al* conducted a meta-analysis of data from seven randomised controlled trials involving SMBG and concluded there was no evidence of improved glycaemic control associated with frequent blood glucose testing (369). However the studies included in the meta-analysis were methodologically poor, lacking in statistical power and three of the trials had follow-up of 6 months or less. The authors also acknowledged that the effectiveness of SMBG was largely dependent on the type and quality of diabetes education which patients receive. The findings of Coster *et al* were supported by the cross-sectional study of Patrick *et al*, which involved 200 non-insulin treated patients with type 2 diabetes (370).

In contrast to these findings, the large cohort study of Karter *et al* involving over 24,000 patients with type 1 and type 2 diabetes found that SMBG was associated with clinically and statistically better glycaemic control regardless of diabetes type or therapy (371). Murata *et al* also found intensified SMBG improved glycaemic control in 201 insulin-treated veterans with type 2 diabetes, with SMBG providing a strong stimulus for improved self care (372). In a large observational study of 2855 patients with type 2 diabetes, Franciosi *et al* found a higher frequency of SMBG was associated with better glycaemic control in patients who were able to adjust insulin doses, whereas no relationship was found in all other patients irrespective of treatment type (373).

Thus the value of SMBG in patients with type 2 diabetes remains controversial although it is likely to be of benefit in selected patients, particularly in those on insulin therapy or those where safety is a prime indictor for SMBG (222).

Summary of POCT Studies for Diabetes and Renal Disease in Ambulatory Settings

While there is a clear need for further outcome studies especially randomised control trials, there is sufficient evidence to conclude that POCT, particularly for HbA1c and lipids, can be effective in monitoring response to therapy and achievement of therapeutic targets at least for diabetes management in ambulatory care settings. There is limited evidence to support the observation that POCT increases clinician and patient satisfaction, but no evidence on the clinical or cultural effectiveness of POCT for diabetes and renal disease management in the Australian Indigenous health setting apart from the study of Simmons (42) and papers published by the author in this research program.

SUMMARY - GAPS IN LITERATURE AND HOW THESE ARE ADDRESSED BY THIS PROGRAM OF RESEARCH

Table 2.25 summarises the main findings of this literature review and identifies the current gaps in the POCT knowledge base that are relevant to this thesis.

POCT now has a major role in the primary care setting where the care of patients with chronic disease is being increasingly devolved. POCT devices are available for diabetes and renal disease management although, apart from the study of St John et al (310) and those of the author (presented in Chapter 3 of this thesis), their analytical performance has not been evaluated under Australian conditions. POCT can also have clinical and operational benefits under appropriate conditions.

The Australian Indigenous medical service is an important primary care setting in Australia and the burden of diabetes and renal disease represents one of the greatest contemporary challenges facing the health care system in this country. Therefore, intuitively the Australian Indigenous health service would appear to represent a very appropriate setting in which to conduct POCT.

Other factors which suggest that the Australian Indigenous health service would be a suitable niche for POCT include:

- Over 90% of Aboriginal medical services are located in rural and remote Australia, where access to mainstream laboratory services is often poor,
- Aboriginal Heath Workers could potentially be trained as POCT operators, although such a role had never been undertaken before and they have had no previous knowledge or formal training in diagnostic pathology testing,
- The accessibility and convenience of POCT, as well as immediate feedback of results, may prove attractive for Indigenous patients. Western standards of laboratory practice are often

culturally inappropriate because Indigenous patients have difficulty attending follow-up visits to receive laboratory results (and hence treatment) due to other social and cultural priorities,

- Community control and ownership is a crucial cultural element to successful implementation and uptake of health programs; with POCT being conducted by the Aboriginal Health Worker on-site in the community, the sense of community control is fostered and enhanced.

Nonetheless, despite this potentially exquisite cultural fit of POCT, the Australian Indigenous health care setting also presents one of the most challenging environments in which to conduct POCT. Most rural and remote Indigenous health services endure difficult working conditions, including extremes of heat, humidity and dust, regular power fluctuations, inadequate lighting and refrigerator space, and poor access to IT services, support and infrastructure. Staff turnover among both health professional and administrative staff is extremely high, making health programmes (including POCT) difficult to sustain (13).

However, as reiterated many times in this chapter, this literature review revealed that the application of POCT had not been previously addressed in the Australian Indigenous health care setting. The key research question examined in this thesis was thus: Could POCT models for the prevention and management of diabetes and renal disease be developed and implemented in the Australian Indigenous medical service setting, models that would prove analytical sound and both clinically and culturally effective? The papers presented in the subsequent chapters address and answer this question.

The literature review also revealed that chronic disease is a major health problem for non-Indigenous Australians (albeit not to the same significant levels as Indigenous people). Many of these patients, particularly in rural and remote communities, suffer similar access barriers to pathology and other specialist services. As a concluding component of this research program, the transferability and adaptability of my Indigenous POCT models to other primary care settings was investigated, with these findings presented in Chapter 7.

Table 2.25: Summary of key findings of this literature search, the gaps identified in the current literature, and how and where these gaps have been addressed in this thesis/program of research. (Table continues to page 136).

Topic	Key Findings/Gap Identified in the Literature	How Gap Addressed in this Thesis/Program of Research	Relevant Chapter(s)
General			
Primary aim of literature review - search for the evidence for the use and application of POCT in the primary care Australian Indigenous health care setting	The literature was totally replete of published papers on POCT in Australian Indigenous health care setting, apart from the research conducted directly or collaboratively by the author.	The purpose of this program of research was to develop and implement models for the application of POCT for diabetes and renal disease in the Australian Indigenous health care setting.	Chapters 3-7
Definition of POCT	No single definition was available that appropriately addressed all aspects of POCT.	Definition proposed in the literature review.	Chapter 2
Organisation and Management	There were no standards or guidelines exclusively written for establishing and managing POCT in a primary care community-based setting, including the Australian Indigenous health setting; apart from the interim standards and guidelines being trialled in the POCT in General Practice Trial.	Models for establishing and managing POCT in the Australian Indigenous health setting were developed for the Umoona, QAAMS and POCT in Aboriginal Hands Programs, with particular focus on training Aboriginal Health Workers as POCT operators and managing analytical quality.	Chapters 5 and 6
Evidence base for effectiveness of POCT	While some evidence was available for the broad effectiveness of POCT in hospital and primary care settings (excluding diabetes and renal disease), no studies have been conducted in the Australian Indigenous primary care setting.	Studies of clinical and cultural effectiveness of POCT in different Australian Indigenous health settings have been undertaken.	Chapter 6

Topic	Key Findings/Gap Identified in the Literature	How Gap Addressed in this Thesis/Program of Research	Relevant Chapter(s)
POCT for Renal Disease and Diabetes			
1. Prevalence	There is an extremely high burden of diabetes and renal disease in Indigenous Australians.	POCT programs have been implemented to prevent and manage these major contemporary diseases.	Chapters 5 and 6
2. Overview of tests available and clinical utility	Although the clinical utility of HbA1c, urine microalbumin and lipids is well established, the measurement of these tests by POCT has not been previously undertaken in the Australian Indigenous health setting.	POCT for HbA1c, urine ACR and lipids was implemented in Australian Indigenous medical services.	Chapters 5 and 6
3. POCT devices A. Analytical evaluations	Apart from St John *et al* (310), no evaluations of POCT analysers for diabetes and renal disease have been reported under Australian conditions – either in the laboratory or the field.	Field and laboratory evaluations of POCT analysers were undertaken in Australia to validate this technology.	Chapter 3
3. POCT devices B. Analytical goals for POC tests for diabetes and renal disease	No analytical goals are available specifically for POC tests for diabetes and renal disease.	Paper was written promulgating analytical goals for the use of POC tests for diabetes management in non-laboratory settings.	Chapter 4
3. POCT devices C. Analytical performance in the Australian Indigenous health setting	There are no published results from external Quality Assurance Programs on analytical quality of POCT for diabetes and renal disease in Australian Indigenous medical services.	National Quality Assurance Programs were established for HbA1c and urine ACR POCT for diabetes and renal disease and data on analytical performance collected and analysed over 7 years.	Chapter 5
4. Evidence for the effectiveness of POCT for diabetes and renal disease management	No evidence was found in this literature search for the clinical or cultural effectiveness of POCT for diabetes and renal disease management in the Australian Indigenous health care setting, apart from the study of Simmons (42).	Studies of clinical and cultural effectiveness of POCT in different Australian Indigenous health care settings have been undertaken.	Chapter 6

Topic	Key Findings/Gap Identified in the Literature	How Gap Addressed in this Thesis/Program of Research	Relevant Chapter(s)
5. Transferability of POCT Models	No evidence on the transferability of POCT models to other clinical settings was found.	POCT models in Australian Indigenous health services were adapted for use in a rural country hospital and General Practices in Australia.	Chapter 7

SECTION 2: PUBLISHED PAPERS

INTRODUCTION TO PUBLISHED PAPERS

The 19 peer-reviewed papers presented in the following five chapters were published in national and international journals specifically selected by the author because they targeted the professional audiences of most relevance to, and with greatest interest in, the field of POCT.

The *Clinical Biochemist Reviews* and the *Australian Journal of Medical Science* are the official journals of the Australasian Association of Clinical Biochemists (AACB) and the Australian Institute of Medical Scientists (AIMS), the professional bodies representing clinical biochemistry and laboratory medical scientists in Australasia and Australia respectively. The *Annals of Clinical Biochemistry* is the international journal of the Association of Clinical Biochemists in the United Kingdom. *Point of Care* is a new international journal affiliated with the Critical and Point-of-Care Testing Division of the American Association for Clinical Chemistry (AACC) and it is the only journal with a specific focus on POCT.

Rural and Remote Health is the only international electronic journal focussing on rural and remote health research, education, practice and policy. The *Medical Journal of Australia* is Australia's premier journal of medical practice and clinical research.

The *Aboriginal and Islander Health Worker Journal* is the oldest and principal peer-reviewed journal representing the Aboriginal Health Worker professional group in Australia.

In addition to these papers, a peer-reviewed book chapter the author was invited to write in the second edition of the book *Point of Care Testing* is included in the published works. *Point of Care Testing*, edited by Price, St John and Hicks (14), is widely regarded as the definitive global text book on the subject of POCT.

Collectively these papers and the book chapter have enabled me to strategically disseminate my research findings to a wide audience of clinical biochemists, medical scientists, experts in the field of POCT, clinical researchers, health professionals working in the field of rural and remote health where the application of my POCT models has most relevance and, importantly to the wider Aboriginal Health Worker profession in Australia.

As first author of these papers, my publication philosophy has been to be as inclusive as possible with co-authors to foster the spirit of collaboration and a sense of collective ownership of the POCT models I have implemented in the Indigenous health care setting. As emphasised throughout this thesis, the engagement and empowerment of Aboriginal Health Workers and the Indigenous community in general has been absolutely pivotal and crucial to the success of my POCT models in this setting.

CHAPTER 3

ASSESSMENT OF ANALYTICAL PERFORMANCE OF POCT DEVICES USED IN THIS PROGRAM OF RESEARCH

INTRODUCTION TO CHAPTER 3

The four papers presented in this chapter describe studies undertaken by the author in both the laboratory and the field to evaluate and validate the analytical performance of the POCT devices used in this research program (both prior to their introduction into a POCT model and in an on-going sense). These studies principally involved an assessment of the analytical accuracy and/or precision of the POCT device(s).

IS THE BAYER DCA 2000 ACCEPTABLE AS A SCREENING INSTRUMENT FOR THE EARLY DETECTION OF RENAL DISEASE?

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Annals of Clinical Biochemistry 1999; 36: 393-394.

STATEMENT OF AUTHORSHIP

IS THE BAYER DCA 2000 ACCEPTABLE AS A SCREENING INSTRUMENT FOR THE EARLY DETECTION OF RENAL DISEASE?

Annals of Clinical Biochemistry 1999; 36: 393-394.

SHEPHARD, M.D.S. (Candidate)

Conceived research question, designed evaluation, performed sample analysis, interpreted data, wrote manuscript and acted as corresponding author.

Signed . ... *Date* 18/11/2006

BARRATT, L.J.

Commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed . ..... *Date* 18.11.06

SIMPSON-LYTTLE, W.

Commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed ..... *Date* 12/11/2006

Is The Bayer DCA 2000 Acceptable As A Screening Instrument For The Early Detection Of Renal Disease?

The urine albumin:creatinine ratio (ACR) test first became available as a POC test on the Bayer DCA 2000 in Australia in 1998. This study was undertaken to answer the research question: Was the analytical performance of the urine ACR test acceptable for potential use in the Indigenous medical service setting (specifically the Umoona Tjutagku Health Service at Coober Pedy in South Australia's far north)? The study represented the first scientific evaluation of this POC test in Australia. The study was also particularly timely because there were calls in the literature in the late 1990s from leading Australian clinical researchers advocating the urgent need to develop simple community-based screening programs (including the measurement of urine ACR) for recognising and managing renal disease risk factors in an Australian Indigenous population that had become burdened with escalating rates of renal disease (235, 350, 352).

The study validated for the first time under Australian conditions that the urine ACR test on the DCA 2000 was precise, accurate and diagnostically reliable and, with its simple operation and the availability of an on-site urine ACR result in 7 minutes, the DCA 2000 would be an ideal device for use in the remote Indigenous community setting. The study thus provided the impetus for the use of the urine ACR POC test in the Umoona Kidney Project.

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Is the Bayer DCA 2000 acceptable as a screening instrument for the early detection of renal disease?

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Additional key phrases: early renal disease; urine albumin:creatinine ratio; specificity; predictive value for microalbuminuria

The analytical capabilities of the Bayer DCA 2000 System point-of-care instrument (Bayer Australia Ltd, Pymble, NSW, Australia) have recently been upgraded to include the measurement of the urine albumin:creatinine ratio (ACR).[1] Microalbuminuria, defined as a urine ACR between 3·4 and 34 mg/mmol for females and between 2·5 and 34 for males,[2] is a well-established predictor for diabetic nephropathy and clinical proteinuria in the non-diabetic.[3] The use of the urine ACR measurement as a screening test for the early detection of renal disease in high-risk population groups, such as Aboriginal Australians, has recently been advocated.[4,5]

Through a co-operative partnership with the Umoona Tjutagku Health Service, the Renal Unit at Flinders Medical Centre has recently begun a program for the early detection and prevention of renal disease with the 500-strong Umoona Aboriginal community at Coober Pedy in South Australia's far north. The first phase of the study involves screening the community for its risk factors for renal disease, the cornerstone of which is the measurement of urine ACR. The Bayer DCA 2000 instrument was selected as the instrument of choice for this phase of the program, but prior to its implementation, the analytical and diagnostic performance characteristics of the machine were evaluated.

METHODS AND PATIENTS

The Bayer DCA 2000 instrument uses a reagent cartridge (Bayer DCA 2000 Microalbumin/Creatinine Catalogue Number 0611) which provides a quantitative measurement of albumin (by immunoturbidimetry, using a polyclonal goat anti-human albumin antiserum) and creatinine [by spectrophotometry using 3,5-dinitrobenzoic acid (DNBA) at alkaline pH], as well as calculation of the ACR, all within a 7-min window. Common potential interfering substances with colorimetric urine creatinine methods, such as glucose, acetoacetic acid, bilirubin and cephalolothin, were shown by Bayer to produce a bias of less than ±5% using the DNBA method.[6] The measuring ranges of the instrument are: urine albumin 5 to 300 mg/L, urine creatinine 1·3 to 44·2 mmol/L, and urine ACR 0·11 to 226 mg/mmol. Calibration parameters are encoded onto a calibration card provided with each reagent kit (which contains ten cartridges). Urine albumin, creatinine and ACR results are displayed for each test sample.

Low and high control samples (Bayer DCA 2000 Microalbumin/Creatinine Low and High Control kit, Catalogue Number 6012) were analysed daily on the DCA 2000 over a 15-day period to assess between-run imprecision.

Sixty random; spot urines from diabetic subjects (64% males and 36% females) were analysed over a 30-day period by both the DCA 2000 (using six reagent kits) and by routine methods at the SouthPath laboratory, Flinders Medical Centre [urine albumin by nephelometry using the Beckman Array (Beckman Instruments Inc, Fullerton CA, USA) and urine creatinine by a kinetic Jaffe method on an Hitachi 917 (Boehringer Mannheim GmbH, Mannheim, Germany)]. These urines had a range of concentrations/ratios (by the SouthPath methods) of urine albumin 4 to 235 mg/L, urine creatinine 2 to 24 mmol/L, and urine ACR 0·4 to 34 mg/mmol.

RESULTS

Between-day coefficients of variation ($n = 15$) for each measurement on the DCA 2000 were: 3·0% and 2·4% for urine albumin (at levels of 34 and 201 mg/L, respectively), 2·1% and 1·8% for

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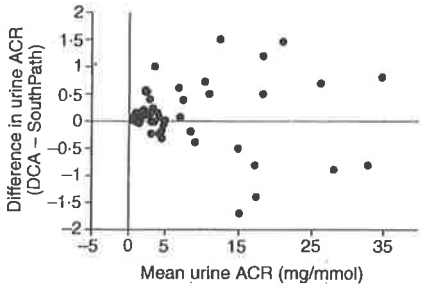

FIGURE. *Bland–Altman plot showing the difference in urine albumin:creatinine ratio (ACR) results between the Bayer DCA 2000 and the SouthPath laboratory routine methods. See text for manufacturers' details.*

urine creatinine (8·8 and 36·7 mmol/L), and 3·4% and 2·3% for urine ACR (for ratios of 3·8 and 5·5). These levels of imprecision are better than those achieved by the top 20% of laboratories participating in the Royal College of Pathologists of Australasia – Australasian Association of Clinical Biochemists Chemical Pathology Quality Assurance Programs group (8·2% for urine albumin, 2·4% for urine creatinine, June 1998 cycle) (J Gill, personal communication).

For the 60 urines tested, the DCA 2000 showed excellent correlation with the SouthPath methods (regression analysis slopes = 1·05, 1·03 and 0·99, and $r = 0·99$, 0·99 and 1·00 for urine albumin, urine creatinine and urine ACR, respectively).

The figure displays the difference in results between the two methods for urine ACR. The overall mean difference for ACR between the two methods was 0·119 (standard error 0·071); $P = 0·100$, not significant.

Of the 60 urines tested, 34 (57%) were classified as normal and 26 (43%) as microalbuminuric (ACR between 3·4 and 34 mg/mmol) by the SouthPath methods. There was only one urine sample where a difference in diagnostic classification for microalbuminuria would have been made using the DCA 2000 (SouthPath ACR 2·8, normal; DCA 2000 ACR 3·8, microalbuminuria – false positive). The DCA 2000 thus exhibited the following comparative diagnostic performance characteristics for microalbuminuria: sensitivity 100%, specificity 97%, predictive value of a positive test 96%, and predictive value of a negative test 100%.

CONCLUSION

This evaluation showed that the Bayer DCA 2000 provides a precise, accurate and diagnostically reliable measurement of urine ACR. In addition to its analytical capabilities, the DCA 2000 has many other characteristics which make it an ideal screening instrument for the early detection of renal disease in a remote clinical setting, such as the Umoona Aboriginal community at Coober Pedy; it is portable, simple to use, requires no sample or reagent preparation, provides quick turnaround of results (7 min) and is cost effective (an ACR on the DCA 2000 being over three times less expensive than the standard government reimbursement for a laboratory urine albumin and urine creatinine determination).

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ASSESSMENT OF THE POINT-OF-CARE CHOLESTECH LIPID ANALYSER FOR LIPID SCREENING IN ABORIGINAL COMMUNITIES.

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STATEMENT OF AUTHORSHIP

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SHEPHARD, M.D.S. (Candidate)

Conceived research question, designed evaluation, analysed and interpreted data, wrote manuscript and acted as corresponding author.

Signed .... *Date* 1/12/2006

TALLIS, G.

Commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed .... *Date* 1-12-06

Assessment Of The Point-Of-Care Cholestech Lipid Analyser For Lipid Screening In Aboriginal Communities.

Following the successful application of POCT in the Umoona Kidney Project and the QAAMS Program, the author received many enquiries from Indigenous medical services about the measurement of blood lipids by POCT. At this time, the Cholestech LDX device was the only POCT device available in Australia that performed a full lipid profile on a single blood sample but there were no published evaluations on its analytical performance in this country. This paper therefore examined the research question: Was the analytical performance for lipid testing on the Cholestech LDX acceptable for potential use in the Indigenous medical service setting?

The study validated for the first time under Australian conditions that lipid testing on the Cholestech was analytically sound, particularly for use in cardiovascular risk assessment. This study provided the impetus for using the lipid POCT device, in conjunction with the DCA 2000, for chronic disease risk assessment and management in the Point-of-Care Testing in Aboriginal Hands Program.

Original Article

Assessment of the point-of-care Cholestech lipid analyser for lipid screening in Aboriginal communities

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Abstract

Cardiovascular disease is the leading cause of mortality in Aboriginal Australians. Screening for cardiovascular disease risk factors, notably elevated blood lipids, is urgently needed. The small, portable Cholestech machine (Point-of-Care Diagnostics) can enzymatically measure total cholesterol, triglyceride and HDL cholesterol (without the prior need for precipitation of other lipoproteins) on 35µL of capillary or venous whole blood in under 5 minutes. It also calculates LDL cholesterol. Its suitability for use in Aboriginal communities was assessed. Fifty-one volunteers had their lipids measured on capillary and venous whole blood samples on the Cholestech. These results were compared with those obtained by Center for Disease Control (CDC)-certified methods on the Hitachi 917. The correlation (r^2) between the Cholestech and Hitachi machines for both capillary and venous whole blood samples was ≥ 0.96 for total cholesterol, ≥0.99 for triglyceride, and ≥0.92 for HDL- and LDL cholesterol. The mean percentage difference between results on the Cholestech and Hitachi for both sample types was less than 2% for total cholesterol and triglyceride analyses and less than 5% for HDL- and LDL cholesterol. A positive bias of 6% was observed on the Cholestech at HDL cholesterol concentrations greater than 1.2 mmol/L. Within-day precision (CV%) on whole blood samples ranged from 0.9 to 3.5% for total cholesterol, 1.6 to 2.5% for triglyceride and 6.3 to 7.9% for HDL cholesterol. There was no significant difference between capillary and venous whole blood lipid measurements performed on the Cholestech. With its simple operation, fully automated nature, sound analytical performance and ability to produce a full lipid profile in under 5 minutes, the Cholestech would be suitable for the Aboriginal health care setting.

Keywords - Cholestech, point-of-care technology, screening, lipids

Introduction

Cardiovascular disease is the leading cause of mortality in Aboriginal Australians, with mortality rates due to coronary heart disease and stroke being twice those of non-Aboriginal Australians (1-3). Of particular concern are the high death rates from coronary heart disease among young and middle-aged Aboriginal people, with death rates for people aged 25-44 years being more than 10-times those of other Australians (2). Risk factors for cardiovascular disease in Aboriginal people include hypertension,

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diabetes, obesity, tobacco and alcohol consumption, lack of physical activity and high blood lipids (2-7).

Screening for cardiovascular disease risk factors, notably elevated blood lipids, has been carried out in selected Aboriginal communities and parts of Australia. For example, the prevalence of dyslipidaemia was examined in a study of over 1000 Aboriginal people from Central Australia, the Kimberley in Western Australia and Cape York in Queensland was 36% (4).

In another study of over 350 Aboriginal people from a community west of Alice Springs, 68% of men and 46% of women over 35 years of age had raised cholesterol levels, while 51% of men and 27% of women had elevated triglyceride concentrations (5). In a country Victorian screening program, 30% of over 120 Aboriginal males tested had cholesterol levels greater than 6.5 mmol/L while 56% had triglycerides greater than 2.0 mmol/L (6). In the Tiwi Islands, 50% of over 850 adults screened had dyslipidaemia, notably high triglycerides (7).

Perhaps even more disturbing is the prevalence of lipid disorders found in a recent study in the Kimberley region of 74 Aboriginal children and adolescents (mean age 18.5 years). Nearly a quarter of these young Aboriginal people had hypercholesterolaemia, while 12% had elevated LDL cholesterol concentrations (8). Clearly, further well co-ordinated, community-controlled and culturally-appropriate lipid screening programs are urgently needed in Aboriginal communities nationally to identify people with disorders of lipid metabolism and to provide these people with the opportunity to participate in intervention programs aimed at lowering their risk for cardiovascular disease.

A major barrier to effective lipid screening in many rural and remote Aboriginal communities is limited access to pathology laboratories. Aboriginal health services may be several hundred, even thousands, of kilometres from the nearest pathology service and blood samples may take up to several days to reach that service, particularly if air transport is limited or unavailable. The return of results to the community and then to the individual patient incurs further delays, while patient follow-up may not be possible.

The ability to perform on-site testing for blood lipids using point-of-care technology would address many of the current problems associated with effective delivery of a lipid screening service. The small, portable Cholestech machine (Point-of-Care Diagnostics) can measure total cholesterol, triglyceride and HDL cholesterol, without the prior need for precipitation of other lipoproteins, on 35µL of capillary or venous whole blood in under 5 minutes. It also calculates LDL cholesterol. The analytical performance of the Cholestech machine was assessed in the laboratory, with the view to testing the machine in the Aboriginal health care setting for lipid screening and on-going management.

Materials and Methods

Samples

Fifty-one volunteers had their lipid levels measured on capillary (fingerprick) and venous whole blood samples on the Cholestech (Point-of-Care Diagnostics, Artarmon, NSW) and on venous plasma by the SouthPath laboratory, Flinders Medical Centre, South Australia.

After sitting for five minutes, each subject had a capillary and venous whole blood sample collected less than five minutes apart. The capillary sample for the Cholestech was taken from the upper side corner of the chosen finger, with the first drop of blood being wiped away. Venous whole blood was collected by venepuncture into a heparinised blood tube. After testing the venous whole blood sample on the Cholestech, the remaining blood was sent to SouthPath, where it was centrifuged for five minutes at 5,000 rpm and venous plasma separated for subsequent analysis.

The Cholestech system

Thirty-five microlitres of sample (capillary or venous whole blood) is placed in the sample well of the Cholestech reagent cassette, and loaded into the instrument. Once in the machine, plasma is separated from red blood cells using a glass fibre

screen. Plasma is directed to individual analyte-specific, solid phase reagent pads containing reactants. Resultant colour is measured by reflectance photometry.

Total cholesterol and triglyceride are measured enzymatically using a Trinder's indicator system with N-ethyl-N-sulfohydroxypropyl-*m*-toluidine sodium salt (9).

HDL cholesterol is isolated from other lipoproteins following their precipitation in the cassette using dextran sulphate/magnesium acetate (10). The filtrate containing HDL cholesterol is then directed to the HDL cholesterol reaction pad, where cholesterol in this fraction is measured enzymatically as above.

LDL cholesterol is calculated using the Friedewald formula (LDL cholesterol = Total Cholesterol - HDL cholesterol - Triglyceride/2.2) (11). This formula provides an adequate indirect estimate of LDL cholesterol, provided the sample has a triglyceride concentration less than 4.5 mmol/L and is free of chylomicrons (11). For these reasons, fasting samples are the specimen of choice for LDL cholesterol calculation by the Friedewald formula.

Calibration information is encoded on a magnetic strip on each cassette and is read by the analyser during each analysis. Calibration is set by the manufacturer using pooled human whole blood or sera that have assigned values traceable to the National Committee for Clinical Laboratory Standards (for total cholesterol) and Centres for Disease Control Reference Methods (for triglyceride and HDL cholesterol).

The Cholestech is capable of measuring analyte concentrations within the following ranges: total cholesterol 2.6 to 12.9 mmol/L, triglyceride 0.5 to 7.3 mmol/L, and HDL cholesterol 0.4 to 2.6 mmol/L. Patients with results exceeding the instrument's wide assay limits for any of these analytes should have a fresh, fasting venous sample collected and sent to the laboratory for accurate quantitation.

Comparative method

Total cholesterol, triglyceride and HDL cholesterol were also measured on separated venous plasma by routine methods at the SouthPath laboratory, Flinders Medical Centre. Total cholesterol and triglyceride were measured enzymatically on the Hitachi 917 analyser (Roche Diagnostics, Germany). HDL cholesterol was measured enzymatically on the Hitachi following precipitation of very low and low density lipoproteins from plasma with phosphotungstic acid/magnesium chloride (12).

All methods are certified through participation in the Centers for Disease Control- National Heart, Lung and Blood Institute (CDC-NHLBI) Lipid Standardisation Program (Centers for Disease Control and Prevention, Atlanta, Georgia).

Precision studies

Within-day precision studies (n=10) were performed on fresh venous whole blood samples from three volunteers. Between-run precision studies (n = 10) were conducted using liquid quality control material (Cholestech LDX Controls, Level 1 and Level 2, Catalogue Number 10-983). During the evaluation, Level 1 and Level 2 controls were run in an alternate manner every time a new reagent kit was opened. A single lot number of reagent was used throughout the evaluation.

Statistical analyses

Passing/Bablock linear regression analysis was used to assess the correlation between analytical measurements on the Cholestech and Hitachi analysers (13,14). Slope, intercept, correlation coefficient (r^2) and standard error (Sy.x) are calculated using the Passing/Bablock analysis. If the test method (Cholestech) showed good agreement with the comparative method (Hitachi), the slope would be close to 1.00, the intercept near to 0, the correlation coefficient close to 1.00, and the standard error small.

Results

Range of analyte concentrations tested

The range of analyte concentrations found in the 51 subjects tested in this study was: total cholesterol 3.1 to 8.5 mmol/L, triglyceride 0.5 to 7.8 mmol/L, HDL cholesterol 0.7 to 2.6 mmol/L and LDL cholesterol 1.6 to 5.7 mmol/L (Hitachi, venous plasma values).

Method comparison

The correlation between the Cholestech and Hitachi machines is shown for each analyte and each sample type using Passing/Bablock linear regression plots (Figure 1).

The correlation (r^2) between the Cholestech and Hitachi for both capillary and venous whole blood samples was ≥0.96 for total cholesterol, ≥0.99 for triglyceride, and ≥0.92 for HDL cholesterol and LDL cholesterol.

The mean % difference between results on the Cholestech and Hitachi for both sample types was less than 2% for total cholesterol and trigylceride analyses and less than 5.5% for HDL cholesterol and LDL cholesterol. A positive bias of 6% was observed with capillary HDL cholesterol on the Cholestech at concentrations greater than 1.2 mmol/L.

Comparison between capillary and venous whole blood

The mean percentage difference between capillary and venous whole blood lipid measurements performed on the Cholestech was 0.8% for total cholesterol, 0.4% for triglyceride, 2.3% for HDL cholesterol and 2.7% for LDL cholesterol ($p>0.05$, not significant by the paired *t*-test, except for HDL cholesterol where $p=0.029$). This indicates that capillary sampling provides lipid results equivalent to those obtained using venous whole blood.

Precision

Within-day precision (coefficients of variation) on three fresh whole blood samples ranged from 0.9 to 3.5% for total cholesterol, 1.6 to 2.5% for triglyceride and 6.3 to 7.9% for HDL cholesterol. Between-run precision on the two liquid controls (Levels 1 and 2) were 3.2 and 3.4% for total cholesterol, 3.1 and 3.0% for triglyceride, 2.2 and 2.4% for HDL cholesterol.

The median imprecision achieved by all Australasian laboratories using all methods in the most recent cycle of the Royal College of Pathologists of Australasia-Australasian Association of Clinical Biochemists General Serum Chemistry Quality Assurance Program was 2.5% for total cholesterol, 3.8% for triglyceride and 5.2% for HDL cholesterol (J Gill, personal communication).

Practicability of the Cholestech

The Cholestech machine proved very robust during the laboratory evaluation. Across more than 200 analyses, no instrument breakdowns or cartridge error messages were recorded. An administrative staff member with no previous laboratory experience performed much of the evaluation. This person was able to conduct analyses after less than half an hour's training, and commented on its ease and simplicity of use.

Discussion

With heart disease being today's greatest single cause of Aboriginal mortality, the need to characterise cardiovascular risk profiles among Aboriginal people is clearly a pressing concern. Screening for elevated blood lipids is an important component of identifying risk.

The ability to perform on-site lipid testing in the Aboriginal community setting offers considerable advantages to both Aboriginal patient and doctor. In particular, the ability to conduct testing and have the result immediately available to the patient means that the results are more relevant and timely for the patient, while the doctor can act more expediently on the results and tailor subsequent management accordingly.

In our laboratory evaluation, the Cholestech point-of-care lipid analyser demonstrated excellent analytical performance characteristics for total cholesterol and triglyceride. HDL cholesterol measurements on the Cholestech showed a small positive bias at concentrations greater than 1.2 mmol/L and greater imprecision than total cholesterol and triglyceride analyses on whole blood samples. However, overall performance for this analyte was considered satisfactory for screening purposes where the combination of low HDL cholesterol (less than 1.0 mmol/L) and high triglyceride (greater than 2.0 mmol/L) is of particular clinical concern.

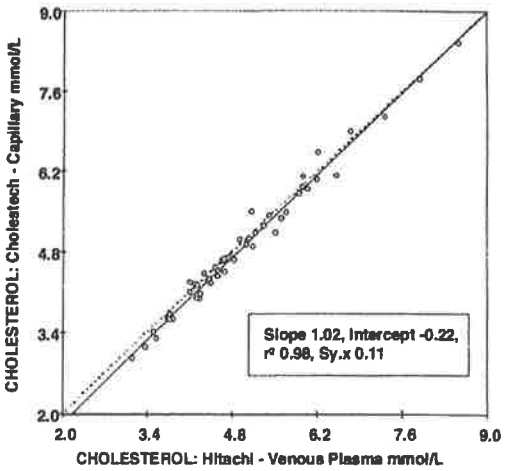
The machine's ability to measure HDL cholesterol in less than five minutes, without the need for prior precipitation of other lipoproteins, is a major practical advantage for field use.

Previous studies have suggested that lipid analyses performed on capillary fingerprick samples produced results that were lower than those found on equivalent venous whole blood samples (15). This was considered to be due in part to contamination (dilution) of capillary whole blood with tissue fluid, and to the dependence of fingerprick sampling on good technique.

However, with the development of better guidelines for fingerprick sampling (including adherence to wiping away the first drop of blood), recent data, including the present study, shows that the more convenient capillary (fingerprick) whole blood sampling is a suitable analytical surrogate for the more invasive, more technically difficult venepuncture sampling (16).

With its simple operation, fully automated nature, sound analytical performance and ability to produce a full lipid profile in under 5 minutes, the Cholestech offers a robust, practical option for first-line lipid screening in the Aboriginal health care setting.

Together with the concurrent development of community education programs targeting nutrition, exercise and smoking and alcohol reduction strategies, the Cholestech machine has the potential to play an integral role in reducing the burden of cardiovascular risk that currently afflicts Aboriginal people.



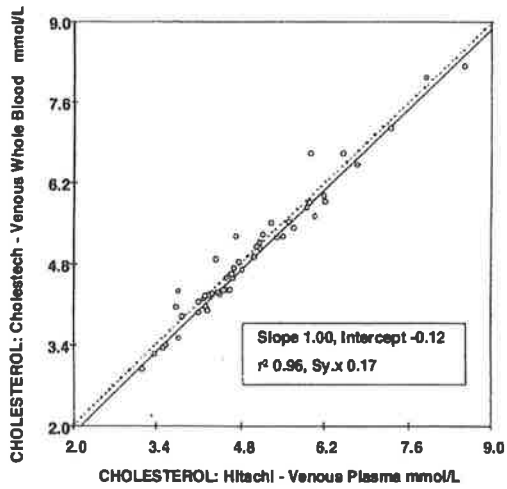
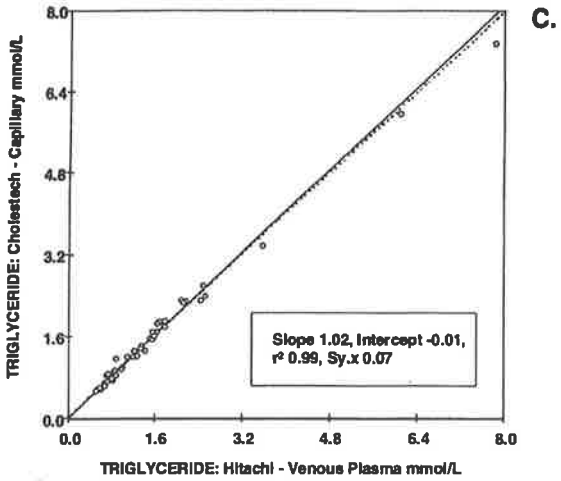
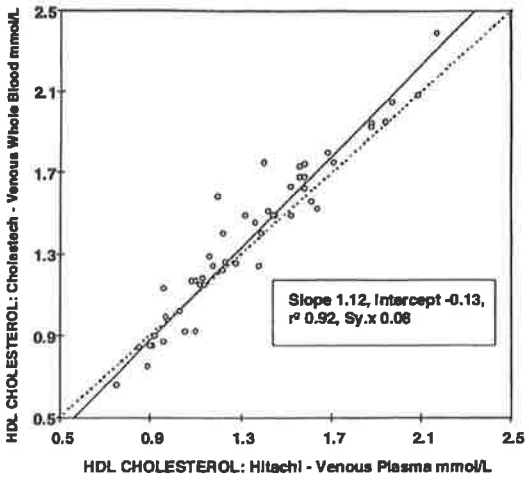


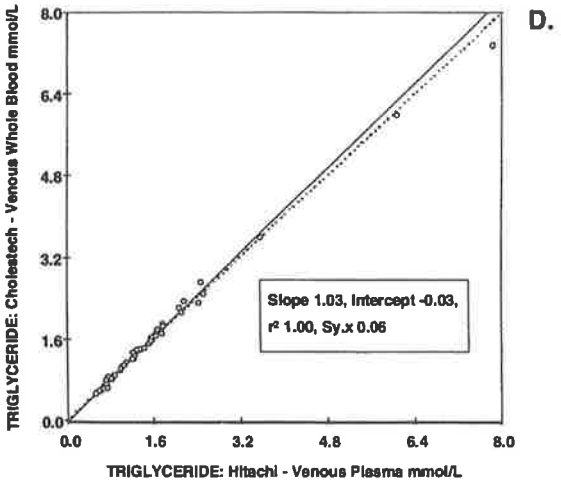
Figure 1. (A-H) Passing/Bablock linear regression plots showing the correlation observed between the Cholestech (y-axis) and the Hitachi (x-axis) for each lipid analyte (cholesterol, triglyceride, HDL cholesterol and LDL cholesterol) and for each sample type tested on the Cholestech (capillary and venous whole blood). The solid line represents the line of best fit between the two instruments as determined by the linear regression equation, while the hatched line represents the line of equivalence.

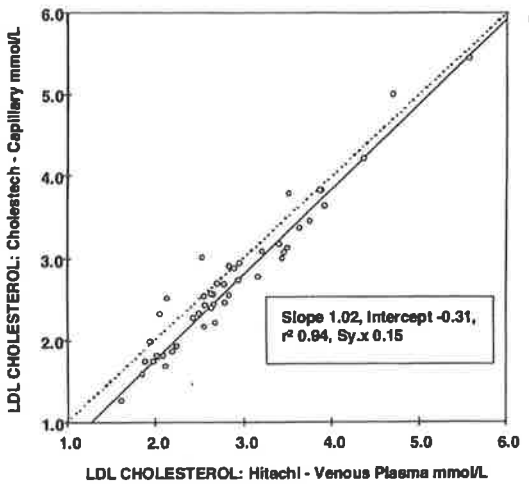
Acknowledgments

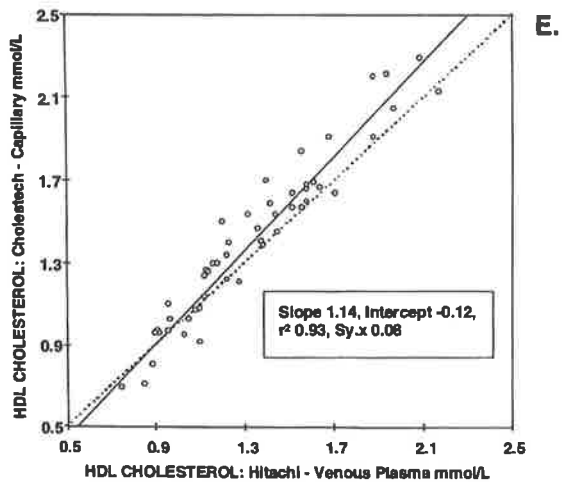
The author would like to thank Lily Mickalov and Karan Lavender for their technical assistance in performing lipid analyses on the Cholestech. Dr Malcolm Whiting, (SouthPath, Flinders Medical Centre) performed comparative Hitachi analyses.

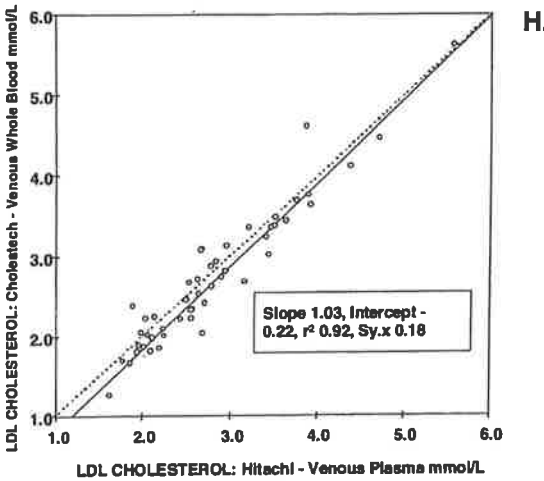

C.
TRIGLYCERIDE: Cholestech - Capillary mmol/L
TRIGLYCERIDE: Hitachi - Venous Plasma mmol/L
Slope 1.02, Intercept -0.01,
r² 0.99, Sy.x 0.07
0.0
1.6
3.2
4.8
6.4
8.0


F.
HDL CHOLESTEROL: Cholestech - Venous Whole Blood mmol/L
HDL CHOLESTEROL: Hitachi - Venous Plasma mmol/L
Slope 1.12, Intercept -0.13,
r² 0.92, Sy.x 0.08
0.5
0.9
1.3
1.7
2.1
2.5


D.
TRIGLYCERIDE: Cholestech - Venous Whole Blood mmol/L
TRIGLYCERIDE: Hitachi - Venous Plasma mmol/L
Slope 1.03, Intercept -0.03,
r² 1.00, Sy.x 0.06
0.0
1.6
3.2
4.8
6.4
8.0


G.
LDL CHOLESTEROL: Cholestech - Capillary mmol/L
LDL CHOLESTEROL: Hitachi - Venous Plasma mmol/L
Slope 1.02, Intercept -0.31,
r² 0.94, Sy.x 0.15
1.0
2.0
3.0
4.0
5.0
6.0


E.
HDL CHOLESTEROL: Cholestech - Capillary mmol/L
HDL CHOLESTEROL: Hitachi - Venous Plasma mmol/L
Slope 1.14, Intercept -0.12,
r² 0.93, Sy.x 0.08
0.5
0.9
1.3
1.7
2.1
2.5


H.
LDL CHOLESTEROL: Cholestech - Venous Whole Blood mmol/L
LDL CHOLESTEROL: Hitachi - Venous Plasma mmol/L
Slope 1.03, Intercept -
0.22, r² 0.92, Sy.x 0.18
1.0
2.0
3.0
4.0
5.0
6.0

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POINT-OF-CARE TESTING OF HbA1c AND BLOOD GLUCOSE IN A REMOTE ABORIGINAL AUSTRALIAN COMMUNITY.

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Point-Of-Care Testing Of HbA1c And Blood Glucose In A Remote Aboriginal Australian Community.

Prior to commencing this research program, the author had considerable experience in using the Bayer DCA 2000 for POC HbA1c testing in the diabetes clinic and in the laboratory at Flinders Medical Centre. Its analytical quality had been validated by regular (unpublished) patient comparison and precision studies conducted in the laboratory setting and through its consistently sound performance in the RCPA Glycohaemoglobin external quality assurance program for laboratories (141).

This paper described a collaborative research study which addressed the research question: Was the DCA 2000 robust enough to maintain analytical accuracy for HbA1c POCT when testing was conducted in very remote Indigenous medical service which experienced extreme conditions of heat and humidity? The study was undertaken by the author and researchers from the Princess Margaret Hospital for Children, the Western Australian Country Health Services – Kimberley Region, and the School of Population Health and Telethon Institute of Child Health Research from the University of Western Australia. The author co-wrote this paper with Dr David Martin as joint principal authors.

A second POCT device, the HemoCue glucose analyser, was also evaluated as part of this study but was not used in any of the POCT research models presented in this thesis.

This study verified the robustness of the DCA 2000 and confirmed its sound analytical quality in the remote Indigenous setting, with results obtained by comparative POC and laboratory testing being statistically, analytically and clinically similar.

Point-of-care testing of HbA_{1c} and blood glucose in a remote Aboriginal Australian community

David D Martin, Mark D S Shephard, Hayley Freeman, Max K Bulsara, Timothy W Jones, Elizabeth A Davis and Graeme P Maguire

ABSTRACT

Objectives: To assess the accuracy of point-of-care (POC) measurements of capillary blood glucose and glycosylated haemoglobin (HbA_{1c}) levels in a remote Aboriginal community with high diabetes prevalence.

Design: Cross-sectional study comparing POC capillary glucose and HbA_{1c} results with those from corresponding venous samples measured in a reference laboratory.

Participants and setting: 152 residents aged 11–76 years (representing 76% of population aged over 11 years) had POC glucose measurement in November 2003; 88 with POC glucose level ≥ 5.0 mmol/L, or self-reported diabetes, had POC HbA_{1c} and laboratory glucose and HbA_{1c} measurements.

Main outcome measures: POC fasting capillary levels of glucose (HemoCue Glucose 201 analyser, Medipac Scientific, Sydney) and HbA_{1c} (DCA 2000+ analyser, Bayer Australia, Melbourne); correlation and mean difference between capillary POC and venous blood laboratory measurements of glucose and HbA_{1c}.

Results: Mean and median POC capillary glucose levels were 7.99 mmol/L and 6.25 mmol/L, respectively, while mean and median laboratory venous plasma glucose concentrations were 7.63 mmol/L and 5.35 mmol/L. Values for POC capillary HbA_{1c} and laboratory HbA_{1c} were identical: mean, 7.06%; and median, 6.0%. The correlation coefficient *r* for POC and laboratory results was 0.98 for glucose and 0.99 for HbA_{1c}. The mean difference in results was 0.36 mmol/L for glucose (95% CI, 0.13–0.62; limits of agreement [LOA], −2.07 to 2.79 mmol/L; $P = 0.007$) and < 0.01% for HbA_{1c} (95% CI, −0.07% to 0.07%; LOA, −0.66% to 0.66%; $P = 0.95$), respectively.

Conclusions: POC capillary HbA_{1c} testing, in particular, offers an accurate, practical, community-friendly way of monitoring diabetes in rural and remote clinical settings. POC capillary glucose results should be confirmed by a laboratory test of venous plasma if the results are likely to significantly influence clinical decisions.

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Type 2 diabetes mellitus and its sequelae are a major cause of premature mortality in Aboriginal Australians and Torres Strait Islanders today.[1] Whereas this disease did not seem to exist in Australia before European settlement,[2] reported prevalence rates in the last decade have ranged between 10% and 30%, depending on the study populations and screening methods, and have shown an increasing trend.[3]

Effective diagnostic and management tools are needed. From the viewpoints of the community members and their on-site carers, an ideal diabetes monitoring program would combine immediate and easily interpretable results with direct feedback to the individual, and would be linked to an effective long-term follow-up program. Point-of-care (POC) testing of blood glucose and glycosylated haemoglobin (HbA_{1c}) levels would meet these requirements if shown to be accurate and reliable in the remote, hot and humid conditions characteristic of many Indigenous communities.

The Bayer DCA 2000+ glycohaemoglobin analyser (Bayer Australia, Melbourne, Vic) is being increasingly used for POC HbA_{1c} testing in remote and rural clinical settings, through the Australian Government's Quality Assurance for Aboriginal Medical Services (QAAMS) Program,[4,5] which now involves over 60 services across Australia. The HemoCue Glucose 201 analyser (Medipac Scientific, Sydney, NSW) is a new-generation, hand-held glucose meter that is now widely used in Australia.

We conducted a study in a remote Indigenous community in northern Western Australia to examine the accuracy of POC capillary HbA_{1c} and glucose measurements for monitoring diabetes in difficult environmental working conditions, with extreme heat and humidity.

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METHODS

This project was part of a community-based capacity-building program designed by the Unity of First Peoples of Australia (UFPA) and Western Australian Country Health Services — Kimberley region, to improve primary and secondary prevention of chronic metabolic diseases in Indigenous Australian communities.

Setting and participants

The study was part of a larger study investigating the prevalence of diabetes, obesity and related health problems. It was conducted between 25 October and 2 November 2003 in a remote Aboriginal Australian community, located about 300 km inland from Broome in the Western Kimberley region. The community has a population of 200–250. All residents aged 12 years or older were encouraged to participate in the study. Cooperation with the community

1 Characteristics of study participants ($n = 152$), and point-of-care (POC) and laboratory results for those who had both POC and laboratory testing ($n = 88$)*

Variable		Adults		Children (non-diabetic)
		Diabetic	Non-diabetic	
Total		($n = 36$)	($n = 76$)	($n = 40$)
No. of females (%)		27 (75%)	42 (53%)	23 (57%)
Age in years	Mean (SD)	50.5 (14.1)	37.5 (15.4)	13.7 (1.7)
	Range	(18.4–76.3)	(27.3–76.3)	(11.0–17.5)
Diabetes or POC glucose ≥ 5.0 mmol/L*		($n = 36$)	($n = 38$)	($n = 14$)
POC glucose (mmol/L)	Mean (SD)	11.16 (4.58)	5.87 (1.04)	5.87 (1.30)
	Median (range)	11.0 (3.4–22.1)	5.5 (4.5–10.1)	5.3 (5.1–10.1)
Laboratory glucose (mmol/L)	Mean (SD)	11.50 (5.62)	5.23 (1.00)	4.71 (1.03)
	Median (range)	11.8 (3.0–28.3)	5.0 (3.9–9.1)	4.5 (4.0–8.2)
POC HbA_{1c} (%)	Mean (SD)	9.17 (2.22)	5.80 (0.41)	5.33 (0.42)
	Median (range)	9.5 (5.6–13.2)	5.8 (4.9–6.7)	5.4 (4.2–5.8)
Laboratory HbA_{1c} (%)	Mean (SD)	9.15 (2.40)	5.74 (0.38)	5.53 (0.34)
	Median (range)	9.4 (5.5–13.4)	5.7 (4.9–6.6)	5.6 (4.7–6.1)

* POC assay of HbA_{1c} and laboratory assay of both glucose and HbA_{1c} were conducted only for people with self-reported diabetes or POC glucose level ≥ 5.0 mmol/L. HbA_{1c} = glycosylated haemoglobin.

school enabled 40 school children aged 11–18 years to participate.

Informed written consent was obtained from each participant in the weeks before the monitoring week. For those aged under 16 years, informed written consent was also obtained from a legal guardian (usually the mother or grandmother). Approval was obtained from the local community council to use pooled data.

Protocol

For the 2 months preceding the study week, three experienced UFPA carers (DDM, HF and GPM) lived in the community to establish a good relationship with community members, gather population statistics, assess and optimise knowledge about diabetes and lifestyle, and prepare the community for the assessment.

Participants were interviewed to obtain a basic medical history and underwent a physical examination. They were asked to fast overnight (unless currently receiving medication for diabetes) before collection of blood and urine samples the following morning for POC and laboratory investigations.

All participants had POC measurement of fasting capillary glucose level. Those with a glucose level < 5.0 mmol/L (equivalent to fasting venous plasma glucose level < 5.5 mmol/L[6]) were assumed not to have diabetes and not tested further (unless known to be taking medication for diabetes).

Participants with a fasting capillary glucose level ≥ 5.0 mmol/L, and those with self-reported diabetes, were immediately followed up with POC capillary HbA_{1c} assay of the same capillary blood sample and with venepuncture for subsequent measurement of HbA_{1c} and glucose levels in a reference laboratory.

Participants with a laboratory venous plasma glucose level in the range 5.5–11.1 mmol/L underwent an oral glucose tolerance test (OGTT) with 75 g of diluted anhydrous glucose on a subsequent day.

Diabetes was defined as:

- fasting plasma glucose level ≥ 7.0 mmol/L; OR
- 2-h plasma glucose level ≥ 11.1 mmol/L by OGTT; OR
- existing diagnosis of diabetes confirmed in medical chart.[7,8]

Glucose and HbA_{1c} measurements

Point-of-care methods

Capillary glucose level was measured on site in a 5 μL fingerprick blood sample by a HemoCue Glucose 201 analyser. This measures glucose enzymatically using glucose dehydrogenase and produces a result within 4 minutes.

Capillary HbA_{1c} was measured on site in a 1 μL sample of whole blood by a Bayer DCA 2000+ analyser. This measures HbA_{1c} immunochemically, producing a result in 6 minutes.[9] Blood samples for HbA_{1c} testing were transferred to reagent cartridges and analysed immediately after collection to ensure they did not dry out, causing measurement errors.

POC analyses were performed in a room open to the outside environment, in which temperature varied between 27°C and 31°C. For HbA_{1c} measurement, which can be affected by high temperature, we followed the manufacturer's recommendations to check that reagents had not been exposed to excessive heat (indicated by a heat-sensitive colour pad on the front of each reagent box), and to recalibrate the analyser and test a quality control sample each time a new box of reagents was opened.

Laboratory methods

Laboratory tests were performed at Derby PathCentre, Derby, WA (glucose), and the Western Australian Centre for Pathology and Medical Research, Perth, WA (HbA_{1c}).

For glucose analysis, venous whole blood samples were collected in containers with fluoride-EDTA as preservative, then centrifuged at room temperature for 10 minutes at ≥ 800 g. Supernatants were stored at 0°C for less than 4 hours before being transported on ice by road to Derby (3–4 hours' drive). Venous plasma glucose level was measured enzymatically on the Vitros 250 Analyser (OrthoClinical Diagnostics, Rochester, NY, USA) using glucose oxidase spectrophotometric dry chemistry.

For HbA_{1c} measurement, part of each original whole blood sample was transferred to a container with EDTA as preservative, and flown on ice 2000 km to Perth. HbA_{1c}

2 Comparison of point-of-care and laboratory results for 88 participants with capillary glucose level ≥ 5.0 mmol/L or known diabetes

	Glucose (mmol/L)		HbA_{1c} (%)	
	POC	Laboratory	POC	Laboratory
Mean	7.99	7.63	7.06	7.06
Median	6.25	5.35	6.0	6.0
Range	3.4–22.2	3.0–28.3	4.2–13.2	4.7–13.4
Mean difference (95% CI)	+ 0.36 (0.13–0.62) ($P = 0.007$)*		0.002 (–0.07 to 0.07) ($P = 0.95$)*	
Limits of agreement	–2.07 to 2.79		–0.66 to 0.66	

* By paired t test. POC = point of care. HbA_{1c} = glycosylated haemoglobin.

was measured using cation-exchange high performance liquid chromatography (HPLC) on the Bio-Rad Variant II (Bio-Rad Laboratories, Hercules, USA). This has mean intra- and inter-assay precision (coefficients of variation) < 2%. This assay is certified by the US National Glycohemoglobin Standardization Program as traceable to the Diabetes Control and Complications Trial reference method.[10]

Laboratory results were available after 1 day for glucose, and after 3 days for HbA_{1c}.

Statistical methods

Data were analysed using JMP software[11] and are presented as mean and 95% confidence intervals unless otherwise stated. Linear regression analysis was performed and Pearson's correlation coefficient (r) was calculated for each analyte. The two-tailed Student's t test was then used to compare POC and laboratory measurements for paired samples, with $P < 0.05$ representing statistical significance. Bland and Altman plots[12] were used to calculate mean difference (bias) and limits of agreement (LOA) between the two methods. Regression analysis was performed on the Bland and Altman plots to determine whether bias was constant or proportional to concentration.

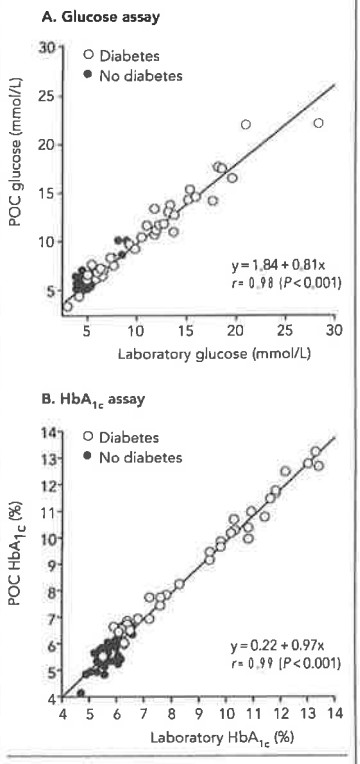
Power calculations using 0.05 for α and β suggested that 26 participants would be required to detect a 1 mmol/L difference in means between laboratory plasma glucose and POC capillary glucose levels, and that 12 participants would be required to detect a 0.5% difference between laboratory and POC HbA_{1c} results.

RESULTS

POC capillary glucose measurements were made in 152 individuals, including 40 children aged between 11 and 18 years (Box 1). These 152 represented 76% of the population aged over 11 years in the community, and included 82% of residents with known diabetes. POC capillary HbA_{1c} measurements and laboratory analyses of venous blood were subsequently performed in 88 of these people (all with capillary glucose level ≥ 5.0 mmol/L or self-reported diabetes).

Prevalence of diabetes was found to be 32% in adults (36 of 112) and 0 in children. The prevalence of impaired fasting glucose could not be reliably assessed as 40% of participants were not properly fasting. Similarly, the prevalence of impaired glucose tolerance was not calculated as the OGTT was performed only in participants with fasting plasma glucose levels in the range 5.5–11 mmol/L. None of the patients with diabetes were receiving renal dialysis treatment at the time of the study.

3 Bivariate plot comparing point-of-care and laboratory results ($n = 88$)



POC = point of care.
HbA_{1c} = glycosylated haemoglobin.

Comparison of glucose results

POC capillary glucose level is compared with laboratory plasma glucose level for the same patients in Box 2. Glucose concentrations determined by the two methods were significantly correlated ($r = 0.98$; $P < 0.001$) (Box 3A). However, actual values differed significantly between the two methods ($P = 0.007$ by paired t test). The mean difference was +0.36 mmol/L (95% CI, 0.13–0.62 mmol/L), with lower and upper LOA, −2.07 and 2.79 mmol/L (Box 4A). The difference in glucose concentration between the two methods was concentration dependent ($r = 0.69$; $P < 0.001$), with the POC measurement generally higher than the laboratory measurement at glucose concentrations < 10 mmol/L by POC measurement, and lower at concentrations > 10 mmol/L.

Comparison of HbA_{1c} results

POC capillary HbA_{1c} concentration is compared with laboratory plasma HbA_{1c} concentration in the same patients in Box 2. Median values for HbA_{1c} concentration by the two methods were identical (6.0%), as were mean values (7.1%). Results by the two methods were significantly correlated ($r = 0.99$; $P < 0.001$) (Box 3B), and the mean difference between them was neither statistically nor clinically significant (0.002%; 95% CI, −0.07% to 0.07%; LOA, −0.66% to 0.66%; $P = 0.95$ by paired t test) (Box 4B). The difference was greater than 0.5% in five of the 88 samples, only one of which was in the HbA_{1c} range 6%–10%. The very small bias observed was constant across the range of HbA_{1c} concentrations measured ($r = 0.05$; $P = 0.14$).

DISCUSSION

Indigenous Australians in regional Australia often live in isolated communities that are a significant distance from pathology laboratories. For example, in our study, the nearest laboratories able to measure glucose and HbA_{1c} concentrations were 300 km and 2000 km away, respectively. POC pathology testing is therefore a desirable alternative to laboratory testing, provided it gives comparable results. Our study aimed to assess the accuracy and reliability of POC glucose and HbA_{1c} tests compared with laboratory tests of venous samples transported to the nearest laboratory.

For HbA_{1c}, the values obtained by POC and laboratory testing were statistically, analytically and clinically identical. Thus, POC testing for HbA_{1c} using the Bayer DCA 2000+ analyser has demonstrated acceptable accuracy for field use in this remote Australian Aboriginal community. However, we could not assess the precision (or reproducibility) of these tests, because of the small number of quality control samples tested. Certainly, it is important that the precision of HbA_{1c} measurement approaches 3% or less, to ensure that clinically significant changes in serial HbA_{1c} concentrations can be detected.[13] In the QAAMS Program (currently being conducted in 60 Aboriginal medical services across Australia), precision of HbA_{1c} measurement using the Bayer DCA 2000+ is monitored continually. For the past 5 years, the median between-site precision has averaged 3.5%,[4] while during 2004 it averaged 2.9%.[14]

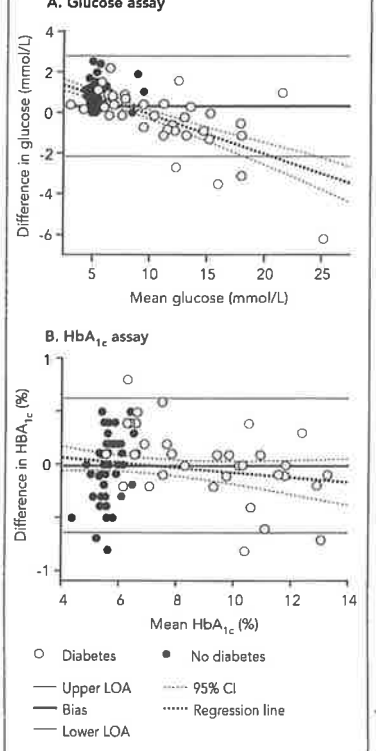
We found that the POC and laboratory results for glucose concentration were reasonably correlated but showed a concentration-dependent difference. Many variables could account for this. The time available for training local staff to use the HemoCue glucose

meter was very limited; appropriate and detailed training is critical for staff conducting tests outside the laboratory environment. Other factors potentially contributing to the observed difference include the different samples collected (capillary versus venous blood) and tested (whole blood versus centrifuged plasma), and the effects of transportation on the laboratory samples.[6] A further study comparing glucose concentrations measured by the HemoCue meter and the Vitros Analyser using the same venous samples after appropriate staff training would be necessary to fully investigate the observed differences.

We did not formally survey the satisfaction of patients and health professionals with POC testing. However, non-laboratory staff in the community (Aboriginal health workers and nurses) were able to operate the DCA 2000+ after on-site training. POC testing provides the opportunity for immediate feedback and counselling, making it an ideal tool for inexpensive on-site motivational management of diabetes. Patients expressed their appreciation of the simultaneous education and opportunity to "see what happens with their blood". They generally preferred fingerprick collection to venepuncture. Other studies in both Indigenous and non-Indigenous settings have also shown that POC HbA_{1c} testing can improve diabetes control when linked with aggressive clinical management regimens and specialist support.[15-17]

This study shows that HbA_{1c} can be conveniently and accurately measured by POC testing with the Bayer DCA 2000+ analyser in rural and remote clinical settings. This form of testing is suitable for regular HbA_{1c} monitoring across all concentrations. The study also opens the way to investigate the contribution of POC HbA_{1c} testing to diagnosis of diabetes when it is uncertain whether the patient has fasted. POC glucose testing has a useful role in screening for diabetes risk, as well as self-monitoring for people with known diabetes, and it is important that the performance of different glucose meters is known in specific clinical settings. However, the diagnosis of diabetes should still rely on confirmatory tests of plasma glucose concentration in the laboratory.[6]

4 Difference (Bland and Altman) plot for point-of-care versus laboratory results



Plot of the difference between results for each patient (POC – laboratory result) against the mean of the two results. Horizontal lines represent bias (mean difference between POC and laboratory results) and its limits of agreement (LOA), while sloping lines represent the regression line and its 95% confidence limits.

For glucose measurement, bias was + 0.36 mmol/L. The regression line (difference = 1.88 – 0.19 mean) indicated that bias varied significantly with glucose concentration ($r = 0.69$; $P < 0.001$).

For HbA_{1c} measurement, bias was close to 0, and the regression line (difference = 0.16 – 0.023 mean) indicated that it did not vary significantly with HbA_{1c} concentration ($r = 0.05$; $P = 0.14$)

POC = point of care.
HbA_{1c} = glycosylated haemoglobin.

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COMPETING INTERESTS

The supporting sources (see Acknowledgements) had no role in study design, data collection, analysis or interpretation, or in writing the article.

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ASSESSMENT OF THE PRACTICABILITY AND ANALYTICAL PERFORMANCE OF A POINT-OF-CARE AFFINITY CHROMATOGRAPHY HAEMOGLOBIN A1c ANALYSER FOR USE IN THE NON-LABORATORY SETTING.

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STATEMENT OF AUTHORSHIP

ASSESSMENT OF THE PRACTICABILITY AND ANALYTICAL PERFORMANCE OF A POINT-OF-CARE HAEMOGLOBIN A1c ANALYSER FOR USE IN THE NON-LABORATORY SETTING

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Assessment Of The Practicability And Analytical Performance Of A Point-Of-Care Affinity Chromatography Haemoglobin A1c Analyser For Use In The Non-Laboratory Setting.

When this research program commenced in 1997, the Bayer DCA 2000 was the only POCT device for HbA1c measurement in Australia. However, with the increased interest in POCT in Australia generated by my work and the impending POCT in General Practice Trial, a new POCT device for HbA1c - the BioRad Micromat 11 - was brought onto the Australian market around 2002.

This study was conducted to answer the following research questions:

- How did the analytical performance of the new Micromat POCT device compare with that of the established DCA 2000 and the routine laboratory method used for HbA1c measurement at Flinders Medical Centre?
- Was the Micromat's performance acceptable for potential use in rural and remote Australia?

The results of this research study confirmed the sound analytical performance of the DCA 2000, but showed that the Micromat's poor imprecision and the high degree of technical expertise needed to operate the device limited its reliability and practicability in rural and remote settings.

Short Report

Assessment of the practicability and analytical performance of a point-of-care affinity chromatography haemoglobin A_{1c} analyser for use in the non-laboratory setting

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Abstract

Background Haemoglobin A_{1c} (HbA_{1c}) is a pivotal pathology test used around the world for the long-term management of patients with diabetes. Point-of-care testing (POCT) provides a convenient means for conducting HbA_{1c} testing outside the laboratory.

Methods The practicability and analytical performance of the Micromat II POCT HbA_{1c} analyser (Bio-Rad Laboratories, USA), which has affinity chromatography as its methods principle, was evaluated in Australia and compared with the DCA 2000 POCT device (Bayer Australia) and a laboratory-based high-performance liquid chromatography (HPLC) method.

Results Overall between-day imprecision over 10 days was 1.9% for the laboratory HPLC method, 2.2% for the DCA 2000 and 7.0% for the Micromat II. In a second study over the same time period, the Micromat II's imprecision was 6.4%. The mean difference between the Micromat II and the laboratory method in a patient comparison ($n = 100$) was −0.25% (lower and upper limits of agreement −1.79 to 1.30).

Conclusions The imprecision obtained with the Micromat II was inferior to both the DCA 2000 and laboratory methods and did not meet current internationally accepted precision goals for this analyte. The Micromat II's poor imprecision can be explained by the high degree of technical expertise needed to perform the test; its use by non-laboratory health professionals such as nurses and Aboriginal health workers in rural and remote Australia cannot be recommended.

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Introduction

Diabetes mellitus, with its associated long-term microvascular complications, is a major global health problem. The measurement of haemoglobin A_{1c} (HbA_{1c}) provides an assessment of glycaemic control over the preceding three months and is a pivotal pathology test for the long-term management of patients with diabetes. The analytical imperative for precise and accurate HbA_{1c} measurements arises from its clinical use in tracking changes in glycaemic control over time and determining whether patients have achieved Australia clinical targets.

In Australia, the DCA 2000 point-of-care analyser (Bayer Australia, Melbourne, Australia) has been used widely in rural and remote locations and in indigenous and non-indigenous health settings for monitoring HbA_{1c} levels through point-of-care testing (POCT) models including the national Quality Assurance for Aboriginal Medical Services (QAAMS) Programme and the Diabetes Management Along the Mallee Track project.[1–2] The DCA 2000 measures HbA_{1c} by immunoassay on 1 μL of capillary whole blood in 6 min and, in these programmes, this instrument has proven reliable and analytically sound in the hands of non-laboratory POCT operators.

In 2002 a new POCT HbA_{1c} analyser, the Micromat II (Bio-Rad Laboratories, CA, USA), was introduced into Australia. The small bench-top device uses affinity chromatography to measure HbA_{1c} on 10 μL of capillary whole blood in approximately 5 min. This study was conducted to determine its practicability and

analytical performance relative to the DCA 2000 analyser and a laboratory-based high-performance liquid chromatography (HPLC) method, and to assess its potential application as a POCT HbA_{1c} analyser in rural and remote Australia.

Methods

Analytical principle of Micromat II POCT haemoglobin A_{1c} method

The capillary blood sample was initially diluted, lysed to release haemoglobin, mixed with a boronate affinity resin to bind the glycated haemoglobin fraction, and then loaded onto the Micromat II analyser. The non-glycated fraction was collected in an optical chamber and the total haemoglobin concentration determined spectrophotometrically. The bound HbA_{1c} fraction was washed and eluted, and its concentration also was measured spectrophotometrically. The HbA_{1c} fraction was expressed as a percentage of the total haemoglobin.

The Micromat II method is not subject to interference by uraemia or the haemoglobin variants HbS, HbC and HbF and, like the DCA 2000, is traceable to the Diabetes Control and Complications Trial reference method.

Comparative POCT and laboratory methods

At the South Path laboratory at Flinders Medical Centre, Adelaide, comparative POCT and laboratory HbA_{1c} measurements were performed using the Bayer DCA 2000 and cation-exchange HPLC with a Pharmacia Mono-S column, respectively.[3]

Assessment of precision

Between-day imprecision was assessed using daily analysis of three patient samples with HbA_{1c} concentrations of 5.5%, 6.9% and 9.8% over a 10-day period. An HbA_{1c} of less than 6% generally indicates a person does not have diabetes; an HbA_{1c} of 7% is a target for optimal glycaemic control in patients with diabetes, while an HbA_{1c} of 10% is reflective of a person with diabetes whose glycaemic control is poor. A second assessment of imprecision was also made with the Micromat II only, using three further patient samples with similar HbA_{1c} concentrations across the same time period.

Assessment of accuracy

Blood samples were collected from 100 patients with and without diabetes (median HbA_{1c} 7.1; range 4.6–20.1%) and were analysed over a 10-day period by the three methods, according to the manufacturer's specifications. Agreement between methods was assessed by Passing Bablock regression analysis and Bland–Altman plots using the Analyse-It statistical package (Analyse-It Software Ltd, Leeds, UK).

Results

Assessment of precision

The between-day imprecision recorded by each instrument for the three different patient HbA_{1c} levels is shown in Table 1.

The overall between-day imprecision was 1.9% for the laboratory HPLC method, 2.2% for the DCA 2000 and 7.0% for the Micromat II. Due to the poor imprecision exhibited by the Micromat II, a second precision study was undertaken for this instrument using three further patient samples with HbA_{1c} concentrations of 5.4, 6.9 and 9.7%. The overall imprecision recorded by the Micromat II for these samples was 6.4%.

Assessment of accuracy

The Passing Bablock correlation coefficient (r) was 0.94 for the Micromat II versus the laboratory method, and 0.96 for the DCA 2000 versus the laboratory. Using Bland–Altman analysis, the mean difference between the Micromat II and the laboratory method was −0.25% (lower and upper limits of agreement [LOA] −1.79 to 1.30) (Figure 1). For the DCA 2000 and the laboratory method, mean difference was −0.36% (LOA −1.34 to 0.62).

Table 1 *Between-day imprecision observed at three different HbA_{1c} concentrations*

	Patient HbA_{1c} concentration (%)		
Analysers	5.5	6.9	9.8
HPLC MonoS	2.2	2.2	1.2
Bayer DCA 2000	3.1	1.8	1.7
Micromat II	9.0	5.8	6.1

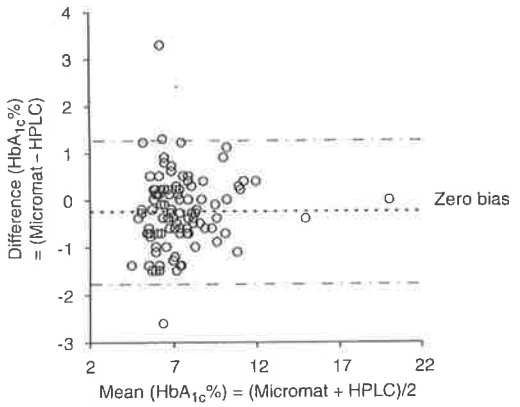

Figure 1 *Bland–Altman difference plot for comparing the Micromat II versus the laboratory-based cation exchange HPLC method*

Discussion

This study investigated the analytical performance of a POCT analyser for HbA_{1c} that used affinity chromatography as its methods principle and compared it with current POCT and laboratory benchmarks. The overall between-day imprecision obtained with the Micromat II across two separate precision studies (6.7%) was inferior to both the DCA 2000 and laboratory methods and did not meet internationally accepted precision goals for this analyte (less than 3%).[4] Tight imprecision is critically important when monitoring glycaemic control in diabetes patients over time, and this clinical requirement demands that POCT HbA_{1c} methods must exhibit precision equivalent to laboratory-based HbA_{1c} methods. Methods with poor imprecision (or high degree of analytical noise) can potentially mask clinically significant changes in glycaemic status and their use in the POCT environment cannot be recommended. The poor imprecision exhibited by the Micomat II in our hands can largely be explained by the high degree of technical expertise needed to perform the test. There are a number of manual steps requiring precise timing and the POCT operator is not able to leave the instrument during the entire reaction sequence.

Accuracy of HbA_{1c} measurement is important because there are set targets for the management of diabetes; for example, an HbA_{1c} of 7% or less is considered to represent optimal glycaemic control in a diabetes patient. The mean bias observed with the Micromat II was slightly less than that observed for the DCA 2000 in this study; however, the LOA between the POCT device and the laboratory method were much tighter with the DCA 2000 compared with the Micromat II. This evaluation represents the fourth patient comparison between the DCA 2000 and the laboratory undertaken by our group (two being conducted in laboratory settings and two in field settings). The overall bias recorded by the DCA 2000 relative to the MonoS laboratory method across these four studies was 0.08% (−0.36% present study, 0.18% [LOA −0.9 to 1.2] in a previous unpublished laboratory comparison [$n = 42$], −0.1% [LOA −1.1 to 0.8) in field study 1 [$n = 39$] and −0.02% [LOA −0.65 to 0.61] in field study 2 [$n = 118$]).[5–6]

The Micromat II system is innovative in its design, uses a well-established methods principle of affinity chromatography and is not subject to interference by uraemia or haemoglobin variants. Other POCT HbA_{1c} devices available in the market (such as the Cholestech GDX and Provalis Glycosol HbA_{1c} tester) also use a methods principle identical to that of Micromat II. Like the Micromat II, poor imprecision was also observed with the Cholestech GDX device in a recently published study.[7]

In conclusion, the poor imprecision observed with the Micromat II, together with the labour-intensive and technically demanding nature of its test procedure, severely limits the device's practicability in the community setting. Its use by non-laboratory health professionals such as nurses and Aboriginal health workers in rural and remote Australia cannot be recommended, based on the results of this study.

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CHAPTER 4

QUALITY SPECIFICATIONS FOR POCT DEVICES USED IN THIS PROGRAM OF RESEARCH

ANALYTICAL GOALS FOR POINT-OF-CARE TESTING USED FOR DIABETES MANAGEMENT IN AUSTRALIAN HEALTH CARE SETTINGS OUTSIDE THE LABORATORY.

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Point of Care 2006; 5: 177-185.

Analytical Goals For Point-Of-Care Testing Used For Diabetes Management In Australian Health Care Settings Outside The Laboratory.

The setting of analytical goals for the performance of routine pathology tests is an important component of laboratory practice and there is now a considerable published literature on goals for most laboratory tests (130, 132, 159). However, despite the increase in global uptake of POCT devices and their use in primary care, the setting of analytical goals specifically for the non-laboratory POCT environment remained largely unaddressed in the published literature.

This landmark paper therefore answered the key research questions:

- Were laboratory-derived analytical goals relevant to POCT conducted outside the laboratory? and
- What were appropriate analytical goals for common POC tests (namely HbA1c, lipids and urine ACR) used for diabetes management in Australian health care settings?

The paper systematically discussed current approaches to analytical goal setting for laboratory methods, reviewed published data on analytical goals for the candidate tests, examined current state-of-the art laboratory performance, and recommended for the first time analytical goals for the precision, accuracy and total error of these POC tests which were designed to be relevant, practical and attainable in the non-laboratory environment.

Most of the goals recommended in this article have been used to assess the analytical performance of the POCT devices employed in the Australian Government's POCT in General Practice Trial (36, 113). Indeed the impetus to publish this paper came from the author's involvement with the Australian Government's Technical and Clinical Working Party of the POCT Subcommittee, Quality Use of Pathology Committee, where I was invited to review current literature and make recommendations on analytical goals for use in the Trial.

Analytical Goals for Point-of-Care Testing Used for Diabetes Management in Australian Health Care Settings Outside The Laboratory

Mark D. S. Shephard, MSc, MAACB

Abstract: Diabetes mellitus is a major global health problem. Pathology testing for hemoglobin A1c (HbA1c), lipids, and urine albumin/creatinine ratio (ACR) has an important role in the management of diabetes patients. Each of these markers can be performed by point-of-care testing (POCT). This article focuses on setting analytical goals (quality specifications) for the imprecision, bias, and total allowable error of these selected POC tests in the public health environment in Australia. The article reviews published data on analytical goal setting for laboratory tests, considers the factors that set POCT apart from the laboratory, compares laboratory-based analytical goals with state-of-the-art performance, and then sets analytical goals that are designed to be relevant for nonlaboratory POCT environment. The desirable analytical goals for imprecision are the following: HbA1c, 3%; cholesterol, 3%; triglyceride, 5%; high-density lipoprotein cholesterol, 4%; low-density lipoprotein cholesterol, 4%; urine albumin, 10%; urine creatinine, 6%; and urine ACR, 12%. The analytical goals for total allowable error are the following: HbA1c, 4%; cholesterol, 10%; triglyceride, 15%; high-density lipoprotein cholesterol, 15%; low-density lipoprotein cholesterol, 15%; urine albumin, 12.5%; urine creatinine, 7.5%; and urine ACR, 15%. The recommended analytical goals are designed to be flexible and refinable as more data, particularly from clinical outcome studies, become available. They have the potential to be adopted by countries outside Australia, given the limited published data on analytical goals specifically for the nonlaboratory POCT sector.

Key Words: analytical goals, point-of-care testing, diabetes management, non laboratory setting

(*Point of Care* 2006;5:177–185)

Diabetes mellitus is a major global health problem that has reached epidemic proportions in many parts of the world. It was estimated that there were 160 million people with diabetes worldwide in the year 2000, and this figure was predicted to climb to more than 280 million by the year 2025, the majority of whom will have type 2 diabetes.[1,2] Diabetes causes significant morbidity and mortality among people with this disease, primarily from the cardiovascular and renal complications and retinopathy arising from the disease. In the United States, diabetes-related costs account for approximately 12% of the national health budget.[2]

In Australia, the number of adults with diabetes has trebled since 1981. A major recent study (the Australian Diabetes, Obesity and Lifestyle Study) reported a prevalence rate of 7.5% in people older than 25 years. In addition, the rate of impaired glucose metabolism was 16%, and it was estimated that for every known case of diabetes, there was 1 undiagnosed case.[2] In Australia's indigenous population, prevalence rates of diabetes are of particular concern, being 2 to 3 times that of non-Aboriginal Australians.[3]

Pathology testing has an important role in the management of patients with established diabetes and in the monitoring of complications of the disease. Hemoglobin A1c (HbA1c) and urine albumin/creatinine ratio (ACR) are well-established biochemical tests that form part of a patient's regular diabetes review, as is the lipid profile of tests (total cholesterol, high- and low-density lipoproteins [HDL and LDL, respectively] cholesterol, and triglyceride). Hemoglobin A1c provides a long-term measure of a patient's glycemic control, urine ACR can detect early stages of diabetic nephropathy, whereas dyslipidemia characterized by high plasma triglyceride and low HDL cholesterol concentrations is common in type 2 diabetes. Each of these markers can readily be performed by point-of-care testing (POCT). During the past 7 years in particular, there has been considerable uptake of POCT for diabetes management in Australian public health care settings outside the laboratory, particularly in Aboriginal medical services, country hospitals, and, more recently, general practice.[4–9] There has been also been an increase in the number of POC instruments available in the diagnostic market place offering the ability to conduct tests in public health care settings. When selecting a POCT instrument for use outside the laboratory, it is crucial to consider its analytical performance and to be aware of analytical concepts such as precision, accuracy, and total error (refer to Glossary of Key Terms). It is therefore also crucial that analytical goals are set to critically assess the competency of POCT instruments being used for clinical decision making for diabetes management in settings outside the laboratory in Australia.

This article therefore focuses on setting analytical goals (or analytical quality specifications) for the performance of

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HbA1c, urine ACR, and lipid POC tests used for diabetes management in Australia. The article describes current approaches used to set analytical goals for laboratory methods, discusses the relevance of these approaches to POCT, reviews available published data on analytical goals for the candidate tests and how these goals relate to current state-of-the-art performance in Australia, and makes recommendations on analytical goals for these tests that are relevant and appropriate for the POCT public health environment in Australia. Goals have been set for the imprecision, bias (inaccuracy), and total allowable error for each POC test (refer to Glossary of Key Terms). Many of the analytical goals recommended in this article have been adopted for use by the Australian Government's Department of Health and Ageing in a major new trial of POCT in General Practice in Australia (see accompanying article in this issue).[10]

Approaches Used to Set Analytical Performance Standards in Laboratories

There is an internationally accepted, 5-tiered hierarchical model for the setting of analytical goals for the imprecision, bias, and total allowable error of laboratory tests (Table 1).[11–13] Where data are available from more than 1 approach, models higher in the hierarchy are considered to hold greater weighting than those from lower levels.

The highest quality standard is required when analytical quality has a direct effect on medical decision making in a specific clinical situation. As described later, HbA1c is an example of a test where this standard should be applied. Analytical goals for broader clinical need can be derived from biological variability or from clinical survey on how clinicians use test results. Biological variation data (both within individual and between individuals) are now available on more than 300 analytes.[14,15]

Three classes of analytical goals (minimal, desirable, and optimal), based on fractions of within-individual biological variation, have also been developed for the imprecision of commonly measured tests.[12–15] The desirable analytical goal for most biochemical analytes is that the analytical imprecision (coefficient of variation, CVa) should be less than one half of the average within-person biological variation (0.5 CVw).[12] However, for those analytes for which the desirable goals derived using this formula are readily achievable with current methodology, it is recommended that an optimal analytical goal be used, based on the formula CVa < 0.25 CVw.[12] For those analytes for which desirable goals are not readily attainable using current methodology, a minimum analytical goal is recommended, based on the formula CVa < 0.75 CVw.[12]

Many national and international groups have also set profession-defined analytical goals (eg, the recommendations of the National Cholesterol Education Program [NCEP] in the United States, which have been widely used to set goals for lipid analyses).

Government or external quality assurance program organizers also set analytical quality specifications. In Australia, the Royal College of Pathologists of Australasia (RCPA) Quality Assurance Programs Pty Ltd Chemical Pathology Group is the major provider of external quality assurance (proficiency testing) programs for clinical chemistry laboratories. This group sets analytical goals for total allowable error (which they call "allowable limits of performance") for all biochemical tests offered through their programs.[16]

TABLE 1. Hierarchical Approach for Procedures to Set Analytical Goals

Level	Approach	Procedure
1	Specific clinical need	Clinical outcome studies
2	Broad clinical need	Biological variation
		Clinical survey
3	Profession defined	Experts panels
		National/international guidelines
4	Proficiency testing	Specifications from external quality assurance organizers or regulation
5	State of the art	Published data from external quality assessment schemes or literature

How Relevant Are Laboratory-defined Analytical Goals for POCT Settings Outside the Laboratory?

As an overarching principle, analytical goals for POCT should be equivalent to those used for laboratories to ensure the use of POCT does not compromise standards of patient care and clinical decision making. Fraser has stated that the internationally accepted hierarchical approach to setting analytical goals should be adopted in, and is appropriate for, all settings in which laboratory medicine is practiced, including POCT.[17]

However, it is important to acknowledge that the POCT environment, particularly in rural and remote Australia, is often very different to the laboratory setting. First, long-term retention of staff as POCT operators is an ever-present problem for rural and remote health services, creating difficulties in sustaining not only POCT but other health programs in general. For many rural and remote health services using POCT, refrigerator space, efficient and timely delivery of reagents and quality products, regular power fluctuations, poor lighting, heat, dust, and humidity within the working environment are all real issues that can impact on the ability to deliver and sustain a quality POCT service. Second, there needs to be a balanced approached to goal setting. There is limited value in setting analytical goals that are too stringent and which current POCT (and/or laboratory) instruments cannot achieve. On the other hand, there is a clinical imperative to ensure that excessive analytical noise from POCT methods does not mask clinically significant changes in patient results. Minimum analytical goals for the imprecision of nonlaboratory-based POCT should be set (along with desired and optimal goals) where sufficient data are available with the proviso that performance outside the minimum goal should be investigated and acted upon by the clinician responsible for clinical governance of POCT and the POCT site operator. Third, when assessing analytical performance in POCT environments against published literature, it should be noted that the majority of published

evaluations of POCT instruments have been conducted in the laboratory setting (ie, away from the field site where the POCT instrument is to be used) by trained laboratory staff (rather than the staff who would normally be required to perform POCT in the field). Analytical goals may also vary depending upon the intended purpose of the test. For example, different goals may be needed for diagnosis versus monitoring of test results and for monitoring an individual patient at 1 health service compared with different sites. The analytical goals recommended in this article are for goals for patient management within a given health service.

HEMOGLOBIN A1C

Goals for Imprecision

Results from clinical outcome studies such as the Diabetes Control and Complication Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) have firmly established the importance of tight glycemic control in reducing the complications of diabetes.[18,19]

In the DCCT study, for example, 1441 patients with type 1 diabetes were randomly allocated to either an intensively treated or a conventionally treated group. The intensively treated group had a mean HbA1c level of 7.2% during a 6.5-year period, whereas the conventionally treated group had a mean HbA1c of 9.1%. The risks of developing retinopathy, microalbuminuria, and neuropathy (all complications of diabetes) were reduced by 76%, 39%, and 60%, respectively, in the intensively treated group.[18] In the UKPDS study, 3867 patients with type 2 diabetes were randomly assigned to intensive and conventionally treated groups. Over 10 years, the mean HbA1c level was 7.0% in the intensively treated group and 7.9% in the conventionally treated group. Although the difference in mean HbA1c levels was not as striking as in the DCCT trial, there was still a 21% and 34% reduction in retinopathy and microalbuminuria end points in the intensively treated group from the UKPDS trial.[19]

From 1997 to 2002, the American Diabetes Association (ADA) recommended a target HbA1c of less than 7% for optimal glycemic control, whereas treatment with more intensive therapy was recommended for HbA1c levels of greater then 8%.[20] More recently, the ADA have recommended the optimal HbA1c target for individual patients should be as close as possible to normal (HbA1c, <6%) without significant hypoglycemia.[21]

Collectively, the DCCT and UKPDS clinical outcome studies and the ADA recommendations concerning glycemic targets emphasize the critical requirement for low imprecision in monitoring serial HbA1c measurements in the individual patient with diabetes.

This has led professional bodies and expert groups to recommend a general tightening of analytical goals for imprecision of HbA1c assays during the past decade. The National Glycohemoglobin Standardization Program in America requires that an HbA1c method must have a total (between-run) imprecision of 4% or less to achieve National Glycohemoglobin Standardization Program certification.[22] Many expert groups representing clinical and chemical pathology organizations from the United States, United Kingdom, and Australia have recommended imprecision goals of 3% (within laboratory) and 5% (between laboratory) for HbA1c.[23–26] More recently, an international workshop representing distinguished bodies including the International Diabetes Federation, the International Federation of Clinical Chemistry (IFCC), and the ADA produced a consensus statement advocating an optimal imprecision goal for HbA1c of 2%.[27,28]

Only methods with an analytical imprecision, or coefficient of variation (CV%), of 3% or less can distinguish statistically between HbA1c treatment goals of 7% and 8%[29]; coefficient of variation is a statistical measure of imprecision, calculated as the SD divided by the mean of replicate measurements and expressed as a percentage. At the ADA target of 7% HbA1c, an analytical CV% of 3% equates to an SD of 0.21. Thus, the true result has a 95% probability of lying within the range of 6.58% to 7.42% HbA1c (±2 SD). At an HbA1c of 8%, the level formerly recommended by ADA for a change in therapy, an analytical CV% of 3% equates to an SD of 0.24. Here, the true result has a 95% probability of lying within the range of 7.52% to 8.48% HbA1c. For methods with an analytical imprecision greater than 3%, there will be an increasing degree of overlap in these values. Further, 2 serial HbA1c results must differ by greater than 2.77 SD for there to be at least a 95% probability that they are analytically different.[14] For an HbA1c assay with a CV% of 5%, this means that the 2 HbA1c results would need to differ by >1.0% (at a level of 7%) for the physician to be confident that a clinically significant change has occurred in the patient. For methods with CV%s of 4% and 3%, results would need to differ by more than 0.8% and more than 0.6%, respectively, to be confident there has been a clinically significant change in glycemic status.

Data on biological variation of HbA1c is limited. Early published estimates list the within-person biological variation of glycated hemoglobin in blood as 5.6, from which a desirable imprecision goal of 2.8% can be derived.[13,14] However, more recent estimates indicate the within-person biological variation of HbA1c is 1.9%, leading to a tighter desirable goal of 1.0%.[15,30,31]

Clearly, an imprecision goal of less than 3% is the desirable analytical goal for laboratory HbA1c methods, based on clinical requirement, with an optimal imprecision goal of 2% now being recommended by leading professional groups.

Can these analytical goals be achieved in Australia by laboratory (and POCT) methods? The average imprecision (CV%) recorded by the top 20%, 50% (median), and 90% of laboratories participating in the 2005 RCPA Quality Assurance Programs Glycohemoglobin Program was 1.9%, 2.7%, and 5.1%, respectively (Table 2). Only approximately 55% of analytical systems used in Australia achieved a precision of less than 3%, most of which are high-performance liquid chromatography (HPLC)–based methods. The main POCT device used by laboratories in Australia (the DCA 2000; Bayer, Tarrytown, NY) recorded a CV% of 2.9% in this program during 2005.[32] State-of-the-art data on POCT HbA1c testing outside the laboratory are available through the national Quality Assurance for Aboriginal Medical Services (QAAMS) Program. The Bayer DCA 2000 recorded a median

TABLE 2. Imprecision Observed in 2005 by Laboratories Participating in Quality Assurance Programs Administered by the RCPA Quality Assurance Programs Chemical Pathology Group[16]

Analyte	Program	2005 Cycle Number	2005 Cycle Period	CV%			Concentration Range in Quality Assurance Samples
				Top 20% of Laboratories	50% of Laboratories (Median)	90% of Laboratories	
HbA1c	Glycohemoglobin	22	Jan–Jun	2.0	2.7	5.1	5.3–13.0%
		23	Jul–Dec	1.8	2.6	5.1	
Cholesterol	Special lipids	28	Jan–Jun	1.5	2.3	5.7	2.5–10.5 mmol/L
		29	Jul–Dec	1.7	2.1	3.6	
Triglyceride	Special lipids	28	Jan–Jun	1.9	2.8	5.1	0.5–3.2 mmol/L
		29	Jul–Dec	1.7	2.3	4.6	
HDL cholesterol	Special lipids	28	Jan–Jun	3.9	5.6	10.0	0.7–2.2 mmol/L
		29	Jul–Dec	3.5	4.7	7.7	
Urine albumin	General urine chemistry	41	Jan–Jun	3.4	5.8	12.6	10–130 mg/L
		42	Jul–Dec	3.6	5.7	12.6	
Urine creatinine	General urine chemistry	41	Jan–Jun	2.0	3.3	7.2	2.4–22 mmol/L
		42	Jul–Dec	2.0	3.1	7.4	

Data are presented for the two 6-monthly testing cycles completed by laboratories during 2005.

CV% of 3.2% for quality assurance testing in the QAAMS Program during 2005.[32] A recent comparison of 4 POCT devices for HbA1c in the hands of hospital nursing staff revealed that only the Bayer DCA 2000 was able to achieve a within-batch CV% of less than 3%.[33]

With many laboratory systems currently unable to attain the desirable analytical goal of 3% for HbA1c testing, it would therefore seem inappropriate to impose this goal on POCT devices measuring HbA1c outside the laboratory. It is therefore recommended that a minimum imprecision goal of 4% for POC HbA1c testing be set for this analyte, along with a desirable goal of 3% and an optimal goal of 2%.

Goals for Bias

Routine laboratory methods for HbA1c are based on 3 different analytical principles: those that measure HbA1c by difference in charge (eg, cation exchange HPLC), structure (affinity chromatography) or antigenicity (immunoassay).[23,26] Methods based on these principles measure slightly different glycation products and hence generate slightly different HbA1c results. Some methods may also be subject to interference by fetal hemoglobin, abnormal hemoglobin variants, and uremia seen in renal patients (as a result of carbamylation of hemoglobin from urea-derived isocyanate) or in patients on long term-salicylate therapy.

From a clinical perspective, the use of glycemic targets for assessing management and therapy dictates that there should be no difference between the accuracy of analytical methods. This clinical requirement has led to a pressing need among clinical biochemists to standardize (or harmonize) all HbA1c methods globally. There has been considerable work devoted to this task during the past decade by the IFCC Working Group on HbA1c Standardization.[27,34] The preparation of pure HbA1c calibration material, the establishment of international reference methods, and a reference system is well under way and should lead not only to a minimization of analytical bias between methods but also a reduction in between-method imprecision. With the new reference system close to being implemented globally, the analytical goal for both laboratory and POCT HbA1c methods should be to have zero bias.

Goals for Total Allowable Error

In Australia, the RCPA Quality Assurance Programs Chemical Pathology Group has set an analytical goal ("allowable limit of performance") for HbA1c measurement of ±0.5 at HbA1c concentrations of 10.0% or less and ±5% at HbA1c concentrations of more than 10.0% for their laboratory-based glycohemoglobin program.[17] A goal for total allowable error of HbA1c analysis of 2.7% can also be derived from recent biological variation data.[15] However, given the goal for accuracy is to have no bias and the clinical imperative for HbA1c to have minimal analytical imprecision, it is recommended that the goals for total allowable error for HbA1c POCT measurement should be the same as those set for imprecision.

Although the Bayer DCA 2000, which is the most widely used POCT instrument in Australia, can achieve performance close to the desired goals, many other current POCT analysers will unquestionably have difficulty achieving the recommended analytical goals. However, the clinical requirement for precise and accurate results dictates that stringent goals need to be set for POC HbA1c testing to ensure patient management is not compromised.

LIPIDS

Goals for Imprecision

Most of the data concerning analytical goals for laboratory lipid analysis comes from biological variation studies or is profession derived.

Minimum, desirable, and optimal imprecision goals for lipid testing based on biological variation data are available from several sources and are summarized in Table 3.[13–15] Published data on analytical goals for lipids is available from 2 American expert groups, namely the Centers for Disease

TABLE 3. Goals for Imprecision of Lipid Testing Derived from Biological Variation[15] and the Recommendations of the NCEP[40]

Analyte	Biological Variation (CVw)	Derived Imprecision Goal (CV%)			Imprecision Goal from NCEP (CV%)
		Minimum	Desirable	Optimal	
Cholesterol	6.0	4.5	3.0	1.5	3.0
Triglyceride	21.0	15.8	10.5	5.3	5.0
HDL cholesterol	7.1	5.3	3.6	1.8	4.0
LDL cholesterol	8.3	6.2	4.2	3.6	4.0

Control and Prevention (CDC) through its CDC–National Heart, Lung, and Blood Institute Lipid Standardization Program and the NCEP. The CDC-National Heart, Lung, and Blood Institute Lipid Standardization Program arose in the late 1980s out of a desire to improve the analytical performance of specialist lipid laboratories around the world.[35] The CDC analytical goals are complex because they are concentration dependent and couched mainly in SD rather than CV% terms. The NCEP have been reporting analytical goals for imprecision, bias, and total allowable error for cholesterol since 1988 and for triglyceride, HDL cholesterol, and LDL cholesterol since 1995.[36–39] Goals recommended by the NCEP for the imprecision of lipid analyses is shown in Table 3.[40]

For total cholesterol, an imprecision goal of 3% is the desirable specification for laboratory methods. Is this goal achievable by laboratories in Australia? The average imprecision (CV%) recorded by the top 20%, 50% (median), and 90% of laboratories participating in the RCPA Quality Assurance Programs Special Lipid Program was 1.6%, 2.2%, and 4.7%, respectively, in 2005 (Table 2). Most, but not all of the current laboratory analytical systems, achieved the desirable imprecision goal. For POCT outside the laboratory in Australia, a minimum imprecision goal of 5%, based on rounded biological variation, is therefore recommended. An optimal goal of 2% can also be set based on the current performance base achieved by the better Australian laboratories.

For triglyceride, the desirable goal for imprecision derived from biological variation (10.5%) is twice that recommended by the NCEP (5%) because triglyceride exhibits a large degree of within-person biological variation (21%). The average imprecision (CV%) recorded by the top 20%, 50% (median), and 90% of laboratories participating in the 2005 RCPA Quality Assurance Programs Special Lipid Program was 1.8%, 2.6%, and 4.9%, respectively, in 2005 (Table 2). It is therefore recommended that the NCEP-derived desirable imprecision goal of 5% is more appropriate for this analyte than the corresponding goal from biological variation. A minimum imprecision goal of 7.5% for POCT outside the laboratory, which represents the approximate midpoint between goals of 10.5% from biological variation and 5% from the NCEP is also recommended and should readily be achievable in the nonlaboratory environment. An optimal goal of 2% can also be set based on the current performance base achieved by the top 20% of Australian laboratories.

For HDL cholesterol, an imprecision goal of 4% is the desirable performance standard from both NCEP and biological variation data. However, the average imprecision (CV%) recorded by the top 20%, 50% (median), and 90% of laboratories participating in the RCPA Quality Assurance Programs Special Lipid Program was 3.7%, 5.2%, and 8.9%, respectively, in 2005 (Table 2). These data indicate that current laboratory methods struggle to meet the desirable goal and this goal is too tight to be imposed on POC HDL cholesterol testing outside the laboratory. Historically, HDL cholesterol has been a technically demanding and time-consuming assay in the laboratory environment, and the fact that HDL cholesterol can be performed by POCT at all is quite a remarkable technological feat. In Australia, HDL cholesterol concentrations are also generally reported to 1 decimal place. For these reasons, it is recommended that a minimum goal for imprecision of POC HDL cholesterol testing be set at 6% (which is slightly higher than the minimum goal derived for biological variation). An optimal goal of 3.5% can also be set based on the current performance base achieved by the top 20% of Australian laboratories.

LDL cholesterol is not measured directly by routine laboratory or POCT lipid analysers, rather it is a calculated value based on the Friedewald formula.[41] This formula provides an adequate surrogate measurement of LDL cholesterol only when the sample has a triglyceride concentration less than 4.5 mmol/L and is free of chylomicrons. Analytical errors in each of the tests measured in calculating the formula (total cholesterol, HDL cholesterol, and triglyceride) are additive. It is therefore recommended that a minimum imprecision goal of 6% (from biological variation) and a desirable imprecision goal of 4% (from both biological variation and NCEP recommendations), respectively, be set for LDL cholesterol. An optimal goal of 3.5% can be set from biological variation but would be extremely difficult to achieve with laboratory, let alone, POCT methods.

Goals for Bias

The following goals can be derived from biological variation data and NCEP recommendations: total cholesterol, 4.0% and 3%, respectively; triglyceride, 10.7% and 5%, respectively; HDL cholesterol, 5.2% and 5%, respectively; LDL cholesterol, 6.8% and 4%, respectively. However, the profession-driven NCEP recommendations would seem more appropriate to apply to laboratory and POCT methods.

Goals for Total Allowable Error

A comparison of goals for total allowable error derived from biological variation and the recommendations of the

TABLE 4. Goals for Total Allowable Error of Lipid Testing Derived from Biological Variation[15] and the Profession-based Recommendations of the NCEP[40] and the RCPA Quality Assurance Programs Pty Ltd[16] in Australia

Analyte	Biological Variation (%)	NCEP (%)	RCPA Quality Assurance Programs
Total cholesterol	9.0	8.9	±0.50 ≤10 mmol/L ±5% >10 mmol/L
Triglyceride	28.0	14.8	±0.20 ≤2 mmol/L ±10% >2 mmol/L
HDL cholesterol	11.1	12.8	±0.20 ≤2 mmol/L ±10% >2 mmol/L
LDL cholesterol	13.6	12	Not available

NCEP and the RCPA Quality Assurance Programs are shown in Table 4.

Using the first 2 approaches, goals for total allowable error are generally comparable for cholesterol (approximately 9%), HDL cholesterol (12%), and LDL cholesterol (13%). For triglyceride, the goal from biological variation is influenced by large within- and between-person variation and is therefore much wider than the NCEP goal. Given that most current methods for triglyceride (including POCT) are of good quality, the NCEP goal for total allowable error of 15% is considered most appropriate. To allow for the vagaries of the nonlaboratory POCT environment outlined in the introduction, recommended total allowable error goals have been rounded to 10% for total cholesterol and 15% for both HDL and LDL cholesterol.

URINE ACR

Microalbuminuria can be defined in terms of either a urine ACR in a first morning urine, a urine albumin excretion rate (AER) in a timed (overnight) urine sample or urinary albumin excretion per day. The measurement of urine ACR on a first morning sample has proven clinically popular in Australia because it is convenient for the patient and does not require a timed collection or measurement of urine volume.

Goals for Imprecision

The following minimum, desirable, and optimal imprecision goals for urine albumin and creatinine can be derived from biological variation data: 27%, 18% and 9% for urine albumin and 18%, 12%, and 6% for urine creatinine.[14,15]

Given the wide within-person biological variation observed with urine albumin, the National Academy of Clinical Biochemistry (NACB) has argued that a lesser degree of precision is required for this analyte. They have recommended that "the analytical imprecision (CV%) of methods to measure microalbuminuria should be <15%."[26]

From state-of-the-art laboratory data, the average imprecision (CV%) recorded by the top 20%, 50% (median), and 90% of laboratories participating in the 2005 General Urine Chemistry Program run by the RCPA Quality Assurance Programs Chemical Pathology Group was 3.5%, 5.8%, and 12.6%, respectively (Table 2). All but a small minority of infrequently used methods achieved the profession-based NACB goal.

In the national QAAMS Program for urine ACR POCT on the Bayer DCA 2000 in Australian Aboriginal medical services, participating services (n = 30) achieved an average imprecision of 8.3% for urine albumin (as well as 4.6% for urine creatinine and 4.4% for urine ACR) during the past 3 years.[32]

These 2 sets of data indicate the goal for urine albumin proposed by the NACB can readily be achieved using current laboratory and POCT methodology. It is therefore recommended that the desirable goal be set at 10%, closer to the optimal goal derived from biological variation data.

For urine creatinine, the desirable imprecision goal from biological variation data is 12%. However, once again, current Australian laboratories can readily achieve this goal. The average imprecision (CV%) recorded by the top 20%, 50% (median), and 90% of laboratories participating in the 2005 RCPA Quality Assurance Programs General Urine Chemistry Program was 2.0%, 3.2%, and 7.3%, respectively (Table 2). As mentioned above, the average imprecision for POC urine creatinine testing in the national QAAMS Program for urine ACR was 4.6%. It is therefore recommended that the desirable imprecision goal for POCT urine creatinine be set at 6%, consistent with the optimal goal derived from biological variation data.

To calculate the desirable imprecision goal for the urine ACR, it is necessary to add the recommended goals for urine albumin (10%) and creatinine (6%) according to the following formula:

$$\text{Total CV\% for ACR} = (CV_{Alb}^2 + CV_{Creat}^2)^{1/2}$$

Thus, the calculated desired goal for imprecision for urine ACR is 12%. This was readily achieved by the DCA 2000 POCT instrument in the QAAMS Program, but detailed data on the performance of other POCT microalbumin analysers is not available in Australia as yet.

Goals for Bias

There is only extremely limited data available on accuracy goals. Goals calculated from biological variation data appear to be too wide to be of practical or clinical use (urine albumin, 16.4%; urine creatinine, 8.6%).

Traditionally, almost all laboratories have used immunochemical methods to measure urine albumin. However, the recent reporting of a previously unrecognized nonimmunoreactive form of urine albumin in diabetes patients separated

TABLE 5. Summary of Analytical Goals Recommended for POCT Instruments Used for Diabetes Management in the Public Health Setting in Australia

Analyte	Goal for Imprecision (CV%)			Goal for Total Allowable Error (%)
	Minimum (%)	Desirable (%)	Optimal (%)	
HbA1c	4	3	2	4
Total cholesterol	5	3	2	10
Triglyceride	7.5	5	2	15
HDL cholesterol	6	4	3.5	15
LDL cholesterol	6	4	3.5	15
Urine albumin	—	10	—	12.5
Urine creatinine	—	6	—	7.5
Urine ACR	—	12	—	15

by size-exclusion HPLC has raised considerable global debate among clinical biochemists about the accuracy of urine albumin measurements.[42-45] The IFCC has now formed a working group on the standardization of the microalbumin assay in urine.[46] Their charter is to establish a reference procedure and reference methods for the measurement of urine (micro)albumin, to undertake a chemical and immunochemical characterization of the various forms of albumin in urine, and to decide upon the optimum analyte for the assessment of microalbuminuria.

Goals for Total Allowable Error

Analytical goals for total allowable error derived from biological variation data are too wide and of limited clinical relevance (urine albumin, 46%; urine creatinine, 28%).

In the RCPA Quality Assurance Programs' General Urine Chemistry Program, "allowable limits of performance" of ±4 for concentrations of up to 20 mg/L and ±20% at concentrations greater than 20 mg/L have been set for urine albumin and ±0.5 at 5 mmol/L or less and ±10% at concentrations greater than 5 mmol/L for urine creatinine.

In the QAAMS urine ACR Program, goals for total allowable error of 12.5% for urine albumin, 7.5% for urine creatinine, and 15% for urine ACR have been set by the program organizers.[5] They would seem relevant, appropriate, and readily achievable for the POCT environment.

DISCUSSION

This article focuses on setting analytical goals for the performance of selected common POC tests used for diabetes management in Australia. The article reviews the current data on analytical goal setting in laboratories, addresses the factors that set POCT apart from the laboratory environment, compares laboratory-derived analytical goals with current state-of-the-art performance, and then sets goals for POCT conducted in the nonlaboratory environment. The analytical goals recommended in this article are summarized in Table 5. They aim to be appropriate and achievable for diabetes management in the nonlaboratory POCT setting in Australia and ensure that the quality of patient care is not compromised. Analytical goals have been set for the imprecision, bias, and total allowable error for each POC test where sufficient data are available. A minimum imprecision goal has been recommended for each blood analyte. Point-of-care testing methods that are unable to achieve these minimum goals should be used with caution.

The goals for analytes such as triglyceride and urine albumin should be readily achievable by most POCT analysers. At the other extreme, the goals for HbA1c will undoubtedly present a challenge for POCT manufacturers to develop more innovative and advanced technological and methodological systems to meet the clinical imperative to minimize total analytical error. Diagnostic companies will need to pay particular attention to the automation and quality management of manufacturing processes to ensure within- and between-batch variation in reagents is minimized. The tight goals for HbA1c will also demand that nonlaboratory POCT operators have continuous access to on-going education and training for POC HbA1c testing to ensure competency standards and skills are maintained at optimal levels.

The analytical goals recommended for POCT in this article should be regarded as a starting point for further profession-based discussion, with the goals needing to be flexible and continually reviewed and refined as further relevant data (particularly from clinical outcome studies) become available. The current Australian Point-of-Care Testing Trial in General Practice will provide a suitable environment in which to rigorously assess the validity and appropriateness of the goals recommended by this article. While the purpose of this article was to recommend goals for POCT conducted in the nonlaboratory setting in Australia, it is also envisaged that the promulgated goals will be broadly applicable and relevant for countries conducting POCT in the public health care setting outside Australia.

GLOSSARY OF KEY TERMS

Accuracy The closeness of the agreement between the measured value and the true value of an analyte.

Analyte The pathology test that is being measured.

Analytical goal The level of performance required to ensure that a pathology test fulfills its stated or implied purpose. The terms *analytical goals*, *analytical quality specifications*, and *allowable limits of performance* are used interchangeably in this article.

Between-person biological variation The difference between the homeostatic setting points of individuals.

Bias (or inaccuracy) The numerical difference between the measured value and the true value of an analyte.

Coefficient of variation (CV%) A statistical measure of imprecision, calculated as the standard deviation divided by the mean of replicate measurements and expressed as a percentage. Thus, CV% = (SD/mean) * 100.

CVa Analytical coefficient of variation.

CVw Within-person biological coefficient of variation.

Imprecision (or analytical imprecision) The standard deviation or coefficient of variation of the results in a set of replicate measurements of an analyte.

Point-of-care testing Pathology testing that is performed by or on behalf of the requesting clinician at the time of consultation with the patient, allowing the test result to be used to make immediate, informed decisions (in the context of this article) about patient management.

Precision The closeness of agreement between replicate measurements on the same analyte under specified conditions; precision is also often referred to as the reproducibility, repeatability, or scatter of a set of replicate measurements.

Standard deviation A statistical measure of imprecision (or the dispersion of replicate measurements on the same analyte), calculated as the square root of the sum of the squares of the difference between each data point and the mean divided by the total number of data points minus 1.

Total (analytical) error The sum of the bias and imprecision, usually defined by the formula TE = [bias] + 1.65 * precision, where bias does not have a sign.

Total allowable error The analytical goal or quality specification for total error.

Within-person biological variation The inherent biological variation of an analyte around the homeostatic setting point for that individual.

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CHAPTER 5

DEVELOPMENT OF A QUALITY FRAMEWORK FOR POCT AND ASSESSMENT OF ANALYTICAL QUALITY OF POCT IN INDIGENOUS MEDICAL SERVICES

INTRODUCTION TO CHAPTER 5

The three papers presented in this chapter described the development and implementation of the education, training and quality management framework that underpinned the QAAMS program (and which formed the foundation of all the POCT models described in this research program). The papers also reported, for the first time, on the analytical quality of POCT for both HbA1c and urine ACR conducted nationally by Aboriginal Health Workers as POCT operators. While Aboriginal Health Workers play a crucial role at the coalface of Indigenous health care, they had never before been trained as POCT operators.

As mentioned in Chapter 1, the QAAMS program, which I conceived, initiated, developed, implemented and have managed for the Australian Government since its inception in 1999, has a national focus currently involving 80 Indigenous medical services across Australia (as at March 2007).

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.

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Clinical Biochemistry Reviews 2003; 24: 123-130.

STATEMENT OF AUTHORSHIP

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

Clinical Biochemist Reviews 2003; 24: 124-131.

SHEPHARD, M.D.S. (Candidate)

Conceived research and study design, initiated, implemented and managed study, analysed and interpreted data, wrote manuscript and acted as corresponding author.

Signed .... *Date* 15/12/2006

GILL, J. P.

Assisted with management of quality assurance program and commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed .... *Date* 15/12/06

Results Of An Innovative Education, Training And Quality Assurance Program For Point-Of-Care HbA_{1c} Testing Using The Bayer DCA 2000 In Australian Aboriginal Community Controlled Health Services.

This paper reported on the research findings from the first 3.5 years of operation of the QAAMS Program for HbA1c POCT.

It described, for the first time, the development of a culturally appropriate national education and training program for POCT HbA1c testing by Aboriginal Health Workers that included a quality management framework comprising both quality control and quality assurance testing.

The key research question addressed in this paper was: Could Aboriginal Health Workers from a wide range of Indigenous medical services across Australia perform POC HbA1c quality assurance testing to an analytical standard that was equivalent to laboratory users of the DCA 2000 and which met or approached analytical goals set by the clinical biochemistry profession?

The research findings presented in this paper confirmed, for the first time, that Aboriginal Health Workers conducting POCT on a national scale could indeed achieve an analytical performance that matched laboratory scientists and approached profession-derived analytical goals for laboratory HbA1c testing.

Review Article

Results of an Innovative Education, Training and Quality Assurance Program for Point-of-Care HbA_{1c} Testing using the Bayer DCA 2000 in Australian Aboriginal Community Controlled Health Services

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Abstract

This study describes the development, implementation and management of a multi-faceted quality assurance program called Quality Assurance for Aboriginal Medical Services (QAAMS) to support point-of-care HbA_{1c} testing on the Bayer DCA 2000 in Aboriginal people with diabetes from 45 Australian Aboriginal Community Controlled Health Services.

The quality assurance program comprised four elements: production of culturally appropriate education resources, formal training for Aboriginal Health Workers conducting HbA_{1c} testing, an external quality assurance program and on-going quality management support services including a help hotline and an annual workshop. Aboriginal Health Workers were required to test two quality assurance (QAAMS) samples in a blind sense every month since July 1999. Samples were linearly related and comprised six paired levels of HbA_{1c}. The short and long term performance of each service's DCA 2000 was reviewed monthly and at the end of each six month testing cycle.

The average participation rate over 7 six-monthly QAAMS testing cycles was 88%. 84% of 3100 quality assurance tests performed were within preset limits of acceptability. The median precision (CV%) for HbA_{1c} testing has averaged 3.8% across the past 5 cycles (range 3.4 to 4.0%) and is continuing to improve. The introduction of a medical rebate for HbA_{1c} testing has ensured the program's sustainability.

Through continuing education and training, Aboriginal Health Workers have achieved consistent analytical performance for HbA_{1c} testing on the DCA 2000, equivalent to that of laboratory scientists using the same instrument. This unique quality assurance model can be readily adapted to other Indigenous health settings and other point-of-care tests and instruments.
(Clin Biochem Rev 2003; 24:124-31)

Introduction

Type 2 diabetes is a significant cause of morbidity and mortality among Aboriginal Australians. Aboriginal people suffer between 12 to 17 times more deaths due to type 2 diabetes than non-Indigenous Australians, while overall prevalence rates are within the range of 10-30% and at least two to four times that of the non-Aboriginal population.[1,2]

Studies such as the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) have confirmed that good control of diabetes

is critical to prevent the long-term debilitating complications of this disease such as nephropathy, neuropathy and retinopathy.[3,4] Haemoglobin A_{1c} (HbA_{1c}) is a well-established biochemical marker of diabetes control and can be conveniently measured on the small, portable DCA 2000 point-of-care analyser (Bayer Diagnostics, Melbourne, Australia).

In 1998, the National Diabetes Strategy and Implementation Plan, Australia recommended that a trial of the DCA 2000 for HbA_{1c} testing be conducted in Aboriginal primary health care services.[5] The DCA 2000 was considered to have particular application in the Aboriginal health care setting, notably in rural and remote locations, where access to basic health care is often limited and services may be several hundred kilometres from the nearest hospital laboratory.[6]

In June 1999 the Australian Government's Department of Health and Ageing, through its Office for Aboriginal and Torres Strait Islander Health (OATSIH) and in partnership with the National Aboriginal Community Controlled Health Organisation (NACCHO), commenced a pilot program for on-site HbA_{1c} testing using the DCA 2000. Forty-five Aboriginal Community Controlled Health Services (ACCHS) around Australia participated in the pilot. Aboriginal Health Workers (Aboriginal people trained in primary health care and living in the community setting) performed the testing on behalf of their local or visiting medical officer. Testing was only conducted on Aboriginal people with known diabetes, with a maximum of four HbA_{1c} tests being performed annually on each person. An HbA_{1c} of 7% was considered the target for good control of diabetes in Aboriginal people.[6]

As a requirement of the pilot, the Department of Health and Ageing determined that an on-going surveillance mechanism was needed to ensure point-of-care HbA_{1c} results generated in the field were acceptable for patient care. As a result, the RCPA Quality Assurance Programs Pty Ltd was initially contracted by the Department of Health and Ageing to develop, implement and manage a multi-faceted quality assurance program to support HbA_{1c} testing by Aboriginal Health Workers. (The RCPA Quality Assurance Programs Pty Ltd provides quality assurance programs to laboratories in Australasia in collaboration with the Royal College of Pathologists of Australasia and the Australasian Association of Clinical Biochemists). The Department of Health and Ageing (through its Diagnostics and Technology Branch) have subsequently extended this contract to the end of 2005 and the program has now been integrated into mainstream Aboriginal health care.

The quality assurance program developed by our group is believed to be the first of its type for Indigenous people anywhere in the world. We describe the novel aspects of this program, present the scientific results obtained over its first three and a half years of operation, and comment on the potential of this model to assist chronic disease prevention and management in other Indigenous countries and communities.

Research Design and Methods

Bayer DCA 2000 Instrument

The DCA 2000 point-of-care analyser is small (25cm high by 21cm wide by 25cm deep) and portable (weighing 5 kg). Only one microlitre of whole blood (capillary or venous) is required for the test, with the result available in 6 minutes. The DCA 2000 determines both the concentrations of HbA_{1c} and total haemoglobin, with the ratio being expressed as the percentage HbA_{1c}. HbA_{1c} is measured immunochemically by a method based on inhibition of latex agglutination. Total haemoglobin is measured spectrophotometrically following its oxidation to methaemoglobin by potassium ferrocyanide and the subsequent complexing of methaemoglobin with thiocyanate to form thiocyan-methaemoglobin.[7]

Participation

Forty-five Aboriginal Community Controlled Health Services formed the initial intake of program participants (Figure 1). Every State and Territory of Australia was

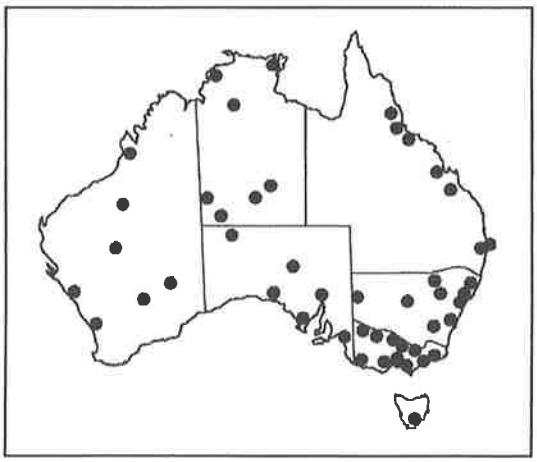

Figure 1. Location of Aboriginal Community Controlled Health Services participating in the QAAMS program during 2002.

represented and the location of participants encompassed a broad spectrum of urban, rural and remote Australia. There have been minor changes to the mix of participants over the past three and a half years due to changing health service priorities and/or Aboriginal Health Worker staff resources. Fifty sites were enrolled in the program at the beginning of 2003.

Quality Assurance Program

The quality assurance program to support HbA_{1c} testing in the Aboriginal community was called QAAMS (Quality Assurance for Aboriginal Medical Services). As tests were being conducted using a point-of-care medical instrument in the community setting by Aboriginal Health Workers, the design of the program needed to be broader and more intensive in its focus than a conventional laboratory-based quality assurance program. Four key elements, namely education, training, quality assurance, and on-going management support services for communities, formed the cornerstone of the QAAMS program.

Education

A culturally appropriate set of education resources was developed in conjunction with senior Aboriginal health representatives, Aboriginal Health Workers, diabetes specialists and scientists. The resources comprised a laminated book, video and a series of posters. Topics covered included diabetes and its complications, the importance of controlling diabetes, the HbA_{1c} test, the DCA 2000 machine and the principles and practice of quality control and quality assurance. The posters included step-by-step guides on how to perform the HbA_{1c} test on the DCA 2000 and how to conduct quality assurance testing on the DCA 2000.

Training

Formal training sessions for 84 Aboriginal Health Workers (and other allied health professionals) from every participating site were held at eight regional centres around Australia over an eight week period from May to July 1999. Training focussed on hands-on practical instruction in how to use the DCA 2000 machine, perform the HbA_{1c} test, and conduct quality assurance testing. Each service also received their education resource kit at the training session. Once back in the community, these resources were used as a refresher course, to train other Aboriginal Health Workers, or for general community education about diabetes.

Quality Assurance

A quality assurance program commenced in July 1999 to monitor the performance of DCA 2000 machines across all participating sites. Since that time, 7 six-monthly testing cycles have been completed to the end of 2002.

At the beginning of each year, all participants were sent a package containing the materials needed to conduct their QAAMS testing. The package included a testing kit containing 24 lyophilised QAAMS samples, each numbered and dated, vials of water for reconstitution of those samples, an information sheet, testing schedule and result sheets. An international Reference Laboratory for Glycohaemoglobin produced the samples for the program. The samples comprised paired and linearly related levels of HbA_{1c} across a range of concentrations from 5 to 14%. Services were required to test two QAAMS samples per month, according to the defined testing schedule that comprised two six-monthly testing cycles per year. Testing could be performed at any time during the month that was convenient to the service, provided the results were received at the QAAMS reporting office by fax or post by the last day of each month. To ensure confidentiality of results, each service was allocated a specific community code number that was stamped on their result sheets and all other printed matter.

Within a week after the closing date for return of results for each month, the QAAMS reporting office sent a graphical report to each individual service (Figure 2). The report compared the results returned by that service with the pre-set target values for each sample and with the range of results from all other services. In addition, the report displayed graphs that documented all previous results returned by the

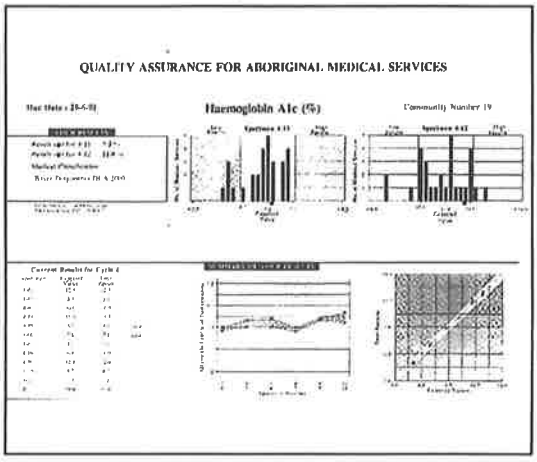

Figure 2. Example of the monthly summary report sent to all QAAMS participants.

Footnote to Figure. For Cycles 1 and 2, the international reference laboratory set target values. For Cycles 3 to 7, the median of all results submitted was used as the target.

service for that particular testing cycle. Through this method of reporting, each service received regular monthly information on the short and long term performance of their DCA 2000 machine.

At the end of each cycle, summary analysis of six months of data (12 specimens) was used to comment on each individual site's precision and accuracy. This data was used to identify individual services that were experiencing significant analytical problems. Services were contacted and an action plan implemented to redress poor performance.

Other Management Services

A help hotline telephone service was established whereby Aboriginal Health Workers could phone the QAAMS office immediately a problem arose, particularly in relation to instrument breakdown or other technical problems and interpretation of quality assurance results. A regular newsletter was also sent to all participants to update them on current issues. Workshops for participants were held in November 2001 and September 2002 and have now become an annual feature on the program's calendar. The workshop provides Aboriginal Health Workers with opportunities for retraining, networking, interactive discussion on all aspects of the program and presentations from participants on how their service is using the program. Representatives from the Department of Health and Ageing and Bayer Australia also attend the workshop. In addition to external quality assurance assessment, the QAAMS program also monitored internal quality control testing conducted by services using kits provided by the manufacturer (Bayer Normal and Abnormal Quality Control kits, catalogue number 5068001, Bayer Australia).

Results

Participation

An overall participation rate of 88% (range 81% to 93%) has been maintained across the first three and a half years (7 testing cycles) of the program. This represents the return of 3100 QAAMS results from a possible 3524. On average, 81% of participating services returned between 10 and a maximum of 12 results each cycle.

Performance Indicators

Across three and a half years of testing, the percentage of returned results that were within preset limits for acceptability was 84% (range 81% to 86%) (Table 1). This represents 2590 acceptable results from 3100 results returned. The limits of acceptability, called allowable limits of performance, were set by the QAAMS program organisers at ±0.5 up to an HbA_{1c} of 10% and ±5% at HbA_{1c} ≥10%. These are the same limits used for the parallel Glycohaemoglobin Quality Assurance Program run by the

	Cycle Number						
Performance Indicator	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Acceptable Results, %	84	84	83	84	81	83	84
Median Precision, CV%*	4.3	4.4	4.0	3.7	4.1	3.9	3.4
Median Bias†, $\%HbA_{1c}$	0.36	0.38	0.18	0.19	0.26	0.19	0.23

* Coefficient of variation (CV%) is calculated by dividing the standard deviation by the mid-point of the service's range of concentrations, expressed as a percentage. The standard deviation is the error of the estimate Sy.x and represents the average standard deviation across the range of concentrations analysed.

†Bias is the average of biases of the service's line of best fit at the lowest, highest and mid-point, irrespective of sign.

Table 1. Key performance indicators in the QAAMS Program, 1999 - 2002

RCPA Quality Assurance Program Pty Ltd for laboratories in Australasia and other parts of the world.

As stated earlier, the 12 samples in each cycle comprised six paired levels of HbA_{1c} concentration that were tested in random order pre-determined by the program organisers.

The use of paired and linearly related samples for QAAMS testing also enabled a direct measure of the precision and accuracy across time of both individual DCA 2000 machines and the group as a whole. The median coefficients of variation (CV%) and bias achieved by services participating in the program is shown for each testing cycle in Table 1. The median precision (CV%) for HbA_{1c} testing has averaged 3.8% across the past 5 testing cycles, with 3.4% being recorded for the most recent testing cycle. Notably the precision achieved by QAAMS participants has been steadily improving since the program began.

How does this level of performance compare to laboratories using the DCA 2000? The RCPA Quality Assurance Programs also runs a laboratory-based Glycohaemoglobin Quality Assurance Program, which uses the same material as that for the QAAMS program. There are approximately 75 DCA 2000 laboratory users in this program. The comparative analytical precision (median CV%) recorded for the QAAMS and the laboratory-based Glycohaemoglobin programs since the QAAMS program began shows that, for the past four testing cycles in particular, Aboriginal Health Workers achieved an analytical performance equivalent to that of trained laboratory scientists and technicians (Figure 3).

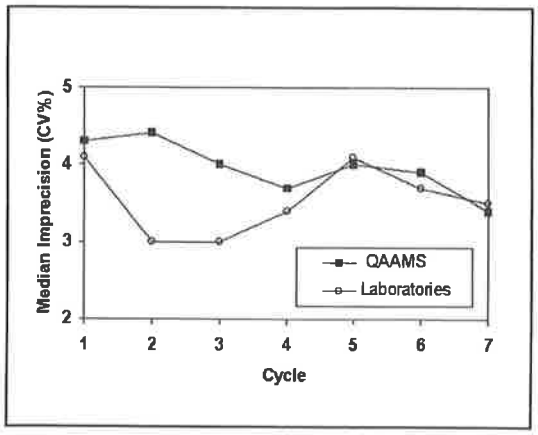

Figure 3. Precision achieved by QAAMS participants and laboratory users of the DCA 2000 across the past seven testing cycles.

How does this performance compare to international consensus criteria on desirable performance standards for HbA_{1c} analysis? The importance of imprecision as a key component of HbA_{1c} analysis is being increasingly recognised by the medical and scientific community world-wide. Based on clinical need from studies like the UKPDS and DCCT and recent recommendations from key professional bodies, there is now widespread international consensus that the desirable precision goal for HbA_{1c} analyses is a CV of less than 3%.[8-13] While there is little specific published information on desirable performance standards for point-of-care HbA_{1c} analysis, it is a generally accepted principle that analytical performance goals for point-of-care testing should be close or equivalent to those used for laboratories. In the most recently completed QAAMS testing cycle (Cycle 7), the point-of-care DCA 2000 analysers in the QAAMS program achieved a median CV of 3.4%, with 43% of QAAMS sites attaining the desired precision goal of less than 3% during this cycle. Whilst acknowledging that the point-of-care DCA 2000 analyser cannot achieve the performance base of state-of-the-art laboratory HPLC technology, the DCA 2000 is unquestionably the most practical and robust HbA_{1c} analyser for use in rural and remote Australia where access to laboratory services is often very limited or non-existent.

Other Management Services

A total of 419 calls were received by the QAAMS help hotline over the past three and a half years, 49% of which were taken during the first year of the program as teething problems and issues of process were being addressed. In addition to incoming calls, the QAAMS Program Manager provided on-going advice and follow-up action for sites whose DCA 2000 machines exhibited poorer performance.

1235 Bayer HbA_{1c} quality control results were returned to the QAAMS reporting office across the three and a half years of the program. As up to seven different lot numbers of Bayer quality control material were being used by QAAMS participants at any one time, it has not been possible to conduct detailed statistical analysis of Bayer quality control results. In the most recent cycle of testing, 95% of all Bayer quality control results returned were within the acceptable limits for the particular lot number of control tested (with the limits of acceptability the same as those used for the testing of QAAMS samples). During 2003/4, a single lot number of Bayer HbA_{1c} control will be sourced for use in the program.

Medicare Rebate for HbA_{1c} Testing

In December 2000 Australia's Federal Health Minister announced that a rebate could be claimed under the government's Medical Benefits Schedule (MBS) for HbA_{1c} tests conducted on the DCA 2000 in Aboriginal Community Controlled Health Services. Provision of this rebate has facilitated the program's integration into mainstream Aboriginal health care by ensuring there was a long-term sustainable funding mechanism for the program. The rebate remains conditional on services continuing to participate in the QAAMS program.

Field Usage of HbA_{1c} Testing

The charter of the QAAMS Program has been to provide education, training and quality management services to support community HbA_{1c} testing rather than to collect or analyse patient data, which remains the property of the participating services. However, participant discussion at QAAMS workshops has revealed HbA_{1c} testing is being carried out in a variety of different community settings. These include the diabetic clinic (with some services establishing new diabetic clinics as a result of being able to perform the test on-site), opportunistic testing in the health service, home visits for patients with diabetes who are unable to attend clinics, community functions and health promotion activities, and field visits to outstations and distant communities serviced by health services.

Further, data collected independently by NACCHO in the first 18 months of the program indicated 2315 Aboriginal people with diabetes were monitored using the DCA 2000 during this period.[14] Subsequently data derived from reagent consumption figures indicate approximately 3000 HbA_{1c} tests were performed in each of the second and third years of the program.

Discussion

Significant advances in medical technology over the past decade have seen the development of point-of-care instruments such as the DCA 2000 that can perform tests for the early detection and management of chronic diseases in the community. Apart from advantages such as portability and small sample size, the DCA 2000 has other advantages that make it particularly applicable to the Aboriginal health care setting.[15] Through appropriate training, Aboriginal Health Workers can perform HbA_{1c} tests, thereby empowering them to take greater responsibility for the health of their own community members. By conducting the tests on-site, ownership and control of health information remains with the community, a factor crucial to the acceptance and success of Indigenous health programs. Immediate availability of a result means that the Aboriginal patient with diabetes does not have to return for a follow-up visit.

The usefulness of the DCA 2000 machine for the early detection of renal disease in a single remote Aboriginal community has been previously demonstrated.[15-17] However, the QAAMS program represents the first time the DCA 2000 instrument has been used in a multi-centred, nation-wide program for monitoring control of diabetes in Aboriginal people.

In March 2001 NACCHO released an independent evaluation on the first 18 months of the QAAMS program.[14] The executive summary of this report viewed the use of the DCA 2000 point-of-care technology as a major opportunity to better care for and manage Aboriginal clients with diabetes within the community setting. It stated that the ability of the point-of-care technology to generate rapid results served as a catalyst to enhance patient self-management, while simplicity of use led to high levels of acceptance by Aboriginal Health Workers nationally. It concluded that the sense of community control was enhanced as a result of management of diabetes becoming more focussed within Aboriginal medical services.

Participation rate and all key performance indicators measured in the QAAMS program have remained constant across the program's three-and-a half year duration. Tight precision for HbA_{1c} measurements in patients with diabetes is particularly important because clinicians monitor serial measurements across time and adjust treatment according to changes in control of diabetes. If the analytical imprecision of the HbA_{1c} method is too wide, it may mask a clinically significant change in control of diabetes. With appropriate education, training and on-going support, Aboriginal Health Workers have shown they can consistently achieve a level of analytical precision for HbA_{1c} testing using the DCA 2000 point-of-care analyser that is equivalent to that of laboratory scientists and technicians using the same instrument. Further, the analytical performance base achieved by QAAMS participants using point-of-care technology is close to current internationally recommended precision goals for HbA_{1c}. We believe this is reflective of the program's intensive on-going commitment to continuing education, training and support for the participating services. Given the geographic isolation of many Aboriginal health services and their often poor access to laboratory services, the point-of-care DCA 2000 clearly represents the most practical and culturally appropriate option for community-based on-site HbA_{1c} measurements on Aboriginal patients with diabetes.

The greatest challenge to the sustainability of the QAAMS program is Aboriginal Health Worker turnover in participating sites and the provision of education and training for new health workers who come into the program from those sites. Since the program's inception in June 1999, 33 services now have a different health worker responsible for the QAAMS program; in 10 of these services there have been more than one health worker change across this period. It is a remarkable testament to the goodwill and vision of the participating services and to the dedication and commitment of the Aboriginal Health Workers concerned that the program's major performance indicators have remained stable across this period in spite of such change. The QAAMS workshop provides at least one opportunity for formal training in a group environment every year.

The QAAMS HbA_{1c} model, based on education, training, quality assurance and on-going quality management support services, provides a sound framework for the appropriate and sustainable use of point-of-care technology outside the laboratory environment. The model can be readily adapted and is transferable to both Indigenous communities in other parts of the world and to other point-of-care instruments and tests. In 2003 an international participant from the Western Pacific has joined the QAAMS HbA_{1c} program. With further Government support, a new QAAMS program for the measurement of urine albumin:creatinine ratio on the DCA 2000 commenced in February 2003, thereby maximising the analytical capabilities of this point-of-care analyser and facilitating further on-site management for Aboriginal people with diabetes.

Acknowledgements

The QAAMS program was made possible by funds from OATSIH (1999-2000) and the Diagnostics and Technology Branch of the Commonwealth Department of Health and Ageing (2001 to the present). The support of Bayer Australia, particularly from Linda Walsh, Stuart Moody, Dean Whiting and Alison Halfnights, is gratefully acknowledged. Lloyd Penberthy, Business Manager of the RCPA Quality Assurance Programs Pty Ltd, is thanked along with the company's Board of Directors for their commitment to the program. Most importantly, as organisers of the QAAMS program, we thank NACCHO and all the participating services for their vision in taking up this program and making it work so successfully at the grassroots level.

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AN INNOVATIVE AUSTRALIAN POINT-OF-CARE MODEL FOR URINE ALBUMIN:CREATININE RATIO TESTING THAT SUPPORTS DIABETES MANAGEMENT IN INDIGENOUS MEDICAL SERVICES AND HAS INTERNATIONAL APPLICATION.

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Annals of Clinical Biochemistry 2005; 42: 208-215.

STATEMENT OF AUTHORSHIP

AN INNOVATIVE AUSTRALIAN POINT-OF-CARE MODEL FOR URINE ALBUMIN:CREATININE RATIO TESTING THAT SUPPORTS DIABETES MANAGEMENT IN INDIGENOUS MEDICAL SERVICES AND HAS INTERNATIONAL APPLICATION

Annals of Clinical Biochemistry 2005; 42: 208-215.

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Conceived research and study design, initiated, implemented and managed study, analysed and interpreted data, wrote manuscript and acted as corresponding author.

Signed .... *Date* 15/12/2006

GILL, J. P.

Assisted with management of quality assurance program and commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed .... *Date* 15/12-06

An Innovative Australian Point-Of-Care Model For Urine Albumin:Creatinine Ratio Testing That Supports Diabetes Management In Indigenous Medical Services And Has International Application.

In 2003, the Australian Government approved a proposal written by the author to develop a new QAAMS program for urine ACR testing on the DCA 2000, which would facilitate enhanced clinical management of Indigenous diabetes patients. This approval reflected the confidence of Government in the QAAMS model, its acceptance of the research findings to date, and its recognition that POCT was a valid means of health service delivery for Indigenous Australians.

However, the research question that needed to be addressed was: Could the key elements of the QAAMS HbA1c program be successfully adapted for the new urine ACR tests and could Aboriginal Health Workers perform this POC test to an acceptable analytical standard?

This paper described the education, training and quality management framework implemented for this new test, reported on the results of both quality control and quality assurance testing across the first two years of the program, and conclusively validated for the first time that Aboriginal Health Workers could be successfully trained as POCT operators for urine ACR POCT and maintain high levels of analytical competency. The paper also provided preliminary comment on the potential international application of the QAAMS model.

As for HbA1c, the multi-centred, large scale implementation of quality assurance testing for urine ACR represented a world first for Indigenous peoples.

Original Article

An innovative Australian point-of-care model for urine albumin: creatinine ratio testing that supports diabetes management in indigenous medical services and has international application

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Abstract

Background Type 2 diabetes is the leading cause of end-stage renal failure in Australia's indigenous people. The measurement of urine albumin:creatinine ratio (ACR) as a marker for early renal disease is an important component of the management of indigenous patients with diabetes.

Methods An innovative national program (Quality Assurance for Aboriginal Medical Services [QAAMS]) for point-of-care (POC) urine ACR testing on the DCA 2000 analyser (Bayer Diagnostics) was established to monitor microalbuminuria in indigenous people with diabetes in 30 Aboriginal and Torres Strait Islander medical services across Australia. Aboriginal health workers perform the ACR test. The QAAMS model provides ongoing education and training, an annual workshop, monthly quality assurance testing and a telephone help hotline. Quality assurance testing is conducted using paired, linearly related samples with a wide range of ACR concentrations (1–25 mg/mmol).

Results The average participation rate across four six-monthly QAAMS ACR testing cycles was 83%. In all, 94% of 1163 quality assurance tests performed were within the preset limits of acceptability. The median precision (coefficient of variation percent for ACR quality assurance testing averaged 5.4%, well within desirable performance specifications. Between-site accuracy was excellent.

Conclusion This unique POC model for supporting diabetes management is the first of its type to be developed for indigenous communities and has considerable potential to be adopted worldwide.

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Introduction

In rural and remote areas of Australia, the geographical isolation of many health centres, particularly those responsible for indigenous (Aboriginal and Torres Strait Islander) communities, means access to laboratory services is often limited, while time delays in transporting samples and receiving results may lead to delayed clinical management and poor rates of patient follow-up. Point-of-care (POC) testing (POCT) provides a practical option for the provision of pathology services in both the acute and chronic clinical contexts as results are available on-site, enabling clinical management to be initiated immediately.

In rural Australia there is a strong clinical need for effective POCT programmes for chronic disease management, in particular in indigenous Australians, with prevalence rates of adult diabetes as high as 30% and rates of end-stage renal disease (ESRD) reaching epidemic proportions in many communities.[1,2] While acknowledging the multifactorial nature of progressive renal failure, diabetic nephropathy is by far the leading cause of ESRD in Australian indigenous people, accounting for 47% of cases compared with 17% in non-indigenous Australians.[3]

To address the ever-increasing burden of morbidity and mortality caused by diabetes and its renal complications, the feasibility of using on-site POC pathology

testing for biochemical markers of diabetes management and locally trained personnel was investigated for the first time.

In 1998, Australia's *National Diabetes Strategy and Implementation Plan* recommended that a trial of the DCA 2000 analyser (Bayer Diagnostics, Tarrytown, NY, USA) be conducted for POC glycated haemoglobin (HbA_{1c}) testing in indigenous primary health-care services.[4] The trial aimed to provide a more accessible and convenient clinical service for monitoring diabetes control and to facilitate greater community control and ownership of diabetes services within indigenous communities. As a result, a national programme for POC HbA_{1c} testing on the DCA 2000 was developed and implemented in 45 Aboriginal Community Controlled Health Services (ACCHS) in Australia in mid-1999. The Australian Government's Department of Health and Ageing funded the programme, which was named Quality Assurance for Aboriginal Medical Services (QAAMS). The programme was based on four key elements: education, training, quality assurance and ongoing support services. The quality assurance component of the programme was developed in partnership with the RCPA Quality Assurance Programs Pty Ltd., which provides quality assurance programmes to laboratories in Australasia in collaboration with the Royal College of Pathologists of Australasia and the Australasian Association of Clinical Biochemists. The QAAMS programme for HbA_{1c} has now become embedded within the health-care system for indigenous people with diabetes, and the DCA 2000 has proven safe, robust and clinically and culturally effective within this setting.[5–7] The QAAMS model is believed to be the first of its type for indigenous people anywhere in the world.

In 2003 the Australian Government's Department of Health and Ageing introduced POCT for urine albumin:creatinine ratio (ACR) on the DCA 2000 within the QAAMS integrated training and quality assurance framework, to provide further management support for indigenous people with diabetes. Urine ACR is a well-recognized biochemical marker for early renal disease (microalbuminuria), as well as an independent risk factor for cardiovascular disease,[8–16] and can conveniently be measured on the DCA 2000. A systematic review on clinical guidelines for diabetes management in the Australian indigenous population recommends that urine ACR is measured annually for all indigenous people with diabetes, six-monthly in those with established microalbuminuria and three- to six-monthly for patients on therapy for established microalbuminuria.[17]

This paper describes the novel aspects of the QAAMS model for POC urine ACR testing on the DCA 2000 in Australian Aboriginal and Torres Strait Islander Medical Services (AMS), which is the first integrated training and quality assurance programme to be developed and implemented for the monitoring of microalbuminuria in indigenous diabetes patients. The paper also reports on the key outcome measures, including ongoing participation rate and results from the first 24 months of quality assurance testing.

Methods

Bayer DCA 2000 Instrument

The DCA 2000 analyser is small (25 cm high × 21 cm wide × 25 cm deep) and portable (weighing 5 kg). In all, 40 μL of urine is required for the ACR test. The first morning urine is recommended as the specimen of choice for ACR measurement, due to its greater sensitivity and specificity and lesser variability compared with the random spot urine.[18,19] The urine sample is loaded into a single, disposable reagent cartridge (DCA 2000 Microalbumin/Creatinine kit, catalogue number 0611, Bayer Australia), which is then inserted into the instrument. The DCA 2000 provides a quantitative measurement of urine albumin by immunoturbidimetry (using polyclonal goat antiserum) and urine creatinine by spectrophotometry (using 3,5-dinitrobenzoic acid at alkaline pH), as well as calculation of the urine ACR. The result is available in 7 min. The measuring range is 5–300 mg/L for urine albumin and 1–44 mmol/L for creatinine. The DCA 2000's lower limit of detection for urine albumin (5 mg/L) is 60 times more sensitive than conventional dipsticks for this analyte. The analytical performance characteristics for ACR measurement on the DCA 2000 have been verified in previous studies in a remote Australian indigenous community setting[20–22] and in the laboratory,[23–26] but not on a comprehensive national scale.

Participation

The QAAMS urine ACR programme commenced in February 2003. The initial intake of AMS was capped at 30 under the conditions of the QAAMS contract with the Australian Government. The location of these participants (all of whom were existing QAAMS HbA_{1c} sites) encompassed urban, rural and remote locations across every mainland Australian State and Territory (Figure 1). These sites service an estimated 2000 indigenous people with diabetes.

Principles of the QAAMS model

The QAAMS model enables POCT for ACR to be conducted on-site within the AMS by an Aboriginal Health Worker (an indigenous person trained in primary health care who lives and works within the community). As health workers are not familiar with laboratory practices and they conduct POCT outside the

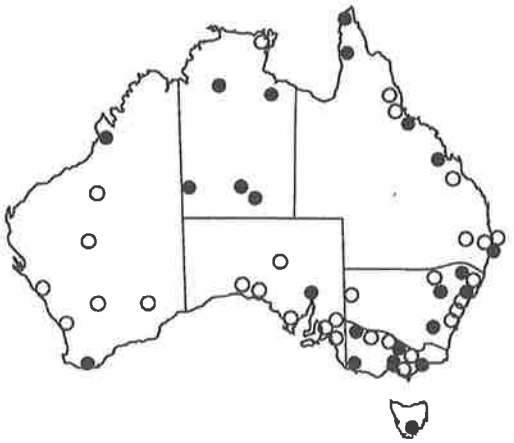

Figure 1 *Location of Aboriginal community-controlled health services participating in QAAMS HbA_{1c} and ACR programmes during 2004. Sites in both the ACR and HbA_{1c} programmes are indicted with an open circle (○), while sites in the in the HbA_{1c} programme only are marked by a closed circle (●).*

laboratory framework, the QAAMS model provides a comprehensive ongoing education and training program, supported by continuous quality assurance testing and other associated management services.

Education

A set of education resources, comprising a training manual and a series of posters, was developed for the QAAMS urine ACR programme. The training manual included the following topics: an overview of renal disease in indigenous Australians, the functions of the kidney, the major causes of renal disease, the natural history of renal disease and the importance of early detection, urine tests for renal disease, the ACR test and the classification of microalbuminuria, how to perform the urine ACR test on the DCA 2000 machine, and the principles and practice of quality control (QC) and quality assurance. Three A3-sized laminated posters with step-by-step instructions on how to perform the ACR test on the DCA 2000 and how to conduct QC and quality assurance testing for ACR on the instrument were produced to consolidate and simplify information presented in the training manual. The training manual was designed to be the primary education resource, while the posters were for day-to-day use with the DCA 2000 machine.

Training

An initial training workshop was held for Aboriginal health workers (and allied health professionals) from participating services in Adelaide, South Australia, in February 2003. Representatives from the Australian Government's Department of Health and Ageing and Bayer Australia also attended the workshop. Participants were given their education resource package and received theoretical and practical instruction from the QAAMS management team about renal disease and the ACR test, how to perform an ACR test on the DCA 2000 machine, and how to conduct quality assurance and QC testing for ACR. Following the workshop, participants returned to their respective medical services and commenced ACR testing on patients with diabetes.

An annual training workshop is also held for participants in the QAAMS ACR Programme. This workshop provides an interactive forum for participants to meet, network, undertake initial or refresher training, deliver presentations about how the programme is being used in their service, and learn about interesting clinical cases from different services. Participants also undertake a practical test and written assessment supervised by the QAAMS Programme Manager and his scientific team and, if successful, they receive a certificate of competency as an approved operator of the DCA 2000 analyser. Only certified operators are able to conduct POCT in participating services. A register of certified operators is held at the central QAAMS office and constantly updated.

The QAAMS Programme Manager also conducts on-site field visits between workshops to sites experiencing difficulties with the programme and/or needing more immediate help with training, as required.

Quality assurance programme

An external quality assurance programme to support ACR testing on the DCA 2000 machines across all participating sites started immediately following initial training in February 2003. Since that time, four six-monthly testing cycles have been completed to December 2004.

An annual package of materials needed to conduct QAAMS ACR testing was sent to each participating site at the beginning of 2003 and 2004. The package included a QAAMS ACR testing kit containing 24 lyophilized samples of human urine, each numbered and dated for testing across two six-monthly testing cycles; 24 sealed plastic pipettes each containing 2 mL of water for reconstitution of the lyophilized samples; an information sheet; testing schedule and result sheets. Australian Scientific Enterprises (ASE) of Sydney, Australia, prepared the samples for the QAAMS ACR programme. The 12 samples per cycle comprise six paired and linearly related levels of ACR that are tested in a random order pre-determined by the program organizers. The samples have a range of values from 1 to 25 mg/mmol for urine ACR (20–230 mg/L for urine albumin and 9–26 mmol/L for urine creatinine). These ACR values cover the full range of levels likely to

be observed in patients with normoalbuminuria (<3.4 mg/mmol) or microalbuminuria (3.5–34 mg/mmol).[1,7,8] Services are required to test two QAAMS samples per month, according to the defined testing schedule. Monthly testing can be performed at any time that is convenient to the service, provided their results are received at the QAAMS reporting office by fax or post by the last day of each month. To ensure the confidentiality of results, each service has been allocated a specific community code number that is stamped on their result sheets and all other printed matter.

Within a week after the closing date for return of results for each month, the QAAMS reporting office send a simplified graphical report to each individual service (Figure 2). The report compares the results returned by that service with the target (median) values for each sample and with the range of results submitted by all other services. In addition, the report displays graphs that document all previous results returned by the service for that particular testing cycle. Through this method of reporting, each service receives regular monthly information on the short- and long-term performance of their DCA 2000 machine for ACR testing. Monthly reports for urine albumin and urine creatinine are also generated, but not sent to participants. The QAAMS Programme Manager holds these reports and uses them, where appropriate, to investigate components of poor analytical performance.

At the end of each testing cycle, summary analysis of six months of data (12 specimens) is used to calculate and rank each individual participant's precision and accuracy for ACR testing. These data are also used to identify individual services that are experiencing significant analytical problems. Services are contacted and a tailored action plan implemented to redress poor performance.

Other management services

In addition to external quality assurance assessment, services are required to conduct internal QC testing to

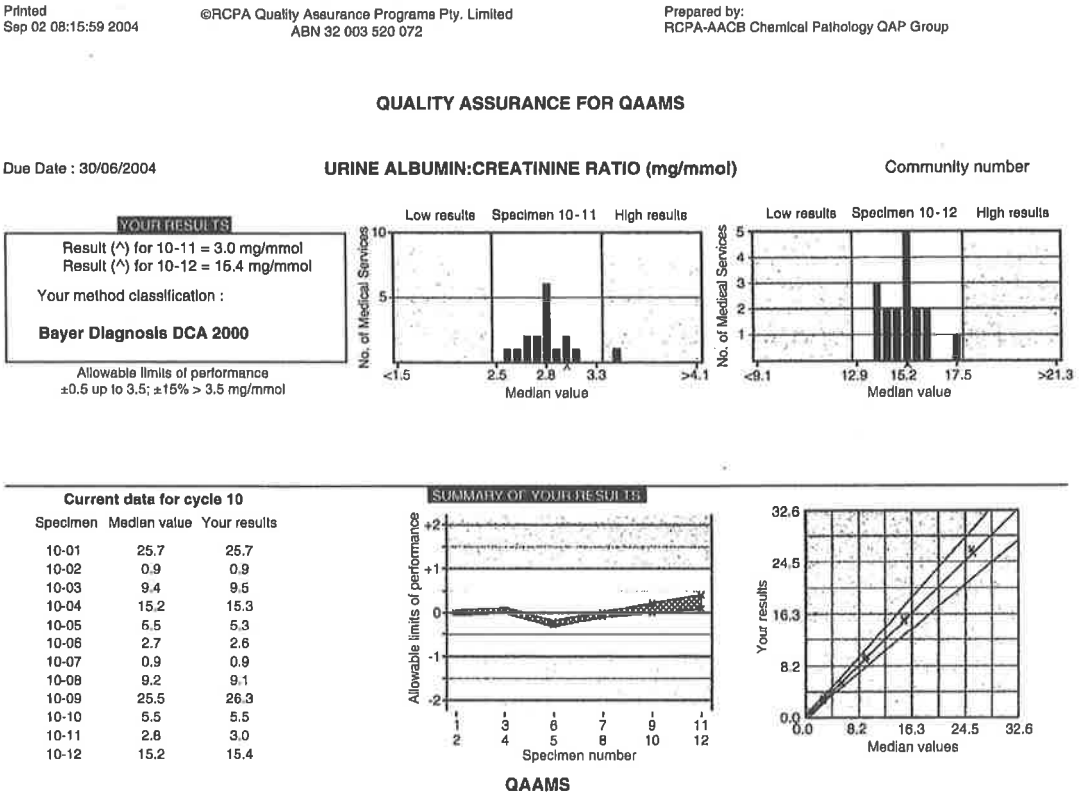

Figure 2 *Example of the monthly summary report sent to all QAAMS ACR participants. As an international primary reference material is not currently available for urine ACR, the median of all results submitted for each sample was used as the target value for that sample.*

provide an immediate on-site assessment of their instrument's performance. Bayer DCA 2000 Microalbumin/Creatinine Low and High Quality Control kits (catalogue number 6916803, Bayer Australia) are used for this purpose. These kits contain lyophilized human urine samples with two ACR levels, approximately 3.5 and 6.5 mg/mmol, depending on the lot number. Services are required to test one of these samples (in an alternating fashion) each time they open a new ACR reagent kit. They are provided with a Bayer Urine ACR QC result sheet showing acceptable limits for each control, preset by the QAAMS management team. Results of QC testing are written on the result sheet and faxed to the QAAMS office. The QAAMS Programme Manager reviews the results and calculates the precision (coefficient of variation percent [CV%]) for each QC sample for each site. Three different lot numbers of Bayer microalbumin/creatinine QC materials have been used across the first 24 months of operation (lot numbers 23, 24 and 9026), providing a sound basis for assessing analytical performance for internal QC testing.

A telephone help hotline service was established whereby Aboriginal health workers could contact the QAAMS office immediately a problem arose, particularly in relation to instrument breakdown or other technical problems and interpretation of quality assurance or QC results. A regular newsletter was also sent to all participants to update them on current issues.

Results

Participation

An overall participation rate of 83% (range 74–91%) has been maintained across the first 24 months (four testing cycles) of the programme. This represents the return of 1163 QAAMS results from a possible 1404. On average, 80% of participating services returned between 10 and a maximum of 12 results in each cycle.

Key analytical performance indicators

Across the first two years of quality assurance testing, the percentage of returned results that were within preset limits for acceptability was 94% for urine ACR (range 88–99%), 84% for urine albumin (range 77–90%) and 85% for urine creatinine (range 83–88%; Table 1). The limits of acceptability or allowable limits of performance, set by the QAAMS program organizers, were ±15% for urine ACR, ±12.5% for urine albumin and ±7.5% for urine creatinine. These limits are the same as those recommended in the Australian Government Department of Health and Ageing's interim *Standards for Point-of-Care Testing in General Practice*.[27] These limits represent a consensus from information on quality specifications derived from biological variation, guidelines from international expert groups and committees, and specifications promulgated by external quality assessment scheme organizers.[28–31]

Table 1 *Percentage acceptable results for urine ACR, albumin and creatinine during the first four QAAMS testing cycles*

	% Acceptable results			
	2003		2004	
Analyte	Cycle 1	Cycle 2	Cycle 3	Cycle 4
ACR	91%	88%	99%	98%
Albumin	80%	77%	89%	90%
Creatinine	83%	83%	87%	88%

Table 2 *Median precision achieved for urine ACR, albumin and creatinine across the first four testing cycles in the QAAMS urine ACR programme*

	Median precision observed (CV%)				
	2003		2004		
Analyte	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Desired precision goal (CV%*)
ACR	7.2%	7.7%	3.6%	3.0%	12%
Albumin	11.8%	13.2%	6.7%	5.9%	10%
Creatinine	4.3%	5.3%	4.2%	4.5%	6%

*Coefficient of variation (CV%) is calculated by dividing the standard deviation of the midpoint of the service's range of concentrations, expressed as a percentage. The standard deviation is the error of the estimate Sy.x and represents the average standard deviation across the range of concentrations analysed.

The use of paired and linearly related samples for QAAMS ACR testing enabled a direct measure of the precision and accuracy of individual DCA 2000 machines and the group as a whole.

The median precision (CV%) achieved by services has averaged 5.4% for urine ACR, 9.4% for urine albumin and 4.6% for urine creatinine across all four testing cycles. The desirable performance specifications for the precision of urine ACR, albumin and creatinine measurements recommended by the Australian Government Department of Health and Ageing's interim *Standards for Point-of-Care Testing in General Practice* are ±12%, ±10% and ±6%, respectively. Precision goals for urine ACR were comfortably met by QAAMS participants across all four testing cycles (Table 2) and also at each of the six levels of ACR tested (Figure 3). Analytical performance for urine creatinine also consistently met performance standards. Precision goals

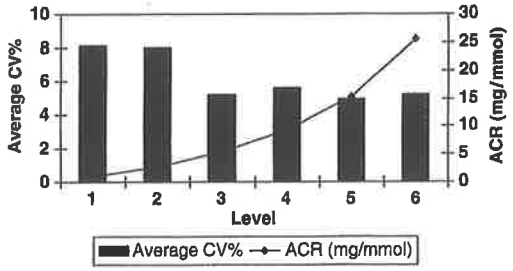

Figure 3 *Average precision (CV%) achieved for the testing of quality assurance samples across six levels of urine ACR during Cycle 3.*

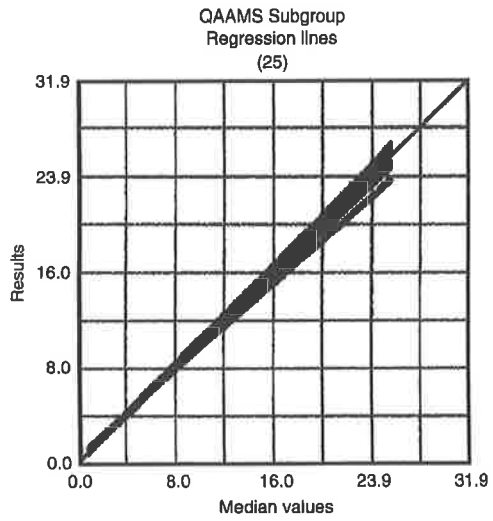

Figure 4 *Accuracy plots for each of the 30 Aboriginal medical services during Cycle 3.*

for urine albumin were achieved for cycles 3 and 4 (during 2004), but not for cycles 1 and 2 (during 2003).

This latter finding can be explained by a stability problem identified with the 2003 QAAMS urine ACR material. Improvements were made to the 2004 QAAMS urine ACR material and no stability issues were reported with this material during 2004. The significant improvement observed in both the percentage acceptable results and precision for urine albumin measurement in Cycles 3 and 4 reflects, at least in part, the improved quality of material used for quality assurance testing.

Accuracy plots for each service participating in Cycle 3, displaying the line of best fit across the full range of ACR values tested, are shown in Figure 4. The distribution of regression lines is very consistent, indicating good between-site accuracy over a wide range of ACR values. This performance has been repeated in Cycle 4.

Other management services

Since the QAAMS ACR programme began, 340 Bayer QC tests have been performed (175 low and 165 high controls, across three different lot numbers of material). The precision (CV%) recorded for internal Bayer QC testing across all the four cycles is shown in Table 3 and is compared with the desired analytical performance goals for precision for each analyte. Precision has generally remained well within performance specifications for all analytes.

Over 400 calls were received by the QAAMS help hotline over the past 18 months; the majority of calls related to the stability problem with the QAAMS material during Cycle 2 and a major audit of each participating site undertaken during Cycle 3. The QAAMS Programme Manager also continues to provide ongoing advice and follow-up action for sites whose DCA 2000 machines exhibit poorer performance.

Table 3 *Precision observed with Bayer internal QC testing for urine ACR on the DCA 2000*

		Precision observed with Bayer QC testing						
		2003			2004			
		Cycle 1	Cycle 2		Cycle 3	Cycle 4		
Test	Level	LN 23	LN 23	LN 24	LN 24	LN24	LN 9026	Precision goal (CV%)
Urine ACR (mg/mmol)	3.7	6.0	8.8	5.7	8.2	6.3	6.5	12%
	6.0	4.8	4.3	4.1	4.8	5.1	5.3	
Urine albumin (mg/L)	35.0	8.8	11.0	6.6	8.1	4.4	7.4	10%
	215.0	4.3	4.7	6.2	4.3	4.0	4.9	
Urine creatinine (mmol/L)	9.0	6.5	5.4	5.1	4.4	6.3	5.2	6%
	35.5	4.1	3.7	4.0	5.1	5.1	5.0	

Three different lot numbers (LN) of QC material have been used across four testing cycles.

Discussion

Type 2 diabetes continues to have a devastating impact on the health of Australia's indigenous people, particularly through the development of serious complications of diabetes – most notably nephropathy.

The progression of diabetic nephropathy from microalbuminuria and overt proteinuria to ESRD can be an incipient, asymptomatic process over many years. However, a number of studies have shown that the early detection of diabetic renal disease, followed by subsequent aggressive clinical management with antihypertensive agents (angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers), can often delay the progression to renal failure.[7,32,33] The role and value of urine ACR testing in detecting microalbuminuria and predicting progression to renal failure in type 2 diabetes is now well established, particularly in the Australian indigenous health setting.[2,7,10–16,20–22]

In rural and remote indigenous communities in particular, on-going quality-assured POC biochemical testing has considerable potential to assist in better management of diabetes, thereby potentially reducing the morbidity and mortality of this debilitating condition. The POC DCA 2000 analyser offers a convenient, accessible, timely and practical way of monitoring urine ACR levels in patients with diabetes. The DCA 2000 has the ability to detect very low levels of protein loss (to 5 mg/L albumin), well before the presence of renal disease can be identified by conventional dipstick urinalysis (at a level of 300 mg/L of urinary protein) or before a rise in blood creatinine occurs (when approximately 50% of nephron function is lost). Urine ACR testing is also a useful management adjunct to blood HbA_{1c} monitoring of glycaemic control performed on the same analyser.

The QAAMS model, which has proven successful for POC HbA_{1c} testing, now provides an opportunity for indigenous medical services across Australia to use the DCA 2000 to monitor albuminuria in their diabetes patients within a quality-assured framework. With its strong emphasis on continuing education and training, Aboriginal Health Workers have demonstrated a level of analytical competency for urine ACR quality assurance and QC testing that consistently meets current desirable performance standards. This should ensure that results of optimal quality are being generated for patients with diabetes being monitored for albuminuria.

The DCA 2000 has again proven reliable and robust in the indigenous setting and has particular application for use in rural and remote locations that are disadvantaged by distance, have limited access to laboratory services, or currently receive unacceptable turnaround times for results from their nearest laboratory.

The QAAMS model, based on education, training, quality assurance and ongoing support services, has been shown to be adaptable to POC pathology tests other than HbA_{1c}, while the Bayer DCA 2000's ability to perform both a blood test for diabetes control and a urine test for microalbumin on-site within a short time interval (15–20 min) provides a powerful and culturally effective platform to improve the management of diabetes in Australia's indigenous medical services.

Challenges confronting the sustainability of the QAAMS ACR programme include maintaining education, training and quality management support services for those sites experiencing high staff turnover and developing a sustainable funding mechanism for the program.

In conclusion, the QAAMS model, with its commitment to providing culturally appropriate education and training, its emphasis of empowering community health workers and community ownership, and its focus on conducting POC testing within a quality assured framework, has significant potential for use in other indigenous community settings around the world where diabetes is a significant health problem and where health services have limited access to laboratory services or are geographically isolated.

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THE ANALYTICAL QUALITY OF POINT-OF-CARE TESTING IN THE 'QAAMS' MODEL FOR DIABETES MANAGEMENT IN AUSTRALIAN ABORIGINAL MEDICAL SERVICES.

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STATEMENT OF AUTHORSHIP

THE ANALYTICAL QUALITY OF POINT-OF-CARE TESTING IN THE 'QAAMS' MODEL FOR DIABETES MANAGEMENT IN AUSTRALIAN ABORIGINAL MEDICAL SERVICES

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The Analytical Quality Of Point-Of-Care Testing In The 'QAAMS' Model For Diabetes Management In Australian Aboriginal Medical Services.

This recently published paper presented updated research data on the analytical quality of POC testing for both HbA1c and urine ACR in the QAAMS Program. It confirmed consistently high levels of analytical quality had been sustained, and continued to improve, over periods of six and a half years for HbA1c and three years for urine ACR.

The paper concluded that the ability to perform both tests by POCT provided a powerful and culturally effective platform to improve diabetes management in Australia's Indigenous people and argued further that the QAAMS model could be expanded internationally.

Report

The Analytical Quality of Point-of-Care Testing in the 'QAAMS' Model for Diabetes Management in Australian Aboriginal Medical Services

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Abstract
Type 2 diabetes mellitus and its major complication, renal disease, represent one of the most significant contemporary health problems facing Australia's Indigenous Aboriginal People. The Australian Government-funded Quality Assurance for Aboriginal Medical Services Program (QAAMS) provides a framework by which on-site point-of-care testing (POCT) for haemoglobin A1c (HbA_{1c}) and now urine albumin:creatinine ratio (ACR) can be performed to facilitate better diabetes management in Aboriginal medical services. This paper provides updated evidence for the analytical quality of POCT in the QAAMS Program. The median imprecision for point-of-care (POC) HbA_{1c} and urine ACR quality assurance (QA) testing has continually improved over the past six and half years, stabilising at approximately 3% for both analytes and proving analytically sound in Aboriginal hands. For HbA_{1c}, there was no statistical difference between the imprecision achieved by QAAMS and laboratory users of the Bayer DCA 2000 since the QAAMS program commenced (QAAMS CV 3.6% ± 0.52, laboratory CV 3.4% ± 0.42; $p = 0.21$, paired t-test). The Western Pacific Island of Tonga recently joined the QAAMS HbA_{1c} Program indicating that the QAAMS model can also be applied internationally in other settings where the prevalence of diabetes is high.

Introduction

Type 2 diabetes mellitus and its major complication, renal disease, represent one of the most significant contemporary health problems facing Australia's Indigenous Aboriginal People.[1-3] The overall prevalence of type 2 diabetes is at least three to four times that of the general population.[1] Hospitalisation rates for diabetes are four times higher for Aboriginal males and six times higher for Aboriginal females compared to non-Aboriginal people. Across Australia, diabetes is responsible for 10.6 times more deaths in Indigenous males and 17.6 times more deaths in Indigenous females than the broader Australian community.[2] Rates of end-stage renal failure (principally as a result of diabetic nephropathy) have risen almost unabated across the past 15 years in many Aboriginal communities.[4-9]

As part of an Australian Government-funded national program called QAAMS which began in 1999, Aboriginal Health Workers from 65 Aboriginal medical services across Australia conduct on-site POCT for HbA_{1c} on the DCA 2000 analyser (Bayer Diagnostics, Tarrytown, NY, USA) to monitor glycaemic control in Aboriginal people with established diabetes.[10-12] Aboriginal health workers are Aboriginal people living and working in the community who have a basic qualification in primary health care. 75% of the participating Aboriginal medical services are located in rural and remote Australia.

In 2003, the QAAMS program expanded to include POC urine ACR testing on the DCA 2000 to further support diabetes management.[13] Urine ACR is a biochemical marker for microalbuminuria or early stages of renal disease which, as mentioned previously, is the major complication of diabetes in Aboriginal people. The initial intake of Aboriginal medical services into the QAAMS urine ACR program was capped by the Australian Government at 30, all of whom were existing sites within the QAAMS HbA_{1c} program. From January 2006, this capping has now been increased to a maximum of 100 Aboriginal medical services for both the urine ACR and HbA_{1c} programs.

The ability to perform both HbA_{1c} and urine ACR tests on-site by POCT provides a powerful and culturally effective platform to improve diabetes management in Australia's

Aboriginal people.[14] However, it is also crucial that analytical performance for conducting POCT in the Aboriginal (non-laboratory) setting meets acceptable analytical performance standards. To measure and maintain the analytical quality of POCT in the QAAMS Program, a broad quality management framework was established. This included a culturally appropriate education and training program with practical and written competency assessment for POCT operators, an internal quality control program and external quality assurance (EQA) testing for HbA_{1c} and urine ACR. This paper provides updated evidence on the analytical quality of POCT in the QAAMS Program, specifically assessed by the results of EQA testing, and also mentions the international applicability of the model.

Methods

The QAAMS Program is a collaborative partnership between the Community Point-of-Care Services Unit within the Flinders University Rural Clinical School and the Royal College of Pathologists of Australasia (RCPA) Quality Assurance Programs Pty Ltd, Chemical Pathology Group, Adelaide, Australia. The QA component of the QAAMS HbA_{1c} and urine ACR programs is modelled on the same principles used by the RCPA Quality Assurance Programs in delivering QA programs for laboratories. However selected design elements have been modified to suit the Aboriginal POCT environment, which, for example, does not have access to deionised water or volumetric pipettes for reconstituting quality assurance samples. Each QAAMS participant is thus provided with lyophilised quality assurance samples and either eye droppers (for HbA_{1c}) or sealed plastic tubes (for urine ACR) with a specific volume of deionised water for making up the samples. Two samples per month are tested across two six-monthly testing cycles per year. The samples for each cycle comprise paired and linearly-related levels of analyte across a range of concentrations from 5 to 14% for HbA_{1c} and 1 to 25 mg/mmol for urine ACR. The use of paired samples enables calculation of imprecision for QA testing on the DCA 2000 for both individual services and the group as a whole.

Services receive a monthly summary report shortly after the end of each month. The report format, which has been published previously, summarises both short and long term analytical performance.[10,13] Each site has its own Community Number to ensure confidentiality of results. At the end of each month, the QA results from all participating services are reviewed. If the QA results returned by a particular service are outside the limits of acceptability established by the program organisers ($\pm$ 0.5 up to an HbA_{1c} of 10% and $\pm$ 5% at HbA_{1c} >10%, and $\pm$ 15% for urine ACR), the service's previous results are assessed for trends over recent months, the service is contacted and the possible reasons for the poor performance are discussed with the POCT operator. Poorly performed services are monitored closely until their performance improves. The QAAMS Program also has a telephone support service (attended during normal business hours). Using this service, POCT operators can contact a member of the QAAMS management team to discuss any technical or analytical issue as it arises.

At the completion of each six-monthly cycle, key performance indicators are calculated including:

- Participation Rate (number of QA results returned as a % of the maximum number of results that could be returned).
- % Acceptable Results (the % of results within preset limits of acceptability set by the QAAMS management team, as stated previously).
- Median within-site imprecision (CV%), calculated by dividing the standard deviation of the midpoint of the service's range of concentrations, expressed as a percentage. Imprecision is considered a crucial performance indicator because serial POCT HbA_{1c} and urine ACR measurements are conducted for patient management in the QAAMS program. It is important that analytical noise is minimised and does not mask clinically significant changes in patient results across time. Current guidelines for Aboriginal and Torres Strait Islander Peoples recommend that HbA_{1c} is conducted every three months, while urine ACR is performed annually if the patient has a normal ACR and six monthly if the patient has microalbuminuria.[15]
- Median within-site bias, which is the average of biases of the service's line of best fit at the lowest, highest and midpoint concentrations, irrespective of sign. For HbA_{1c} samples, a target value was assigned to each sample using an international primary reference method for HbA_{1c} (DCCT Biorex 70 HPLC).[16] For urine ACR samples, the median of all results submitted for each sample was used as the target because no international primary reference measurement systems are currently available.

Results

For HbA_{1c} QA testing, the participation rate across 13 six-monthly testing cycles from July 1999 to December 2005 has averaged 86% (range 73 to 89%). Eighty five percent of 6148 QA results submitted over these 13 testing cycles were within the preset limits of acceptability. The median within-site imprecision (CV%) achieved by services has consistently improved over the six and a half years since the program began (Figure 1), averaging 3.6% across the lifetime of the program and 3.2% across the past three years. Within-site

accuracy has remained steady, with the median bias averaging 0.22% (range 0.17 to 0.38%) across the 13 testing cycles.

It is possible to directly compare the performance of QAAMS Aboriginal medical services with laboratory users of the DCA 2000 (of which there are approximately 70) because the QAAMS and the laboratory-based RCPA Glycohaemoglobin QAP use the same material. The performance achieved for QA testing by Aboriginal medical services and laboratories using the DCA 2000 across the past six and a half years are shown in the Table. The median CV% for laboratory users of the DCA 2000 has averaged 3.4% since 1999 and 3.2% across the past three years. There was no statistical difference between the median CV% achieved by QAAMS and laboratory users of the DCA 2000 since the QAAMS program commenced (QAAMS 3.6% ± 0.52, laboratory 3.4% ± 0.42; t = 1.96, df = 12, p = 0.21, paired t-test).

For urine ACR QA testing, the participation rate across six 6-monthly testing cycles from January 2003 to December 2005 has averaged 85% (range 74 to 91%). Ninety six percent of 1754 QA results submitted over these six testing cycles were within the preset limits of acceptability. The median imprecision (CV%) achieved by services for urine ACR testing has consistently improved over the three years since the program began (Figure 2), averaging 4.4% across the lifetime of the program and 2.9% over the past two years. Within-site accuracy has remained steady, with the median bias averaging 0.42% (range 0.28 to 0.62%) across the six testing cycles.

Discussion

The results presented in this paper confirm that the QAAMS model for POCT HbA_{1c} and urine ACR testing provides a health service delivery system that is analytically sound in Aboriginal hands. The imprecision achieved for HbA_{1c} QA testing by Aboriginal health workers has continually improved across the duration of the QAAMS Program and was statistically equivalent to that achieved by trained laboratory scientists and technicians using the DCA 2000 point-of-care analyser.

Precision goals for HbA_{1c} methods have continually been refined downwards over the past decade as the clinical requirement for tight imprecision has been highlighted through the results of international studies such as the Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study.[17,18] The minimum precision goal for POC HbA_{1c} testing recommended by the Australian Government Department of Health and Ageing's Interim Standards for Point-of-Care Testing in General Practice is 4% and represents a consensus of published information.[19] Many professional bodies have recommended a desired precision goal of 3% for laboratory HbA_{1c} methods, as this degree of precision can statistically distinguish between recommended HbA_{1c} treatment goals of 7% and 8%.[20-22] A recent international workshop advocated the optimal precision goal for laboratory HbA_{1c} methods should be 2% because this level of precision 'justifies clinicians acting on differences of 0.35% to 0.5% as being significant'.[23,24] As can be seen in Figure 1, QAAMS participants achieved a precision base which was just outside the minimum goal in the first year of the program. Over the next three and a half years, services achieved a precision base

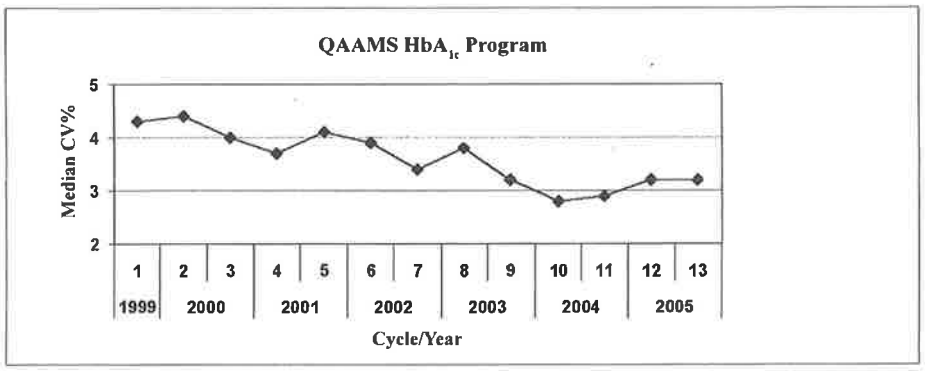

Figure 1. Median Precision Achieved by Aboriginal Medical Services in the QAAMS Program for POC HbA1c testing from 1999-2005.

Table. Comparative precision base (median CV%) over the last equivalent 13 testing cycles: Aboriginal Medical Services (AMS) versus laboratories using the Bayer DCA 2000.

Program	Year	1999	2000		2001		2002		2003		2004		2005	
	Cycle	1	2	3	4	5	6	7	8	9	10	11	12	13
	Type of Service													
QAAMS	AMS	4.3	4.4	4.0	3.7	4.1	3.9	3.4	3.8	3.2	2.8	2.9	3.2	3.2
Glycohaemoglobin	Labs	4.1	3.0	3.0	3.4	4.1	3.7	3.5	3.6	3.3	3.1	3.2	2.7	3.1

that was well within the minimum goal. In 2004, they achieved better than the desired goal of 3%. Over the past year, median performance for HbA_{1c} QA testing in the QAAMS program has stabilised at around the 3% mark, potentially reaching the maximum analytical capability of the DCA 2000 POCT analyser.

The minimum precision goal for POC urine ACR testing recommended by the Australian Government's Department of Health and Ageing's Interim Standards for Point-of-Care Testing in General Practice is 12%, with this goal also representing a consensus of published information.[19,21] As seen from Figure 2, this goal has also been readily achieved by Aboriginal medical services in the QAAMS program.

The analytical performance recorded by QAAMS participants for these two tests represents an outstanding achievement, acknowledging that POCT in the QAAMS program is being undertaken by non-laboratory trained health workers from services scattered across Australia with many services enduring difficult working conditions, particularly in remote Australia, and high rates of staff turnover. It reflects an on-going commitment not only by the QAAMS management team to continuing education, training and competency assessment but also by the dedicated teams of Aboriginal health workers conducting POCT in their services. Whilst this paper has focused specifically on observed improvements in analytical quality, it should be noted that the QAAMS program has also been shown to be both culturally appropriate and clinically effective in improving glycaemic control in Aboriginal hands.[14] In the long term, the QAAMS program aims to collect data on the impact of the program on reduction of morbidity and mortality.

The successful adaptation of the QAAMS model for urine ACR testing in 2003 demonstrates that the model is transferable to other POC tests. The Diabetes Centre from the Western Pacific island of Tonga recently joined the QAAMS

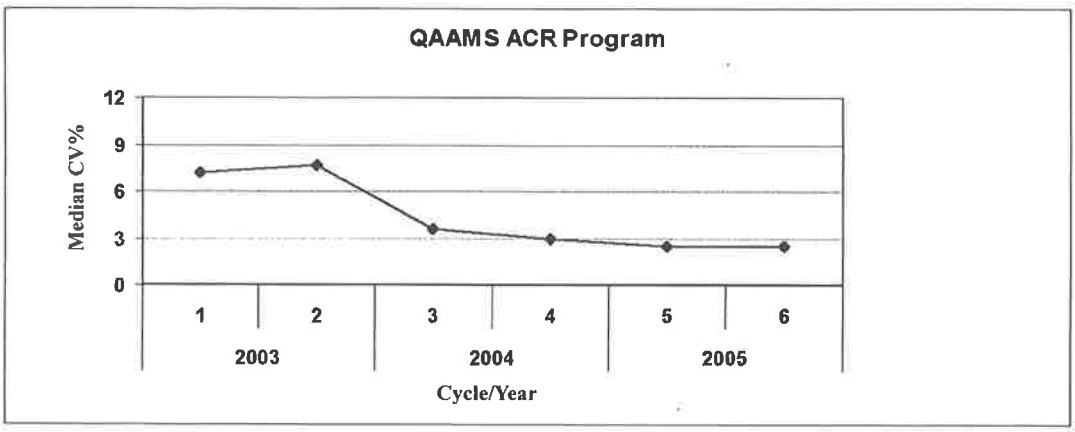

Figure 2. Median Precision Achieved by Aboriginal Medical Services in the QAAMS Program for urine ACR testing from 2003-2005.

network, with the approval of the Australian Government. The QAAMS Program Manager trained a team of health workers from Tonga at the Australian Centre for Diabetes Strategies. A high prevalence of diabetes (15%) has been reported in Tonga, where the disease causes similar problems to those faced by Aboriginal Australians.[25] The Bayer DCA 2000 offered a practical option for the Diabetes Centre to provide better care and monitoring for many of its diabetes patients. The results of recent QA testing in Tonga indicates that sound analytical performance for POCT HbA_{1c} testing can also be obtained in Indigenous health services outside Australia that have access to the same education, training and QA testing framework provided by QAAMS. This finding also confirms the transferability of the QAAMS model to other health settings and illustrates the potential of this POCT model to be expanded internationally to support diabetes management in other countries where the burden of diabetes is similarly high or where health services have limited access to laboratory services due to geographic isolation.

Acknowledgements

The Diagnostics and Technology Branch within the Pathology Section of the Australian Government Department of Health and Ageing are sincerely acknowledged for providing significant funds to support the QAAMS Program continuously over the past six years. The vision and commitment to the program by Jonathan Wraith, John Bacon, Fifine Cahill, Jacquie Millard, Wendy Akers, Pamela McKittrick and Rob Lillie from the Department is gratefully acknowledged, as is the long-standing assistance from Bayer Australia, particularly Dean Whiting and Alison Halfnights. Lloyd Penberthy, recently retired from the RCPA Quality Assurance Programs Pty Ltd, made a significant contribution to the QA component of the QAAMS program through his invaluable scientific collaboration. Scientific colleagues from the Flinders' Community Point-of-Care Services unit, Beryl Mazzachi and Anne Shephard, are thanked for their tireless supporting work with the QAAMS Program.

Competing Interests: None declared.

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Erratum:

In the 2005 May;26(ii)issue of the Journal, page 16 (Appendix) of the article "The Evidence Based Medicine Approach to Diagnostic Testing: practicalities and limit-ations" the reference for Search Findings: should be Kuhlman KA, Hennessey WJ. Sensitivity and specificity of carpal tunnel syndrome signs. American Journal of Physical Medicine & Rehabilitation 1997;76(6):451-7.

CHAPTER 6

EVIDENCE BASE FOR THE CULTURAL AND CLINICAL EFFECTIVENESS OF POCT IN INDIGENOUS MEDICAL SERVICES

INTRODUCTION TO CHAPTER 6

The 10 papers presented in this chapter are grouped according to their program of origin and in the following order - the Umoona Kidney Project, the QAAMS Program and the Point-of-Care Testing in Aboriginal Hands Program. The final two publications, categorised under the 'General' heading, describe all three Indigenous programs. Collectively, these 10 papers describe the cumulative evidence base for both the cultural and clinical effectiveness of the POCT models in this research program. As mentioned earlier in this chapter, the critical importance of evaluating the cultural appropriateness of my POCT models as a research outcome cannot be over-emphasised for, without the engagement of Aboriginal Health Workers as POCT operators and the willingness and acceptance of Indigenous community members to participate in POCT, the POCT models described in this research program would have unquestionably failed.

THE UMOONA KIDNEY PROJECT.

Mark Shephard[1], Michael Brown[2], Maryanne Hudson[2], Cissie Riessen[2] and Janice Braun[2]

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Aboriginal and Islander Health Worker Journal 2000; 24: 12-15.

STATEMENT OF AUTHORSHIP

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Aboriginal and Islander Health Worker Journal 2000; 24: 12-15.

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BROWN, M.

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RIESSEN, C.

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STATEMENT OF AUTHORSHIP

THE UMOONA KIDNEY PROJECT

Aboriginal and Islander Health Worker Journal 2000; 24: 12-15.

SHEPHARD, M.D.S. (Candidate)

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BRAUN, J.

Director of Aboriginal health service, provided administrative supervision at community level and commented on initial draft of manuscript.

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Signed ... . *Date* 1.12.06

The Umoona Kidney Project.

This early peer-reviewed paper provided initial evidence of the cultural approach adopted by the author. It was written collaboratively with the Umoona Aboriginal Health Worker team and deliberatively featured quotations from the team members to illustrate their views on the cultural advantages and effectiveness of POCT.

This paper was intentionally written as a descriptive commentary on the Umoona Kidney Project rather than as an academic tome because I wanted to (i) demonstrate the inclusive nature of the research being undertaken and (ii) ensure that the paper would be readily understood by its target audience – the Australian Aboriginal Health Worker fraternity.

The joint publishing of this paper with Umoona's Aboriginal Health Workers contributed significantly to the cultural acceptance of the Umoona Kidney Project by both the health service and community members and enabled the research outlined in subsequent papers on this program to be conducted in a spirit of mutual trust and respect.

Footnote: The signature of co-author Maryanne Hudson was not able to be obtained due to a severe and long-standing illness rendering her unable to sign her name. The CEO of the Umoona Tjutagku Health Service at the time this project was undertaken (Anne Vanajek) signed the preceding Statement of Authorship on Maryanne's behalf.

The Umoona Kidney Project

BY MARK SHEPHARD, MICHAEL BROWN, MARYANNE HUDSON, CISSIE RIESSEN & JANICE BRAUN

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Introduction

Kidney disease is one of the most serious problems facing Aboriginal Australians[1-6]. Nationally the number of Aboriginal people with advanced, or end-stage kidney disease is six times that of non-Aboriginal Australians[2]. It has recently been predicted that a further 500 Aboriginal people will develop end-stage kidney disease by the year 2004[4,5]. The only treatment options for Aboriginal people with advanced kidney disease are dialysis or transplantation, both of which cause significant social and cultural trauma for the individual and for their family[6].

Early detection of renal disease is critical because, if identified early enough, progression to end-stage kidney disease can be slowed or even prevented. As a result, early detection has the potential to significantly reduce the number of Aboriginal people who may ultimately require dialysis or transplantation.

How the Umoona Kidney Project Came About

In mid-1997, a partnership was formed between the Umoona Tjutagku Health Service (UTHS) and the Renal Unit at Flinders Medical Centre to conduct a renal disease screening and prevention program for adult members of the Umoona Aboriginal community at Coober Pedy in far north South Australia (some 850 kilometres from Adelaide). The request to conduct the project came from the then Director of the UTHS, Waluwe Simpson-Lyttle. (Janice Braun has since replaced Waluwe as Director.) In mid 1998, the partnership was extended to include the Renal Unit at the Women's and Children's Hospital (WCH). This followed the community's desire to include children in the screening and prevention program. As a result, the Umoona Kidney Project provides an integrated family or holistic approach to addressing the community's renal health.

A Real Team Effort

The team working on the project is large and continues to grow. The Umoona Tjutagku Health Service team is Janice Braun (Director), a clinical nurse (Vicki McCormack, who has recently been replaced after 25 years sterling service to the community by Chris Durdin), and Aboriginal health workers (Michael Brown, Maryanne Hudson and Cissie Riessen). The Commonwealth Department of Health and Aged Care (through its Office for Aboriginal and Torres Strait Islander Health) has recently provided additional health worker salary support specifically for the renal project, and a fourth health worker (Gay McLeod) has now joined the team.

The Flinders' renal team comprises Project Manager and Scientist, Mark Shephard, two renal doctors, Lindsay Barratt and Kathy Paizis, a nutritionist, Sally Zeunert, data manager Glen Allen, with computing and administrative support from David Heard and Karan Lavender respectively. The WCH team is made up of two renal doctors (Fred Jureidini and Margie van Renen), senior technical officer Sandra Harris, and a nutritionist Nadia Cerro.

Prior to commencing the project, six months of groundwork was spent with the Umoona Community, listening to the community's thoughts and aspirations about renal disease, and working together to formulate the aims and objectives of the Umoona Kidney Project. This period of community consultation and liaison, facilitated mainly through a series of open community forums during field visits to Coober Pedy, was critical in forming the foundation on which the project has been built. The renal team also consulted with staff from the Coober Pedy Hospital, particularly the Senior Medical Officer, the Director of Nursing and CEO, as well as the local general practitioner at Coober Pedy in the lead up to commencement of the project. In addition, Catherine Morgan, Manager of Karpa Ngarrattendi Aboriginal Health Unit at Flinders Medical Centre, gave important cross-cultural training to the renal team.

Ownership and Direction of the Project

The foundation on which this work is based is that the Umoona community owns the renal project. It is a major long-term objective of the project that a strong sense of Aboriginal ownership continues to be fostered and advanced.

The FMC/WCH renal teams are responsible to the Board of the Umoona Tjutagku Health Service, and report directly to the Director of the Health Service. They work with the community, being respectful of Aboriginal time and space, and remaining sensitive to the cultural priorities of the community.

All data collected during the project (for example on screening, patient management and health promotion activities) remains the property of the Umoona community concerned.

Through community information sessions, community members receive feedback on how the program is progressing, what results have been generated and how the overall health of the community is improving over time. These forums are viewed as a critical priority to reinforce community ownership of the project and as a key strategy in ensuring long-term sustainability.

How Does the Umoona Kidney Project Work?

A major aim of the project is to identify those members of the Umoona community, both adults and children, who may be at risk of developing advanced renal disease. This has been achieved by implementing a screening program that began for adults in June 1998 and for children in November 1998. Participation in the screening program is on an entirely voluntary basis.

The Flinders and WCH renal teams visit the community on a regular basis, around every six weeks during 1999, to carry out the screening (which is conducted at the Umoona health clinic). They work closely with the nurse and health worker team during these field visits. The health screen not only provides information about risk factors for developing renal disease but also the risk of cardiovascular disease, diabetes, and the state of nutrition. It includes a full medical assessment, a family history, and a blood pressure, blood sugar and weight check. In addition, each person also brings along a first-morning urine or "kumbu" sample, which is tested on-site for the urine albumin:creatinine ratio or ACR, using a machine called the DCA 2000. The ACR test is very much the cornerstone of the screening program. It detects low levels of protein in the urine (microalbuminuria), indicating early evidence of renal disease. The DCA 2000 instrument, marketed by Bayer Australia, is portable, simple to use, and provides a quantitative measurement of ACR in seven minutes[7]. Used for the first time *in situ* in an Aboriginal community, it has proven both robust and reliable in this setting. Following a consultation and after reviewing all the screening results, the renal doctor gives each community member immediate feedback on his/her risk factor profiles for renal and other lifestyle diseases.

The role of the health worker team in the screening process is pivotal. As Cissie explains: "We make appointment times for the people to see the renal doctors, we see the people and give them a reminder notice about their appointment, and we give each person a urine container (to collect their specimen for ACR testing) and a brown paper bag to keep the specimen in. On the day the person sees the doctor we provide transport to the clinic if needed, and we measure heights and weights and do fingerprick blood sugar tests."

Between field visits by the renal team, there is also much to do, with the Umoona health team carrying out further screening tests requested by the renal doctors (such as repeat blood pressures, blood sugar levels and dipstick urinalyses). During field visits over the past six months, the health workers have been given regular training sessions about how to use the DCA 2000. Since September last year, the health worker team has been performing urine ACR testing on the DCA between visits of the renal team. This is seen as a critical step in the evolution of the project because it has always been a long-term aim of the project to facilitate Aboriginal control and empowerment of renal screening.

As Michael and Maryanne explain: "Doing the ACR testing ourselves really streamlines the project and spreads out the workload. It gives the community members more choice as to when they have their

Umoona's Aboriginal Health Worker team: Michael Brown, Maryanne Hudson and Cissie Riessen with former clinical nurse Sister Vicki McCormack

urine tested. They can come in at any time and not just when the renal team visits."

By late 1999, 150 adults and 140 children in the community had been screened. Some of the important findings from the screening of adults include:

- Fourteen percent of people had early evidence of early kidney disease or "microalbuminuria", as well as having other risk factors for renal disease. All are either diabetic, diabetic with high blood pressure, or hypertensive. This group is a special focus of the project because we hope to prevent or retard the progression of renal disease in these people through early intervention strategies (as outlined below).
- Eight percent of people had (previously unknown) established renal disease, indicating the critical need for screening and early detection of renal disease in Aboriginal communities.
- Forty two percent of people were not hypertensive or diabetic, but had other risk factors for renal disease, cardiovascular disease and diabetes such as obesity, smoking, and strong family history. Most people in this group were between 20 and 30 years of age, and they will need to be closely monitored in the next ten years for the future development of these so-called "lifestyle diseases".
- Screening has also identified three adults with previously undiagnosed diabetes, 38 adults with previously undiagnosed hypertension, one new case of hepatitis B and one new pregnancy.

Looking at the children,

- At present 14 children/young people are being followed for renal abnormalities detected by the screening project. These abnormalities include significant proteinuria, significant microhaematuria and recurrent urinary tract infections.
- Ten children, who were found to have a raised ACR, are undergoing appropriate renal investigations and two children with mildly elevated blood pressure readings on screening are under regular review.
- In addition, 28 children with minimally elevated ACR levels on initial screening are being followed regularly by analysis of an early morning urine specimen. This enables tracking of ACR levels over time to determine whether they have a potential ongoing renal problem. Eight children have also been identified with significant microhaematuria and are currently being investigated.
- Four children with previously diagnosed renal problems are now under regular review at the Health Service.
- A new non-insulin dependant diabetic (NIDDM) has been diagnosed as a result of screening and a further adolescent is currently being investigated for diabetes. These young people will be managed in the long-term by the regional pediatrician from Port Augusta, Nigel Stewart. Several more young people have been identified as having significant risk factors for Type II diabetes and are receiving appropriate management including dietetic advice.
- Five children with previously unrecognised medical problems (namely, type 2 diabetes, heart murmur, asthma, endocrine and eye conditions) have been found during screening and have been referred to the pediatrician for ongoing management. Eight overweight/obese children are receiving advice and are being reviewed by the WCH nutritionist, both in family and school groups. Many non-renal problems identified during the screening physical examination have been referred to the local general practitioner and/or the regional pediatrician. Many of the children in the community have been found to have a strong family history of significant medical problems, for example hypertension (54%), diabetes (62%), renal disease (32%) and cerebrovascular disease (41%).

Screening will continue to be an on-going priority of the project over the next year. The community has accepted the renal teams from FMC/WCH well. Maryanne says: "The community love the doctors and the whole renal team. They have good trust and respect for the team. Mothers are very keen to come because our children are very important to our community. Having seen the doctors working with their children, many of the parents have now come to see the adult renal team." Michael adds: "The old people also like to see the doctors. Even if they don't have an appointment, they still come in and like to be checked out."

Helping those People At Risk for Kidney Disease

A medication called Coversyl (made by Servier Laboratories) is being offered, again on an entirely voluntary basis, to those adult community members who have been identified during screening and follow up assessment as having high blood pressure, diabetes with early renal disease, or established kidney disease. This medication helps protect both the heart and the kidney. There have been quite remarkable drops in blood pressure in the group of 36 people who have been taking the medication consistently (for example, average lying blood pressures of this group have fallen from 153/92 to normal values of 137/83). There has also been no increase in the degree of microalbuminuria in the group.

Again, the health worker team has a vital role in managing the medication. As Cissie explains: "We deliver tablets as part of a daily morning tablet run to particular clients, and we bring other people to the clinic to collect their weekly dosette of tablets."

A range of culturally appropriate health promotion strategies has been initiated concurrently with the provision of medication. These strategies are seen as vitally important for the long-term sustainability of the project and for the improvement of the general health and lifestyle of the community as a whole. They focus on nutrition, hygiene and exercise. The FMC and WCH nutritionists provide individual nutrition counselling following referral by the renal doctors and work with a range of community members and groups in response to particular requests for information and education (notably the Coober Pedy Area School and the Aboriginal Meals Program).

A recent initiative has been the introduction of a Nutrition Training Program for the health worker team. (This is in addition to kidney education sessions that are regularly run by the renal doctors for the health workers, with the topics for discussion and the agenda being set by the health worker team.) Cissie explains the background behind this Nutrition Training Program. "Our health workers have been keen to work with the community to improve nutrition, but we felt that we did not have an appropriate level of knowledge and skills to do this. So we identified for the renal nutritionists some areas where we felt we needed further education. These were general nutrition, nutrition for infants and children, nutrition during pregnancy, nutrition for obesity and heart disease, and nutrition for diabetes and renal disease. (Representatives from the Umoona Child Care Centre, the Child and Youth Health nurse and Aboriginal Education Workers from the Coober Pedy Area School were also invited for the Nutrition for Infants and Children session.) Maryanne continues: "The renal nutritionists have gone away and prepared education sessions on these five topics, and they come up to Umoona for separate visits to teach us about these areas. We can now pass this information on to the community in our own time, and we can focus on those people who need specific help such as young mothers." Michael states: "As part of the first session, we are running a 'healthy tucker' poster competition at the school with a range of sporting prizes including a signed Port Power guernsey."

While discussing sport, the community as a whole is very keen to improve the level of fitness among their children in particular and to promote sport as a healthy activity. Michael has taken a leading role in this area. Recently the renal team has joined forces with the University of South Australia's Physical Education, Exercise and Sport unit, headed by Jim Dollman and David Stuart, who have had a long standing interest in the fitness of South Australian schoolchildren. The University team has begun some preliminary work with the Coober Pedy Area School with a view to improving fitness and awareness of the benefits and opportunities that sport may provide.

Continually mindful of the community ownership of the project, the renal team has enlisted the heath workers' support in conducting a survey within the community to assess attitudes and perceptions of the project. The project must continually evolve and develop in directions that the Umoona community views as appropriate to its needs and priorities.

Summary

In summarising the project to date, Maryanne states: "The Umoona Kidney Project is culturally appropriate for our people. It's been successful largely because of the education we have received from the renal team. We can now go and talk, in an informed way, to the community about kumbu, our kidneys, diet and tucker. We've now got the chance to educate our young children early about kidneys and nutrition. Everyone is happy working with the kidney team."

Just to finish on a rather humourous note with a story that indicates the messages about healthy kidneys are being taken to heart by the community. The children's renal team recently screened a young boy. The next day he turned up at the health clinic with his dog. He wanted the doctor to check his dog's kidneys. The nurse wouldn't let the dog into the clinic, but Dr Fred came outside and put his stethoscope onto the dog. The dog was so surprised, it ran across to the nearest post, cocked its leg and did a kumbu sample on the spot!

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SCREENING FOR RENAL DISEASE IN A REMOTE ABORIGINAL COMMUNITY USING THE BAYER DCA 2000.

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STATEMENT OF AUTHORSHIP

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Australian Journal of Medical Science 2001; 22: 164-170.

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Conceived research and study design, initiated, implemented and managed study, analysed and interpreted data, wrote manuscript and acted as corresponding author.

Signed .... *Date* 19/12/2006

ALLEN, G.

Provided statistical and data management support for the study and commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed .... *Date* 19/12/2006

Screening For Renal Disease In A Remote Aboriginal Community Using The Bayer DCA 2000.

This paper described the initial results of the adult renal disease risk assessment arm of the Umoona Kidney Project, which utilised POC urine ACR testing for the first time in the Australian Indigenous community setting. The key research finding presented in this paper was the high prevalence of previously undiagnosed micro- and macroalbuminuria, as measured by urine ACR POCT. This finding provided initial evidence to support the clinical effectiveness of POCT in the Indigenous setting, specifically in the context of risk assessment. The paper also reported acceptable analytical performance for urine ACR POCT, as assessed by quality control testing, and described the process by which responsibility for community POCT was handed over to Umoona's Aboriginal Health Worker team.

Original Article

Screening for renal disease in a remote Aboriginal community using the Bayer DCA 2000

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Abstract

End-stage renal disease among Aboriginal Australians has reached alarming proportions during the past decade. The early identification of this disease through community screening programs is a key strategy in reducing the long-term financial and cultural burden of the disease. The small point-of-care Bayer DCA 2000 analyser, which tests for urine albumin:creatinine ratio (ACR), was used as a marker for early renal disease in an adult screening program in a remote South Australian Aboriginal community. Nineteen percent of 149 adults screened had previously undiagnosed persistent microalbuminuria (ACR between 3.4 and 33.9 mg/mmol), while a further 9% had persistent overt albuminuria (ACR greater than or equal to 34 mg/mmol). Aboriginal health workers were trained in the operation of the DCA 2000 to enable screening to be an on-going, sustainable activity within the community setting. The DCA exhibited excellent analytical performance characteristics and was robust and reliable throughout the study period.

Keywords - DCA 2000, point-of-care technology, screening, urine albumin:creatinine ratio, microalbuminuria, macroalbuminuria, sustainability

Introduction

During the 1990s there has been a rapid escalation in the number of Aboriginal Australians with end-stage renal disease. Recent age- and sex-adjusted figures indicate Aboriginal people have around nine-times greater risk of developing end-stage renal disease than all other Australians (1). In some parts of Australia, notably the Tiwi Islands, rates of this disease have now reached epidemic proportions and up to 500 new cases of end-stage renal disease among Aboriginal people are predicted by 2004 (2-5). Renal disease in Aboriginal people arises from a combination of metabolic and environmental factors including strong associations with diabetes, high blood pressure, maternal and infant malnutrition, high rates of obesity, low birthweight and recurrent

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childhood infections (5). Many of these factors reflect poor socio-economic status and social disadvantage of Aboriginal people (6,7). The most common form of renal disease in Aboriginal people is glomerular in origin (8) and characterised by albuminuria, as measured by the urine albumin:creatinine ratio (ACR).

There is an urgent need to develop and implement community-controlled, self-sustainable screening programs for the early detection of renal disease in Aboriginal communities nationally, using simple, non-invasive and cost-effective tests, such as urine ACR.

Early detection is critical because albuminuria progresses as a continuum over time, with an increase in urine ACR of 15% per annum being reported in one Aboriginal cohort (9). Further, the magnitude of albuminuria predicts not only end-stage renal disease but also generalised cardiovascular disease and mortality (10,11). The earlier renal disease is detected, the greater the potential to modify the course of the disease through clinical intervention.

Treatment programs using the ACE inhibitor Coversyl (Servier Laboratories) have proven effective in slowing the progression of renal disease in Aboriginal people (12,13). Coversyl not only stabilises renal function but also reduces hypertension, itself a risk factor for renal disease progression. In addition to its value as a screening tool for early detection, the measurement of ACR levels are also important in monitoring the efficacy of treatment.

In the long-term, early intervention should lead to a reduction in the number of Aboriginal people requiring dialysis - at a conservative cost of $75,000 per patient per year (4) - and having to endure the considerable social and cultural trauma associated with family dislocation during this treatment (7).

The point-of-care DCA 2000 (Bayer Australia) is a small, portable instrument that can measure the albumin:creatinine ratio on 40 μL of urine in just 7 minutes. The analytical and diagnostic performance characteristics of the DCA have recently been validated (14) and the instrument was considered suitable for screening for renal disease in the Aboriginal community setting.

In mid 1997, the Renal Unit at Flinders Medical Centre in South Australia formed a partnership with a remote Aboriginal Community Controlled Health Service, 850 kilometres north of Adelaide, to conduct a renal disease screening program among the adult members of the local Aboriginal community.

The program followed a formal request from the Director and Board of this Aboriginal health service to the Flinders' Renal Unit. The screening program aimed to identify those adult members of the community who were at risk for developing end-stage renal disease, and to offer these people the opportunity to participate in tailored intervention programs at both clinical and community levels. The screening program was extended to include children from the community in late 1998, with the Renal Unit from the Women's and Children's Hospital in South Australia joining the partnership.

The measurement of urine ACR on the Bayer DCA 2000 was the cornerstone of the adult screening program. This paper presents an assessment of the clinical, practical and sustainable use of the instrument in the adult renal screening program.

Methods

The Bayer DCA 2000

The DCA 2000 (Bayer Australia, Pymble, NSW) uses a reagent cartridge (DCA 2000 Microalbumin/ Creatinine kit, catalogue number 0611, Bayer Australia) which provides a quantitative measurement of urine albumin (by immuno-turbidimetry, using a polyclonal goat antiserum) and urine creatinine (by spectrophotometry using 3,5-dinitro-benzoic acid at alkaline pH), as well as calculation of the urine ACR, all within a 7-minute turnaround time. There are 10 reagent cartridges per kit. The measuring range for urine albumin is 5 to 300 mg/L, and for creatinine 1 to 44 mmol/L. The DCA's lower limit of detection for urine albumin (5mg/L) is 60-times more sensitive than conventional dipsticks for this analyte.

Low and high control samples (DCA 2000 Microalbumin/Creatinine Low and High Control kit, Catalogue number 6012, Bayer Australia) were used to assess day to day precision with, in general, each control being used alternately to test the first cartridge of a new reagent kit.

Screening of adults

At the request of the community, adult screening was conducted in the health service clinic. Participation in the screening program was entirely voluntary, with each participant giving prior informed consent.

For the first 18 months of the program, a field team from Flinders Medical Centre comprising a nephrologist, scientist, nutritionist and information technologist visited the community at approximately six-week intervals and worked closely with the clinical nurse and Aboriginal health worker team from the Aboriginal health service to conduct adult screening sessions. During this period, the scientist performed the majority of the DCA testing on adults.

For the next 18 months, Aboriginal health workers conducted most of the adult screening, following a detailed skills transfer program (described later). Throughout the three-year study period, the Flinders Medical Centre renal team was responsible to the Director of the Aboriginal health service and its Board.

The adult screening program involved a full medical assessment including a family history, a height and weight measurement for calculation of body mass index, a blood glucose test by glucometer and a blood pressure measurement (both lying and standing). In addition, each participant brought with them a first-morning urine specimen, which was tested on-site for urine ACR on the Bayer DCA 2000 machine and for pH, protein, glucose, blood, leucocytes, nitrite, urobilinogen and bilirubin by qualitative dipstick urinalysis on the Clinitek 50 (Bayer Australia).

The first morning urine was the specimen of choice because it has greater sensitivity and specificity for microalbuminuria than the random spot urine (15). The latter is subject to a higher degree of variability due to postural factors such as physical activity or exercise and hence a higher rate of false positive test results (15). If the urine specimen was found to be dipstick positive for blood, nitrite or leucocytes (other conditions leading to false positive results), urine ACR analysis was not performed and the patient was asked to return with a fresh first-morning specimen in around two weeks.

Classification of albuminuria

The following levels of urine ACR were adopted in assessing risk for renal disease: ACR less than 3.4 mg/mmol, normal; ACR between 3.4 and 33.9 mg/mmol, microalbuminuria indicating early renal disease; and ACR greater than or equal to 34 mg/mmol, macroalbuminuria indicating overt renal disease (16).

If a raised urine ACR (greater than or equal to 3.4 mg/mmol) was found on initial assessment, then the participant was required to submit a further first morning urine specimen for repeat analysis of urine ACR. Both specimens needed to be between 3.4 and 33.9 mg/mmol before a subject was classified as microalbuminuric, and greater than or equal to 34 mg/mmol for being macroalbuminuric. The mean of the two values was used as the baseline ACR for each individual.

Towards the sustainable use of the DCA 2000 at the community level

A long-term goal of the renal screening program was to implement an education and training program for the community's Aboriginal health workers, whereby they would have a sound understanding of kidney disease and be fully trained and competent in the use of the DCA 2000 point-of-care instrument.

This training program was conducted from January to June 1999. Following completion of this program, the Aboriginal health workers were able to conduct community screening in their own time and space, independent of the Flinders Medical Centre renal team from September 1999 onwards.

Ethics approval

Approval to conduct the renal screening program was obtained from the Aboriginal Health Research Ethics Committee of South Australia and the Flinders Medical Centre's Committee on Clinical Investigation.

Results

Analytical performance of the DCA 2000

Between-run coefficients of variation (CV%) (n=46) for each measurement on the DCA across the study period were: 6.9% and 3.6% for urine

albumin (at levels of 36 and 208 mg/L, respectively), 3.2% and 4.1% for urine creatinine (9 and 36 mmol/L) and 6.7% and 5.3% for urine ACR (for ratios of 4.1 and 5.8).

These levels of imprecision compare favourably with the median coefficients of variation obtained by laboratories participating in the Royal College of Pathologists of Australasia's Quality Assurance Program Group's Urine Chemistry Program (5.6% for urine albumin, 3.8% for urine creatinine, July to December 2000 testing cycle, J Gill personal communication).

Across 30 months of field use, no mechanical breakdowns were experienced, while the error rate for cartridge failure was less than 1%.

Screening for Renal disease using the DCA 2000

We now report the results of urine ACR testing performed on the DCA during adult screening. The results of other screening parameters measured are not included in this paper.

From June 1998 when screening commenced until December 2000, 149 adult members of the Aboriginal community were investigated for their risk factors for renal disease, including urine ACR measurement on the DCA 2000. This number represented approximately 65% of the community's adult population. Thirty seven percent of those adults screened were males, and 63% were females. The mean age of adults screened was 41.7 years ± 1.1 (standard error of mean), with an age range from 18 to 78 years. In total, 232 urine ACR measurements were performed on adult subjects on-site in the community clinic across the screening period.

Twenty-eight (19%) and fourteen (9%) of adults were identified as having previously undiagnosed persistent microalbuminuria and macroalbuminuria respectively, following ACR measurement using the DCA (Table 1).

There was no significant difference between gender in the prevalence of microalbuminuria (χ^2=1.34; df=1; p=0.25, NS) or macroalbuminuria (χ^2=0.010; df=1; p=0.92, NS).

The mean and range of ACR values found in the micro- and macroalbuminuric groups are also shown in Table 1. There was no significant difference between gender in the mean ACR values observed in the microalbuminuric group (ANOVA, p=0.56, NS) or macroalbuminuria (ANOVA, p= 0.36, NS).

Table 1.
Albuminuria identified among adult Aboriginal community members using the Bayer DCA 2000.

	Number of People Screened	Prevalence %		Mean ACR (mg/mmol)					
		Microalbuminuria	Macroalbuminuria	Microalbuminuria			Macroalbuminuria		
				Mean	SEM*	Range	Mean	SEM*	Range
Male	55	23.6	9.1	17.8	2.5	3.6-33.1	134.5	56.7	48-349
Female	94	16.0	9.6	14.5	2.5	4.5-30.5	103.7	22.3	37-217
All	149	18.8	9.4	16.0	1.8	3.6-33.1	114.7	23.8	37-349

** SEM = standard error of the mean*

Figure 1 categorises the albumin:creatinine ratios found during screening by age group. Fifty percent of all adults over 45 years of age had either micro- or macroalbuminuria. Twenty five percent of adults aged between 29 and 44 years exhibited albuminuria. A statistically significant association was observed between age and the progression of albuminuria (χ^2 =16.2; df =4, p=0.003).

All subjects with microalbuminuria were either diabetic, diabetic with hypertension, or hypertensive alone. The high rate of microalbuminuria identified in this community is consistent with the findings from Aboriginal communities in other parts of Australia (12,17).

The number of people with previously unknown overt albuminuria was an unexpected and clearly disturbing finding, and further emphasises the need for screening and early detection of renal disease.

Of a total of 232 urine samples tested during the study, 11% had albumin concentrations greater than the upper limit of the DCA's measuring range (300 mg/L) and therefore an on-site quantitative albumin result could not be obtained on these samples at the time of analysis. None of the urine samples had a creatinine concentration greater than 44 mmol/L. A simple dilution technique to enable on-site quantitation of over-range albumin concentrations has subsequently been developed, the results of which will be published elsewhere.

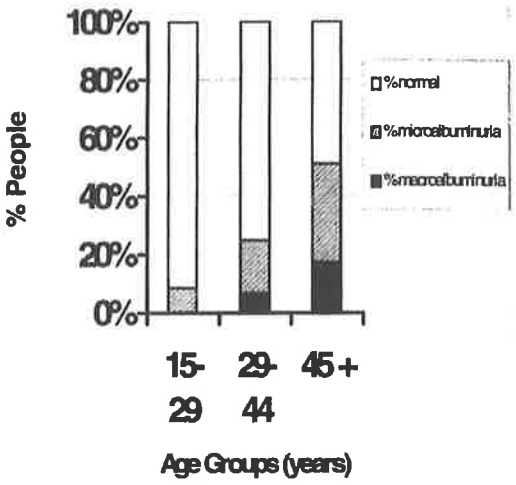

Figure 1: Urine albumin:creatinine ratio category by age group.

Towards the sustainable use of the DCA 2000 at the community level

Figure 2 shows the number of urine ACR tests performed on-site by the service's Aboriginal health workers since education and training initiatives were completed in June 1999. This number is compared with the number of urine ACR tests performed by the field team during visits to the community. The crossover of responsibility for urine ACR testing on the DCA occurred in September 1999. During 2000, there was a 165% increase in the number of urine ACR tests performed by the Aboriginal health workers.

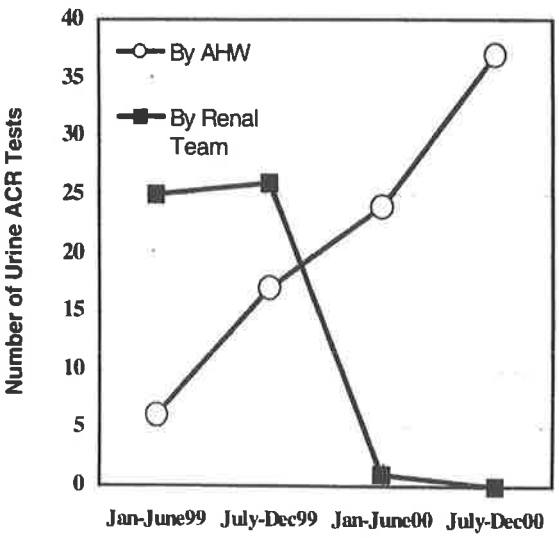

Figure 2: Number of on-site urine ACR tests performed on the Bayer DCA 2000 by the Flinders Medical Centre renal team (Renal Team) and the Aboriginal Health Workers (AHW) from the Aboriginal health service.

Discussion

Screening programs for the early detection of renal disease can be effective in making in-roads into

the current epidemic of renal disease among Aboriginal Australians provided they are community controlled and sustainable at the community level. The point-of-care DCA 2000 meets these requirements because testing for renal disease can be done in the community setting by a trained health worker, the result is immediately available to both the local medical officer and patient, and ownership of the screening information remains in the community.

The large number of adults detected with albuminuria during this screening program confirms a high prevalence of incipient renal disease in this community, while illustrating the clinical and practical usefulness of the DCA 2000.

Common blood markers of renal disease such as urea and creatinine may only begin to rise significantly when 30% to 50% of nephron function has been lost (18). However microalbuminuria may be evident with as little as 10% damage to kidney function (18). The earlier the disease process is detected the greater the chance of retarding the progression of disease through appropriate intervention.

All people identified as at risk for renal disease in this study were given the opportunity to participate voluntarily in both clinical and community-based intervention programs (the results of which will be published later).

The ACE inhibitor Coversyl was offered to those at risk to reduce blood pressure and stabilise renal function. Those persons with macroalbuminuria are now under specialist nephrological care. Information about nutrition, the value of exercise, and alcohol and tobacco consumption reduction strategies has been given to both individuals at risk and to the community in general.

The role of the DCA 2000 in identifying those people with albuminuria has been pivotal to the screening program. The DCA's small, portable nature and its simplicity of operation given appropriate training have resulted in the machine being well accepted by the Aboriginal health worker team. In performing urine ACR tests themselves, health workers have been empowered to take greater responsibility for renal screening in their community.

During the study period, the DCA has continued to demonstrate sound analytical performance and proved robust and reliable in the remote health setting. The only minor deficiency in using the machine in the field was that just over 10% of the urine samples tested were unable to be quantified on-site due to their high urine albumin concentrations. However, as mentioned earlier, this problem has been addressed by the development of a suitable on-site dilution technique.

At the end of 2000, the renal screening program was formally handed over to the Aboriginal health service as a self-sustaining activity.

The Australian Government has noted the successful use of the DCA in the Aboriginal health setting and the full potential of the machine's analytical capability is now being realised. The Bayer DCA 2000 instrument can also measure Haemoglobin A1c (HbA1c) on a fingerprick of blood in six minutes.

HbA1c is an established marker for monitoring control of diabetes. In 1999, the Office for Aboriginal and Torres Strait Islander Health within the Commonwealth Department of Health and Aged Care, in partnership with the National Aboriginal Community Controlled Health Organisation, initiated a program for community-based HbA1c testing using the DCA 2000 in 47 Aboriginal Community Controlled Health Services around Australia (19).

Opportunities for the broader application of point-of-care instrumentation for screening and management of chronic diseases in Aboriginal communities seem considerable.

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ALBUMINURIA IN A REMOTE SOUTH AUSTRALIAN ABORIGINAL COMMUNITY: RESULTS OF A COMMUNITY-BASED SCREENING PROGRAM FOR RENAL DISEASE.

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Albuminuria In A Remote South Australian Aboriginal Community: Results Of A Community-Based Screening Program For Renal Disease.

This paper provided the first international exposure of our research findings from the Umoona Kidney Project. It provided an updated and comprehensive assessment of the adult risk assessment arm of the Umoona Kidney Project by presenting a detailed analysis of all renal disease risk factors measured, and examining the association between albuminuria and selected co-existing risk factors. It also described the broader holistic approach adopted by the project in addressing and raising awareness of chronic disease within the community.

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ORIGINAL RESEARCH

Albuminuria in a remote South Australian Aboriginal community: results of a community-based screening program for renal disease

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ABSTRACT

Introduction: The poverty, poor environmental living conditions and poor health standards experienced by Aboriginal Australians in some communities in rural and remote Australia have been described recently as 'fourth world'. For more than a century Aboriginal people have suffered the effects of dispossession of their land; destruction of their traditional culture and values; and exposure to infectious diseases, alcohol and the Western diet that is high in fat and sugar. Collectively these factors have contributed to the prevalence of chronic disease that afflicts Aboriginal people. In particular, renal disease has emerged during the last decade as a major contemporary health problem for Aboriginal Australians. According to the latest age- and sex-adjusted figures, Aboriginal people now have approximately nine-fold the risk of non-Aboriginal Australians of developing end-stage renal disease. In parts of Australia's Northern Territory, where Aboriginal people represent over 20% of the Territory's population, the rates of end-stage renal disease have been described as 'epidemic', reaching 2700 per million in the Tiwi Islands. In response to a request from the Umoona Tjutagku Health Service in mid 1997, the Renal Unit at Flinders Medical Centre, Adelaide, South Australia, formed a partnership with the health service to conduct a renal-disease screening program for adult members of the Umoona Community at Coober Pedy, a town 850 kilometres north of Adelaide. The partnership was later expanded to include screening for children (conducted by the Renal Unit at the Women's and Children's Hospital, Adelaide, South Australia). The community named the program 'The Umoona Kidney Project'. The Umoona community had recently experienced the dislocation of a number of its older people who suffered from advanced renal disease and were undergoing dialysis in a variety of centres in South Australia and the Northern Territory. As a result, the community had suffered social trauma. Consistent with the

community's overall holistic approach to healthcare, the community wanted the renal program to provide a focus for community awareness of and knowledge about chronic disease, as well as to complement existing health programs.

Objectives: The study objectives were to identify the prevalence of risk factors for renal disease, notably albuminuria, in adults from a remote Aboriginal community, and to examine the association of albuminuria with other risk factors; to empower Aboriginal health workers to self-manage a sustainable, community-controlled renal health program; and to assess the reliability and cultural acceptability of point-of-care technology for detecting renal disease.

Method: The study was a three-year cross-sectional voluntary adult screening program (The Umoona Kidney Project). The study was performed as a partnership between the Flinders Medical Centre Renal Unit and the Umoona Tjutagku Health Service, and it involved nephrologists, medical scientists, Aboriginal health workers and clinical nurses. Setting: Umoona Tjutagku Health Service, 850 km north of Adelaide. Participants: 158 adult members of the Umoona community: 58 males (37%; mean age = 43.8 years, range 23-78) and 100 females (63%; mean age = 39.6 years, range 18-72). Main outcome measures: First morning urine albumin : creatinine ratio measured by the Bayer DCA 2000 point-of-care analyser machine (Bayer Australia, Melbourne, Australia); lying and standing blood pressure; random blood glucose; body mass index; urinalysis.

Results: The study found that of screened adults, 29/149 (19%, 95% C.I. 13%-27%) had persistent microalbuminuria and 13/149 (9%, 95% C.I. 4%-14%) had persistent macroalbuminuria; 62/148 participants (42%, 95% C.I. 34%-50%) had overt hypertension; 35/145 participants (24%, 95% C.I. 17%-32%) had diabetes; 3 participants were newly diagnosed as having non-insulin dependent diabetes; 96/148 participants (65%, 95% C.I. 57%-73%) were either overweight or obese. Strong correlation was observed between the progression of albuminuria and age, all blood pressure categories, blood glucose, body mass index and an increasing number of risk factors.

Conclusions: The Umoona Kidney Project identified a significant community burden of previously unknown incipient and established renal disease that required addressing via clinical- and community-based interventions. The DCA 2000 was a reliable instrument for detecting albuminuria on-site in the remote clinical location and was well accepted by Aboriginal health workers and community participants.

Key words: Aboriginal health, albuminuria, renal disease.

INTRODUCTION

The poverty, poor environmental living conditions and poor health standards experienced by Aboriginal Australians in some communities in rural and remote Australia have been described recently as 'fourth world'[1]. For more than a century Aboriginal people have suffered the effects of dispossession of their land; destruction of their traditional culture and values; and exposure to infectious diseases, alcohol and the Western diet that is high in fat and sugar. Collectively these factors have contributed to the prevalence of chronic disease that afflicts Aboriginal people. In particular, renal disease has emerged during the last decade as a major contemporary health problem for Aboriginal Australians.

Several recent studies have highlighted the cultural and financial burden of this disease[2-5]. According to the latest age- and sex-adjusted figures, Aboriginal people now have approximately nine-fold the risk of non-Aboriginal Australians of developing end-stage renal disease[6]. In parts

of Australia's Northern Territory, where Aboriginal people represent over 20% of the Territory's population, the rates of end-stage renal disease have been described as 'epidemic', reaching 2700 per million in the Tiwi Islands[7-8]. Calls for the introduction of community-based screening programs for the early detection of renal disease have been widely promulgated [4-9].

In response to a request from the Umoona Tjutagku Health Service in mid 1997, the Renal Unit at Flinders Medical Centre, Adelaide, South Australia, formed a partnership with the health service to conduct a renal-disease screening program for adult members of the Umoona Community at Coober Pedy, a town 850 km north of Adelaide. The partnership was later expanded to include screening for children (conducted by the Renal Unit at the Women's and Children's Hospital, Adelaide, South Australia). The community named the program 'The Umoona Kidney Project'.

The Umoona community had recently experienced the dislocation of a number of its older people who suffered from advanced renal disease and were undergoing dialysis in a variety of centres in South Australia and the Northern Territory. As a result, the community had suffered social trauma. Consistent with the community's overall holistic approach to healthcare, the community wanted the renal program to provide a focus for community awareness of and knowledge about chronic disease, as well as to complement existing health programs.

Pathologically, end-stage renal disease among Aboriginal people has been shown to be mainly glomerular in nature[10]. Renal biopsy studies indicate Aboriginal people have increased rates of glomerulomegaly, mesangiocapillary glomerulonephritis, diabetic nephropathy and non-IgA proliferative glomerulonephritis, compared with the non-Aboriginal population[11]. Glomerular damage is characterised by albuminuria[10]. As an integral part of The Umoona Kidney Project, the point-of-care DCA 2000 machine (Bayer Australia, Melbourne, Australia) was used for the first time in an Aboriginal community to detect albuminuria[12]. The small, portable DCA 2000 (dimensions, 24 x24 x27 cm; 5 kg) measures the urine albumin : creatinine ratio (ACR) on 40 mL urine with an on-site result available in 7 min. Prior to its use in the field, the DCA 2000 underwent a full scientific evaluation[13].

This article describes the results of the adult screening program from 1 June 1998 to 31 December 2000, examines the associations between albuminuria and other risk factors for renal disease, and discusses the application of the DCA 2000 point-of-care technology for renal screening in the remote clinical setting.

Method

Community consultation, program ownership and direction

Prior to commencing the adult screening program, clinical and scientific staff from the Renal Unit at Flinders Medical Centre undertook 6 months of community consultation with the Board of the Umoona Tjutagku Health Service and Umoona community members. This consultation was facilitated by a series of open community forums held during field visits to Coober Pedy. At these meetings the community expressed its concerns about renal disease and its aspirations for the program, resulting in the clearly defined aims and objectives of The Umoona Kidney Project. These aims and objectives included the early detection of renal disease among community members by the implementation of a renal screening program. Ownership of the program resided with the community and the Flinders Medical Centre renal team was responsible to, and directed by, the Board of the Umoona Tjutagku Health Service.

Personnel

The Flinders Medical Centre renal team consisted of a scientist-program manager, two nephrologists, a data manager and a nutritionist. The renal team conducted 20 field visits to the community during the project's three-year duration. The Umoona health team consisted of Aboriginal health workers (with four health workers working on the program across its duration), supported by a clinical nurse. The local medical officer at the Coober Pedy Hospital, the town's general practitioner and nursing staff at the hospital also assisted the program

Participants

The adult screening program was open to community members who were 18 years or older, and participation was entirely voluntary. Each of the 158 participants gave prior, signed and informed consent.

Screening

At the request of the community, screening was conducted at the health service clinic and began in June 1998. The Aboriginal health workers recorded each participant's height and weight (for calculation of body mass index [BMI]) and measured their blood glucose using a glucose meter (Medisense; Abbott Diagnostics, Sydney, NSW, Australia). Following these test, participants underwent an initial consultation with one of the visiting nephrologists, during which family and personal medical histories were recorded and a medical examination took place, which included lying and standing blood pressure (BP) measurement.

Each participant brought with them a first-morning urine specimen collected in a 75mL sterile container. The urine was tested qualitatively using Multistix (Bayer Australia) dipsticks on the Clinitek 50 Urine Analyser (Bayer Australia) for the presence of protein, glucose, blood, nitrites and leucocytes. Provided the urine specimen was negative for blood, leucocytes and nitrites, the urine was tested on-site with the DCA 2000 for urine ACR. The urine ACR result was handed to the nephrologist during the initial consultation. The nephrologist then provided the participant with immediate feedback on his or her overall risk-factor profile.

Each participant's baseline screening data was recorded on a single-page proforma and the information was transferred electronically on-site to a patient data-management program (designed using Microsoft Access software).

Risk factor assessment

The following parameters were considered risk factors for renal disease:

- Persistent hypertension (>140/>90 mmHg on at least two separate occasions)
- Random blood glucose greater than 11.1 mmol/L (at least twice)
- Persistent albuminuria (urine ACR >3.4 mg/mmol on a first morning specimen[14] on at least two separate occasions, with the specimens being negative for leucocytes and nitrites)
- Obesity (BMI >30 kg/m^2)
- 'Positive' family or personal medical history, notably a current smoker or consumer of amounts of alcohol greater than 50 g per day for males or greater than 20 g per day for females
- A history of recurrent skin infections.

Repeat measurements necessary to confirm persistent hypertension or albuminuria were conducted either by the Umoona health team between field visits, by the renal team, or by the nephrologist at the next available field visit. The use of first morning specimens for measuring urine ACR was considered preferable to a random sample, which is subject to the potential false-positive effects of posture and exercise and has greater within-person biological variation [15-18].

Following initial clinical review, an action plan was developed for each participant and recorded electronically. This action plan detailed further investigations to be performed (notably repeat BP and urine ACR tests), as well as other clinical information to be collected prior to the next field visit (eg current medications).

Ethics approval

Ethics clearance to conduct The Umoona Kidney Project was obtained from the Aboriginal Health Research Ethics Committee of South Australia and the Flinders Medical Centre Committee on Clinical Investigation.

Results

Participation

By January 2001, 158 adults (approximately 65% of the community's total adult population) had undergone a complete screening assessment. Those screened were 58 males (37%; mean age = 43.8 years, range 23-78) and 100 females (63%; mean age = 39.6 years, range 18-72 years).

Overview of screening results

During the three-year screening program, the team's nephrologists conducted 328 patient encounters: 82 people were seen once, 14 people were seen twice, 66 people were seen three times and five people were seen four times. A total of 232 on-site urine ACR measurements were performed.

The overall mean (± standard error) of measurements conducted during screening is shown for all adults, as well as by gender (Table 1). Diastolic and systolic BP (lying and standing) and weight were higher in males than in females ($p < 0.03$ in all cases, unpaired t-test). Blood glucose levels were higher in female participants than in males but the trend was not significant.

Table 1: Summary of measurements conducted during screening of adult population*

Measurement	All Adults (n = 158)	Male (n = 58)	Female (n = 100)
Age (years)	41.3 ± 1.1	43.8 ± 1.8	39.6 ± 1.3
Blood Pressure (mmHg)			
Systolic, lying	134.0 ± 1.8	140.5 ± 2.9	130.0 ± 2.1
Diastolic, lying	82.0 ± 1.2	85.5 ± 1.8	79.8 ± 1.5
Systolic, standing	131.7 ± 1.9	139.3 ± 3.0	127.1 ± 2.4
Diastolic, standing	84.4 ± 1.2	89.1 ± 1.9	81.5 ± 1.6
Urine ACR (mg/mmol)	13.9 ± 3.3	16.5 ± 6.6	12.4 ± 3.5
BMI (kg/m^2)	28.5 ± 0.7	28.0 ± 0.7	28.8 ± 1.0
Weight (kg)	76.2 ± 1.4	83.1 ± 2.1	72.1 ± 1.7
Blood Glucose (mmol/L)	7.1 ± 0.3	6.6 ± 0.4	7.4 ± 0.4

* Values represent mean ± SEM

Prevalence of risk factors

The overall prevalence of individual risk factors found during community screening is shown (Figure 1).

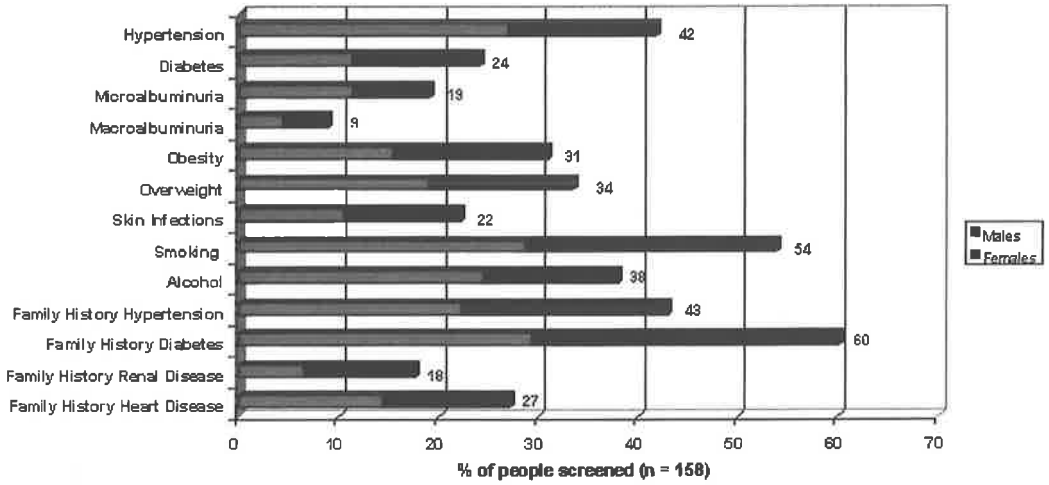


Figure 1: Overall community prevalence of risk factors split by gender. The male : female split shown for each risk factor reflects the relative contribution of gender to the total % of people screened who had positive risk.

Greater than 25% of all adults screened (n = 42/149) had previously undiagnosed persistent microalbuminuria (urine ACR between 3.4 and 34 mg/mol) or macroalbuminuria (>34 mg/mmol). The mean, standard error and range of ACR values found was 16.0 ± 1.8 mg/mmol (3.6-33.1 mg/mmol) for the microalbuminuric group and 114 ± 24 mg/mmol (range 37-349 mg/mmol) for the macroalbuminuric group. Hypertension was found in greater than 40% of the participants (n = 62/148) with a significantly higher rate observed in males (59%) compared with females (32%; p = 0.02, Chi-squared trend analysis). Fifty-eight per cent of participants with hypertension (n = 86/148) were undiagnosed prior to screening. Approximately 25% of all people screened (n = 35/145) had non-insulin dependent (type 2) diabetes mellitus (as assessed by personal history or random blood glucose), and greater than 50% of participants screened also had a positive family history for this condition. Three participants were discovered to have non-insulin dependent diabetes mellitus during screening. Two-thirds of the population surveyed (n = 96/148) was either obese (BMI > 30 = kg/m^2) or overweight (BMI between 25 and 30 kg/m^2). Rates of alcohol and tobacco consumption were high, with greater than 50% of all males drinking to excess and smoking tobacco.

Association between albuminuria and co-existing risk factors

As shown (Table 2), the progression of albuminuria was significantly associated with the following continuous variables: age, diastolic and systolic BP in both lying and standing positions, and blood glucose (p < 0.01 in all cases,

ANOVA). These differences remained significant when controlling for age and sex.

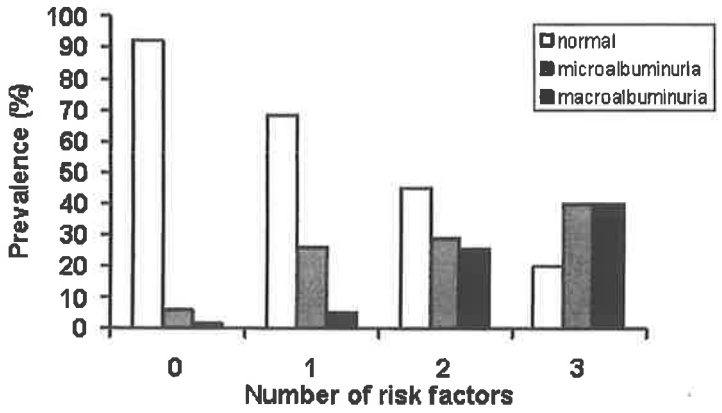
Table 2: The association between measured risk factors and ACR category

Variable	Normal ACR	Microalbuminuria	Macroalbuminuria	
	(*n* = 105)	(*n* = 29)	(*n* = 13)	*p* value
Age (years)	39.1 ± 1.3	44.5 ± 2.4	51.1 ± 3.7	0.003
Blood Pressure (mmHg)				
Systolic, lying	128.2 ± 1.8	143.2 ± 4.1	162.3 ± 5.6	0.002
Diastolic, lying	79.6 ± 1.3	86.0 ± 2.7	93.6 ± 3.5	<0.0001
Systolic, standing	125.8 ± 1.9	139.6 ± 4.1	165.4 ± 6.3	0.007
Diastolic, standing	81.8 ± 1.4	88.7 ± 2.3	99.0 ± 4.5	<0.0001
BMI (kg/m^2)	27.8 ± 0.9	29.7 ± 1.1	32.6 ± 1.1	0.07
Blood Glucose (mmol/L)	6.4 ± 0.3	8.4 ± 0.8	11.1 ± 1.4	<0.0001

Values represent mean ± SEM; normal albumin:creatinine ratio (ACR) <3.4 mg/mmol.

In addition, the categoric variables hypertension, diabetes and obesity all showed strong associations with stratified ACR levels ($p<0.02$ in all cases, logistic regression analysis, data adjusted for age and sex). An association was also observed between albuminuria and an increasing number of these coexisting categoric risk factors (Figure 2). The proportion of people whose ACR was normal decreased as the number of coexisting risk factors increased. The risk of microalbuminuria was significantly increased in the presence of one or more risk predictors while the risk of macroalbuminuria increased significantly in the presence of two or more coexisting risk factors (Chi-squared trend analysis).

Figure 2: Association between albuminuria and an increased number of coexisting risk factors



Other observations during screening

The screening program also identified non-renal conditions including heart failure (n = 1), angina/myocardial infarction (n = 1), hepatitis B (n = 1), pregnancy (n = 1), bronchiectasis (n = 1), active scabies (n = 1), chronic leg ulcers (n = 1) and sub-mandibular abscess (n = 1).

Discussion

This article details the results of the first comprehensive screening program for renal disease undertaken in a remote Aboriginal community in South Australia, using a point-of-care instrument (the Bayer DCA 2000) as the primary screening tool for quantifying microalbuminuria. The program has identified a significant burden of incipient and established renal disease among adult members of this rural Aboriginal community. The high rates of microalbuminuria (n = 29; 19%) and macroalbuminuria (n = 13; 9%) found in this study are the first reported for an Aboriginal community in South Australia. They are generally consistent with rates reported in Aboriginal communities in other parts of Australia. For example, a study of approximately 1100 Aboriginal adults (> 15 years) from eight communities in central Australia, the Kimberley and Cape York areas in northern Australia reported microalbuminuria rates of 22% for men and 27% for women, while the prevalence of macroalbuminuria was 10% for men and 13.5% for women[19]. Microalbuminuria rates of 27% have been observed in a large northern Australian community of approximately 700 people[5,20].

Albuminuria, if left untreated, may progress from microalbuminuria to macroalbuminuria and renal insufficiency arising from overt albuminuria[10,21]. Screening for albuminuria using a simple non-invasive urine test, such as urine ACR, is therefore critical because the earlier albuminuria is detected the greater the chance of modifying the progression of the disease. All community members identified with incipient or overt renal disease in The Umoona Kidney Project were offered and accepted the opportunity to participate in tailored clinical and community-based intervention programs that were aimed not only at reducing the burden of renal disease, but also the high rates of associated hypertension, diabetes and obesity found in this community[22,23]. The clustering of these risk factors with albuminuria is part of the overall metabolic syndrome, and all factors need to be addressed concurrently if an impact is to be made on reducing the chronic disease burden of the community.

Indeed, the screening phase of The Umoona Kidney Project was conducted as part of a broad, family-orientated holistic approach to addressing chronic disease within the Aboriginal community setting. Community awareness programs about renal health, the importance of good nutrition and exercise, and strategies to reduce alcohol and tobacco consumption were conducted at different levels for both Aboriginal Health Workers and adults and children in the community[23]. The Flinders and Women's and Children's renal teams also formed partnerships with a number of community groups including the Umoona Aged Care Services, the Aboriginal Meals Program, the Coober Pedy Area School and the Tjapa Tjuta Child Care Centre. At the request of the Aboriginal health-worker team, a nutrition training program was developed by the team's nutritionists specifically for the health workers; the content, level, timing and length of this training program determined by the health workers themselves[23].

The point-of-care DCA 2000 instrument was the cornerstone of the renal screening program. It proved robust and reliable in a remote clinical setting and demonstrated sound analytical performance characteristics during 30 months of regular field use[12]. The purchase price of the DCA at approximately $AU6500 and the cost of ACR reagent cartridges at approximately $AU9 each, means the DCA point-of-care technology is a cost competitive, practical alternative to the pathology laboratory for remote

communities. The ability of the DCA 2000 to generate an on-site result in 7 min provided an improved service for community members and greater client satisfaction, because results could be discussed with the doctor during the consultation. In the early stages of the screening program, a scientist or technician from the visiting renal team operated the DCA to perform the urine ACR tests. However, following an education and training program in September 1999, Umoona's Aboriginal health-worker team assumed full responsibility for performing urine ACR tests in the latter stages of the program. By performing the tests themselves, health workers have been empowered to take greater responsibility for renal screening in their community, while sustainability and community control and ownership of the program has been ensured. The Umoona Kidney Project was formally handed over to the community in December 2000, with the Flinders renal team still providing clinical, scientific, technical and data management support when appropriate.

Conclusion

The practicability, clinical usefulness and cultural appropriateness of using point-of-care technology in the remote Aboriginal health setting has been clearly demonstrated in The Umoona Kidney Project, and further opportunities exist to broaden the scope and application of point-of-care instruments in community-based screening and management programs.

Acknowledgements

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RESULTS OF AN ABORIGINAL COMMUNITY-BASED RENAL DISEASE MANAGEMENT PROGRAM INCORPORATING POINT OF CARE TESTING FOR URINE ALBUMIN:CREATININE RATIO.

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STATEMENT OF AUTHORSHIP

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Rural and Remote Health 2006; 6: Article 591 (on-line)

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BATTERHAM, M.

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Results Of An Aboriginal Community-Based Renal Disease Management Program Incorporating Point Of Care Testing For Urine Albumin:Creatinine Ratio.

While the previous two papers had demonstrated the usefulness of POC urine ACR measurement in community risk assessment, the clinical effectiveness of this POC test in the management of renal patients had never before been investigated in the primary care setting. This paper therefore examined the key research question: Could urine ACR measurement by POCT be applied in a culturally and clinically effective manner within a management framework for renal disease in an Indigenous health service?

The research findings presented in this paper confirmed, for the first time, the clinical utility of urine ACR POCT as part of a broad clinical management strategy that was effective in stabilising renal function and reducing blood pressure in a group of 35 community members identified as at greatest risk of renal disease.

The paper also presented the results of a community questionnaire, which showed that the Umoona Kidney Project had been culturally effective and well accepted by community.

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ORIGINAL RESEARCH

Results of an Aboriginal community-based renal disease management program incorporating point of care testing for urine albumin:creatinine ratio

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ABSTRACT

Introduction: There has been a significant increase in the burden of renal disease among Aboriginal Australians over the past 15 years. Urine albumin:creatinine ratio (ACR) is a well-established marker of microalbuminuria and can be conveniently performed on the DCA 2000 point-of-care testing (POCT) analyser (Bayer Australia; Melbourne, VIC, Australia) with an on-site result available in 7 min. The application of the urine ACR POCT for renal disease risk assessment was pioneered by our group in the Umoona Kidney Project. This article describes the results of the management arm of the Umoona Kidney Project, which used point-of-care urine ACR testing for the first time within a management framework to monitor albuminuria in patients at highest risk of renal disease. The article also examines the analytical quality of POCT results and overall community acceptance of the Umoona Kidney Project.

Methods: Adults clinically assessed by Flinders Medical Centre renal specialists as being at greatest risk for renal disease were offered the ACE inhibitor (ACEI) perindopril on a voluntary basis. Selected renal markers, including POCT urine ACR (conducted on-site by Umoona's Aboriginal health worker team), plasma electrolytes, urea, creatinine, calculated glomerular filtration rate and

blood pressure were measured six monthly. Regular quality control testing was undertaken to monitor the analytical performance of the POCT analyser. A culturally appropriate questionnaire was designed and implemented to assess community satisfaction with the project.

Results: In all, 231 patient management consultations were conducted over a two year period, with over 70% of patients having four or more (up to a maximum of eight) consultations; 35 patients (mean age 49.2 [±2.3] years, 54% males) participated voluntarily in the management arm. All were overtly hypertensive, hypertensive with other risk factors or had diabetes. The renal status of these patients was followed for a mean of 63 ± 4.5 weeks. In total, 111 POCT urine ACR tests were performed for patient management (mean 3.2 tests per patient). There was no significant difference in POCT urine ACR in the study period with a median (and inter-quartile range) of 5.7 mg/mmol (1.2-15.2) pre-ACEI and 4.3 mg/mmol (1.3-16.7) post-ACEI treatment ($p = 0.50$, Wilcoxon signed ranks test). The calculated glomerular filtration rate altered from 110 to 118 mL/min ($p = 0.019$, paired *t*-test). There was no change in the group plasma potassium, urea and creatinine. Collectively these results indicate a stabilisation in renal function among the management group. Blood pressure (both lying and standing) fell significantly in the study period. The imprecision for urine ACR quality control POCT conducted during the management program was within nationally and internationally accepted precision goals for urine albumin, creatinine and ACR. Fifty community members completed the satisfaction questionnaire. Three-quarters of respondents felt there were no cultural barriers in providing a urine sample for urine ACR POCT.

Conclusions: The management arm of the Umoona Kidney Project was effective in stabilising the renal function and improving the blood pressure of community members identified to be at greatest risk of kidney disease. POCT urine ACR testing can be utilised, not only for community risk assessment, but also for patient management. The Umoona Kidney Project was well accepted by the health service and community members.

Key words: Aboriginal health, management, point of care testing, renal disease, urine albumin:creatinine ratio (ACR).

Introduction

There has been a significant increase in the burden of renal disease among Aboriginal Australians over the past 15 years in particular. Recently, rates of end-stage renal disease (ESRD) among Aboriginal Australians and New Zealand Maori people were reported as being eight-fold that of non-Indigenous people[1]. In Australia, rates of ESRD among Aboriginal people are generally correlated with increasing degrees of remoteness, with some of the highest rates recorded in the desert regions of the Northern Territory, Western Australia, South Australia and far western Queensland[2]. Aboriginal communities from these remote regions often have poor access to health care and general goods and services, especially fresh foods. They may also endure poor environmental living conditions and poor water quality, and suffer social disadvantage which may contribute to their susceptibility to chronic disease[3].

Renal disease is often asymptomatic and, as a result, effective health strategies are needed for the early identification of Aboriginal people at risk of renal disease[4,5]. Once detected, there is a critical requirement for structured renal disease management programs because the natural history of renal disease is amenable to change through the judicious use of antihypertensive agents such as angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers[6-10].

Urine albumin:creatinine ratio (ACR) is a well established biochemical marker of microalbuminuria[11-13] and this test

can now be conveniently performed on the DCA 2000 point-of-care (POC) analyser (Bayer Australia; Melbourne, VIC, Australia)[14]. Point-of-care testing (POCT) enables this pathology test to be performed on-site in the Aboriginal community setting by a trained health professional, with quantitative results available within 7 min. The Community Point-of-Care Services unit at Flinders University conducted the first scientific validation of this new POC test in Australia[14] and pioneered its application in the Aboriginal community setting through the Umoona Kidney Project[15-16].

The Umoona Kidney Project was a cooperative partnership between the Umoona Tjutagku Health Service at Coober Pedy in South Australia's far north, 850 km north of Adelaide, and the renal units at the Flinders Medical Centre and the Women's and Children's Hospital, Adelaide. The project was conducted between 1998 and 2000 and the aims of the adult component of the project were two-fold: to determine the renal disease risk profile among the community's adults, and to implement a management program to monitor those adults at greatest risk of developing ESRD.

The results of the risk assessment arm of the program have previously been reported[15-16]. This article describes the results of the renal disease management program, and investigates the following research questions: can urine ACR POCT be applied in a culturally and clinically effective manner within a management framework, and how well was the Umoona Kidney Project accepted by the community?

Methods

Community consultation

Prior to commencing the management program, clinical and scientific staff from the Renal Unit at Flinders Medical Centre conducted a series of meetings with the community and the Board of the Umoona Tjutagku Health Service to discuss the most culturally appropriate way of introducing the management program. A culturally appropriate community brochure on the Umoona Kidney Project was also developed by the community nurse, members of the Aboriginal health worker team and the program manager, and disseminated to all members of the community.

Ethics approval

Ethics approval to conduct the management arm of the Umoona Kidney Project was obtained from the Aboriginal Health Research Ethics Committee of South Australia and the Flinders Medical Centre Committee on Clinical Investigation.

Flinders renal clinical and scientific team

The Flinders Medical Centre renal team consisted of the program manager/scientist, two renal specialists (one male and one female), a scientist responsible for patient data management and a nutritionist. A Flinders' medical student (MB) was supported through a National Health and Medical Research Council (NHMRC) scholarship to conduct a community satisfaction survey.

Selection of patients for inclusion in the management program

Following completion of the risk assessments, adult members of the community considered at highest risk for renal disease underwent a clinical and pathology review by the Flinders renal specialists. The ACEI perindopril was subsequently offered to members of this group clinically assessed as being likely to receive the greatest benefit from this intervention.

All persons were individually counselled about the potential benefits and side-effects of ACEI medication (in particular angioneurotic oedema and anaphylaxis, which required urgent medical attention). Significant adverse side-effects were required to be reported to Flinders Medical Centre's

Committee on Clinical Investigation and the Clinical Drug Trials Committee.

The following people were excluded from treatment with ACEI: pregnant or breast-feeding women, women at risk of becoming pregnant, persons with a plasma potassium greater than 5.2 mmol/L, and persons who had a demonstrated history of intolerance to ACEI.

Similar to the risk assessment arm, participation of Umoona community members in the management phase of the project was voluntary, and patients could withdraw from taking medication at any time and for any reason. Every patient who voluntarily participated in the study signed a written consent form in the presence of the clinic nurse and an Aboriginal health worker.

Monitoring of patients in the management arm

Adults participating in the management arm were initially given a low dose of ACEI to assess their tolerance and identify any side-effects. Blood pressure, plasma potassium and creatinine were measured within 7 to 10 days after initiation of treatment (via a blood sample sent to the pathology laboratory at Flinders Medical Centre). Subsequently, dosage of medication was titrated to a maximum of 8 mg for each person, with the aim of achieving a target blood pressure of less than or equal to 130 mmHg (systolic) and 80 mmHg (diastolic). If the patient's blood pressure was still high after reaching the maximal effective dose of ACEI, then a calcium channel blocker was added to achieve optimal blood pressure control.

Adults in the management arm were monitored at every field visit through clinical consultation with the Flinders renal specialists. Selected renal markers, including urine ACR by POCT, plasma electrolytes, urea, creatinine, calculated glomerular filtration rate and blood pressure were measured at six-monthly intervals or when deemed appropriate by the specialists. The urine ACR was measured on a fresh first morning urine sample by POCT, with responsibility for urine ACR testing taken by the Umoona Aboriginal health worker team. Dipstick urinalysis was performed prior to urine ACR POCT and a microscopic urine assessment was conducted on-site if the urine specimen exhibited gross proteinuria or haematuria. A 24 hour urine protein estimation was performed on those patients who were or had become macroalbuminuric (urine ACR greater than or equal to 30 mg/mmol). HbA1c was measured at three-monthly intervals for patients with diabetes and 12 monthly for non-diabetics. Possible side-effects (including angioneurotic oedema, persistent cough, hypotension and dizziness) were monitored at every visit.

In addition to on-going specialist renal advice, patients were counselled on the management of other risk factors such as alcohol, smoking and obesity. The Flinders nutritionist also provided dietary advice.

Compliance

Patients in the management arm of the program were required to visit the Umoona clinic on a monthly basis to collect their tablets in individual dosette boxes prepared by the Umoona clinic nurse. Compliance was assessed through monthly tablet counts performed by the clinic nurse and recorded on a manual record system, which detailed the date when a new supply of tablets was given to each patient and the date when the patient returned to collect their next month's supply.

Patients were considered compliant if they took at least 80% of required number of tablets each month. Patients were considered non-compliant if they took less than 50% of their monthly tablets. For patients who were non-compliant or who were unable to attend the clinic, Umoona's Aboriginal health worker team prepared individual dosette boxes which were hand-delivered to patients as part of a 'tablet run' at 8 am each morning.

Electronic documentation of management plans

Patient information was entered electronically into a data management program (designed specifically for the program

using Microsoft Access software). To maintain confidentiality each patient was assigned an individual code number which was used as their unique identifier in their electronic record. The master copy of the electronic data base was held by the scientist responsible for data management, while access to the data base was password protected and restricted to the data manager, project manager, renal specialists and clinic nurse. All biochemical and haematological results and current treatment plans could be reviewed, in chronological sequence, at each clinical consultation by the renal specialist team.

Point of care testing for urine ACR

The program manager delivered a series of continuing education and training sessions about urine ACR POCT for Umoona's Aboriginal health worker team, during which the health worker team was progressively taught how to conduct urine ACR POCT on patients, and how to perform quality control testing to monitor the analytical performance of the DCA 2000. A series of laminated posters were provided to visually demonstrate the step-by-step processes of urine ACR patient and quality testing on the DCA 2000. By the commencement of the management arm of program, Umoona's Aboriginal health worker team had taken over responsibility for urine ACR POCT on the DCA 2000.

The POCT analyser provided a quantitative measurement of urine albumin by immunoturbidimetry, urine creatinine by colorimetry and then calculated the ratio of these analytes[17]. The urine ACR test, performed using DCA 2000 Microalbumin/Creatinine reagent kits (Bayer Australia; Melbourne, VIC, Australia), was completed in 7 min on the DCA 2000.

The DCA 2000 Microalbumin/Creatinine Low and High Control kit (Bayer Australia; Melbourne, VIC, Australia) was used to monitor the analytical imprecision of urine ACR POCT results. A quality control test (alternating between the low and high control) was performed each time a new reagent kit (containing 10 cartridges) was opened. Imprecision was calculated as a coefficient of variation (CV%) from the results of repeated analysis of each quality control sample.

Survey of community satisfaction

The Flinders NHMRC medical student developed a culturally appropriate questionnaire to assess community attitudes towards, and satisfaction with, the Umoona Kidney Project[18]. The satisfaction tool for this project was initially developed in collaboration with behavioural psychologists from the School of Medicine at Flinders Medical Centre. The tool was then validated for its cultural appropriateness through consultation with the manager of the Aboriginal Health Unit at Flinders Medical Centre and the director, health workers and the clinic nurse from Umoona. The Board of the Umoona Tjutagku Health Service approved the final questionnaire. The questionnaire was implemented at the community level by Umoona's Aboriginal health workers, the nurse-in-charge, two community leaders and the medical student.

The questionnaire consisted of a series of general questions, to which multiple responses could be ticked, and a set of more specific questions, based on the 5 point Likert scale[19], with respondents rating their attitude to the questions posed (from 'very much yes' to 'very much no').

Statistical analysis

Analysis of the results from patient management was performed using both the Analyse-It (Analyse-It Software Ltd; Leeds, UK) and SPSS Version 12.0.1 for Windows (SPSS Headquarters; Chicago, IL, USA) statistical software packages.

Results

On-site consultations with the renal specialists

The Flinders renal specialists conducted 231 patient consultations in the two years of the management program,

with over 70% of patients having four or more (up to a maximum of eight) consultations.

Patients entering the management program

Fifty-seven community members were initially assessed as being at risk for renal disease. All were overtly hypertensive (systolic blood pressure greater than 140 mmHg and/or diastolic blood pressure greater than 90 mmHg over three independent blood pressure readings), hypertensive (systolic blood pressure greater than 130 mmHg and/or diastolic blood pressure greater than 80 mmHg over three independent readings) with other risk factors, or had diabetes. Ten patients were excluded from the study because they were already taking ACEI medication, they were women of child-bearing age, their blood pressure had improved through lifestyle changes, or their blood pressure was too unstable to commence treatment. Six males did not wish to participate for personal reasons, while four people no longer lived in the community. Two commenced a low dose of ACEI, but were withdrawn due to a perceived increase in aggression ($n = 1$) or to the effects of headache, itchiness and minor numbness on the right side of the face ($n = 1$). The remaining 35 patients voluntarily entered the management arm of the program. The baseline characteristics of these patients in the management group are shown (Table 1).

Patient management results

The renal and blood pressure status of these patients were followed for a mean of 63 ± 4.5 weeks. There were no significant adverse events reported or observed clinically in this group. At the completion of the study period, 39% of patients were taking 2 mg, 29% were taking 4 mg, 3% taking 6 mg and 29% taking 8 mg of ACEI, respectively. A total of 72% of clients were clinically assessed as compliant, 22% were considered compliant 65% of the time and 5% were non-compliant.

Over the 2 years of the management phase of the project, 111 urine ACR tests were performed by POCT for patient management (mean 3.2 tests per patient). There was no statistical difference in urine ACR levels in the study period (median [and inter-quartile range] 5.7 mg/mmol [1.2-15.2] pre-ACEI and 4.3 mg/mmol [1.3-16.7] post-ACEI treatment $p = 0.50$, Wilcoxon signed ranks test). Categorisation of patients into those exhibiting normoalbuminuria, microalbuminuria and macroalbuminuria (Table 2) revealed a trend towards improving albuminuria although these trends did not reach statistical significance due to small patient numbers (χ^2 test; (χ^2statistic = 0.496, degrees of freedom = 2, $p = 0.780$). One patient with initial microalbuminuria recorded a normal ACR post ACEI. The urine ACR levels in three diabetes patients with initial macroalbuminuria decreased by 27%, 64% and 78% respectively, with each patient falling within the microalbuminuria category post-ACEI treatment. The urine ACR in one patient with microalbuminuria deteriorated from 13.5 to 36.6 mg/mmol post ACEI. This patient was non-compliant in taking medication and was repeatedly hospitalised for other illnesses during the study period. Previous studies have shown that urine ACR levels deteriorate by approximately 15% per annum if antihypertensive treatment is not undertaken[20]. The calculated glomerular filtration rate of the group altered from 110 to 118 mL/min ($p = 0.019$, paired t-test). There was no change in the group's plasma potassium, urea and creatinine (Table 2). Collectively these results indicate a stabilisation in renal function among the management group.

In the study period, there was a sustained and statistically significant reduction in mean blood pressure (both lying and standing) after ACEI intervention (Fig 1). Systolic blood pressure fell from 151±3 mmHg to 137±3 mmHg (lying) and from 147±3 mmHg to 131±3 mmHg (standing) ($p < 0.001$, paired t-test). Diastolic blood pressure similarly fell from 92±2 mmHg to 84±2 mmHg (lying) and from 94±2 mmHg to 84±2 mmHg (standing) ($p < 0.001$, paired t-test).

Table 1: Baseline characteristics of 35 patients taking ACE inhibitor medication (number or percent for each selected parameter).

Parameter	*N* or %
Mean age (SE) in years	49.2 (2.3)
Male (%)	54
Blood pressure >130 and/or >80 mmHg with risk factors	35
Blood pressure >140 and/or >90 mmHg	33
Diabetes mellitus	12

Table 2: Albuminuria status and selected biochemical measures in patient group (n = 35) pre- and post-ACE inhibitor treatment

Parameter	Pre-ACEI	Post-ACEI	*P*-value
Albuminuria status (%)			
Normal ACR (<3.5 mg/mmol)	42%	46%	
Microalbuminuria (3.5<ACR<30 mg/mmol)	35%	38%	
Macroalbuminuria (ACR >30 mg/mmol)	23%	15%	
Biochemical markers	Mean ± SD	Mean ± SD	
Plasma potassium (mmol/L)	4.0 ± 0.1	4.0± 0.1	0.226
Plasma urea (mmol/L)	4.9 ± 0.3	5.1 ± 0.3	0.510
Plasma creatinine (µmol/L)	81± 3	77 ± 3	0.05

ACEI, ACE inhibitor; ACR, albumin:creatinine ratio.

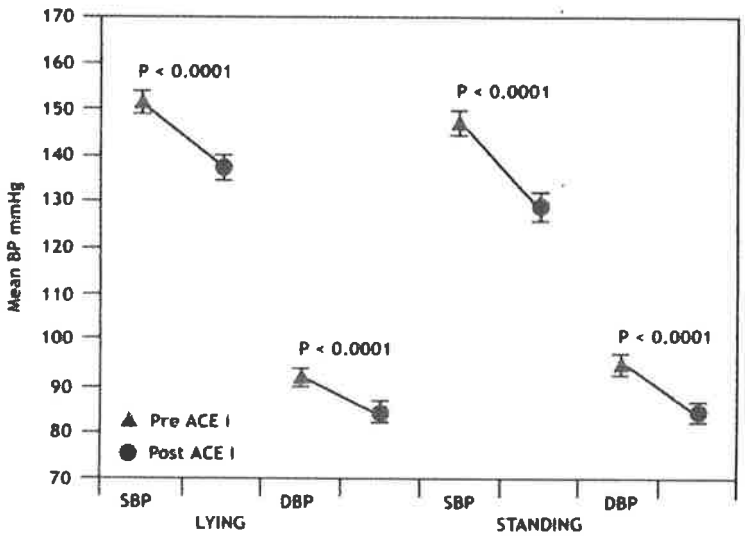

Figure 1: Improvement in mean blood pressure (BP; both lying and standing) in patient group (n = 35) following ACE inhibitor (ACE i) treatment. DBP, diastolic BP; SBP, systolic BP.

Quality testing

For quality control testing conducted during the management phase of the Umoona Kidney Project ($n = 20$), the DCA 2000 recorded an imprecision (coefficient of variation, CV%) of 8.3% and 3.9% for urine albumin (for quality control samples with concentrations of approximately 36 and 210 mg/L respectively), 5.5% and 3.9% for urine creatinine (9 and 35 mmol/L) and 7.4% and 3.0% for urine ACR (ratios of 4.0 and 6.7 mg/mmol). These levels of imprecision are consistent with that observed for quality control testing in the entire life of the Umoona Kidney Project[15] and are well within national and international precision goals of 10%, 6% and 12% for urine albumin, creatinine and urine ACR respectively that have been derived from biological variation and other international consensus data on performance criteria[21-23].

Community acceptance

Fifty community members completed the questionnaire on the Umoona Kidney Project, including 76% of the patients who participated in the program. The results obtained for selected questions relating to this article are shown (Table 3). Over two-thirds of the community were concerned about developing renal disease. Three-quarters felt there were no cultural barriers in providing a urine sample for ACR POCT.

Of respondents, 98% understood the project's educational messages about how regular 'checks' for kidney disease could lessen their risk of developing advanced renal disease and they believed the community was comfortable with the concept of risk assessment. Over 95% were satisfied with the way the Flinders' renal team worked with them as individuals, while 94% agreed the renal team had helped the community overall in addressing renal disease.

In response to the general question *Can you tell me why the kidney team comes here?*, 63% of the 49 respondents ticked the following two responses *Help people at risk of getting bad kidney disease to stay healthy* and *Find out who has bad kidney disease*. One-third ticked the response *Help the community to understand the benefits of treatment*.

Discussion

The Umoona Kidney Project had many unique features which set it apart from other chronic disease programs for Aboriginal Australians. It adopted a strong family-orientated holistic approach (involving both adults and their children) and empowered and encouraged community ownership. Community members received on-site clinical advice (for both renal disease prevention and management) from a team of renal specialists who conducted 24 visits to the community over 3 years. While acknowledging this approach was intensive and difficult to sustain, it occurred in a time when the community did not have its own salaried medical officer. Importantly, POC pathology testing for urine ACR was used for the first time in an Aboriginal community setting in the Umoona Kidney Project. Umoona's Aboriginal health worker team received a continuous, structured education and training program on POCT delivered by the program manager. The health worker team were taught not only how to conduct urine ACR POCT on patients, but they also undertook their own quality testing procedures to assess the performance of their DCA 2000 analyser for urine ACR measurement. These processes provided a significant sense of empowerment for the health workers[24]. For Umoona's community members, the immediacy of the urine ACR POCT result meant they could see the renal specialist and have their treatment modified without the need to attend a follow-up visit to obtain their result. A further unique design aspect of this study was the specific requirement for patients to provide a first morning urine sample to test for ACR in preference to the more easily obtained random sample. The first morning urine is the recommended specimen of choice for the urine ACR test[13]. It provides the most accurate measure of urine ACR, as it is not subject to the wide diurnal biological variation exhibited

by urine albumin and therefore has a much lower rate of false positive results than the random sample.

The value of POCT for community risk assessment has previously been described by our group[15-16] but this article reports for the first time the practical and culturally appropriate use of urine ACR POCT on the DCA 2000 for the management of Aboriginal renal disease. The renal function of the patient group stabilised over the 2 year study period, as measured by POC urine ACR testing and other renal markers. The use of POC urine ACR testing was analytically sound and comparable to the performance expected of a pathology laboratory, while the use of POCT was culturally appropriate and widely accepted within the Aboriginal community setting. Community-based POCT not only raised the cultural awareness of renal disease, but also facilitated the development of a number of other community health promotion programs, particularly centred on nutrition, as previously reported by our group[25].

The efficacy of the ACEI medication in improving renal and cardiovascular function in the Aboriginal health setting has also been confirmed in this study, and our results are consistent with other workers in this field[26-27].

The high level of acceptance of the Umoona Kidney Project by the community was confirmed from the results of the community survey. As further testament to the success of the program, the inaugural director of the Umoona Tjutagku Health Service wrote the following comments in a letter to the program manager at the conclusion of her tenure as Director:

> *In my twenty years of working with Aboriginal people I have never seen such dedication, coupled with sensitivity in a group working with Aboriginal people. The* [renal] *team has built up a feeling of trust amongst community members and has made many friends. The team's willingness to listen and involve the community has provided a good model for future projects.*

Table 3: Summary of questionnaire responses (n = 50) to ascertain community attitudes towards the Umoona Kidney Project

Question	Community members' responses				
	n (%)				
	Very much Yes	A little bit Yes	Don't care	A little bit No	Very much No
Do you worry that you will get bad kidneys?	24(48)	10(20)	1(2)	0	15(30)
Does your culture make it hard for you to have your kidneys checked (by providing a urine sample)?	6 (12)	2 (2)	4 (8)	4 (8)	33 (67)
Do you think that people who have their kidneys checked might save themselves from getting sick?	46 (94)	2 (4)	1 (2)	0	0
Are you happy with the way the kidney team treats you?	38 (95)	1 (3)	1 (3)	0	0
Do you feel the community is happy about individuals having their kidneys checked?	45 (92)	3 (6)	1 (2)	0	0
Do you think the kidney team helps the community?	44 (88)	4 (8)	2 (4)	0	0
Do you think the community is happy with the kidney team?	33 (77)	8 (17)	3 (6)	0	0

It should be acknowledged that this study was conducted in a single community with a relatively small samples size and was not a randomised controlled study. Nonetheless, in December 2000, the Umoona Kidney Project was handed over to the Umoona Community as a self-sustaining activity fully integrated into the health service infrastructure. Both the South Australian Government's Department of Human Services Renal and Urology Services Implementation Plan 2000-2011[28] and the state-wide Iga Warta Aboriginal Renal Disease Summit 1999 endorsed the Umoona model and recommended its expansion to other Aboriginal communities in rural and remote South Australia.

From this pioneering work, a national Australian Government funded POCT program called QAAMS (Quality Assurance for Aboriginal Medical Services) has been developed in which POCT for both HbA1c and urine ACR is used to assist the management of Aboriginal patients with diabetes and associated renal disease[29-31]. Sixty-five Aboriginal medical services encompassing every state and territory in Australia now participate in this unique POCT program. Both the HbA1c and urine ACR POC tests have their own Medicare rebate item number, which enables the costs of performing these tests to be fully refunded to the participating health services and ensures the program is cost-neutral in terms of on-going reagents needed to perform the POC tests and consumables.

Acknowledgements

The Umoona Kidney Project was funded by grants from the South Australian Health Commission (1998), the Office for Aboriginal and Torres Strait Islander Health (OATSIH) in the Commonwealth Department of Health and Aged Care (1999-2000), Servier Laboratories (Australia) Pty Ltd, the Australian Kidney Foundation and Janssen-Cilag Pty Ltd. Dean Whiting and Alison Halfnights from Bayer Australia are also thanked for their support of the Umoona Kidney Project. Our now retired clinical colleague, Dr Lindsay Barratt devoted significant time, commitment and energy to the Umoona Kidney Project. Our close friends and colleagues at the Women's and Children's Hospital (Dr Ken Juriedini, Dr Margie van Renen and Sandra Harris) are gratefully acknowledged for their work on the concurrent children's arm of the project. All members of the Umoona community are sincerely thanked for their participation and long-term support of the Umoona Kidney Project. Maryanne Hudson, Cissie Riessen, Michael Brown and Gaye McLeod worked as Aboriginal health workers during the program, along with Sisters Vicki McCormack and Chris Durden (clinical nurses at Umoona). Ian Crombie (former Chairman of the Board of the Umoona Tjutagku Health Service) and Waluwe Simpson-Lyttle and Janice Braun (former Directors of the Umoona Tjutagku Health Service) all had major input to the success of the program at the community level.

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CULTURAL AND CLINICAL EFFECTIVENESS OF THE 'QAAMS' POINT-OF-CARE TESTING MODEL FOR DIABETES MANAGEMENT IN AUSTRALIAN ABORIGINAL MEDICAL SERVICES.

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Clinical Biochemistry Reviews 2006; 27: 161-170.

Cultural And Clinical Effectiveness Of The 'QAAMS' Point-Of-Care Testing Model For Diabetes Management In Australian Aboriginal Medical Services.

While the analytical quality of POCT for HbA1c and urine ACR in the national QAAMS Program had been verified unequivocally through the results of quality assurance and quality control testing, key research questions concerning the clinical and cultural effectiveness of the QAAMS model remained unanswered until the publication of this significant paper. These were:

- How well had POCT been accepted by key stakeholders in the Indigenous community, namely Aboriginal Health Workers as POCT operators, Indigenous patients with diabetes as consumers of the POCT service and clinicians responsible for management of these patients? and
- Could POCT conducted for the management of diabetes patients be clinically effective and contribute to improvements in glycaemic control?

This paper provided the evidence base to answer these important research questions. A detailed questionnaire distributed to the three stakeholder groups verified, for the first time, that POCT conducted on a national scale had been well accepted as a convenient, practical and culturally appropriate mode of health service delivery by all stakeholder groups. Patient data (n=74) obtained from two participating Indigenous medical services also confirmed, for the first time, that POCT contributed to improved clinical outcomes in this setting, as evidenced by statistically significant reductions in HbA1c levels in these diabetes patients one year after commencing POCT.

The introduction of Medicare rebates for POCT HbA1c and urine ACR testing conducted by QAAMS participants represents a further significant research outcome from the QAAMS Program and has ensured the sustainability of the model.

Report

Cultural and Clinical Effectiveness of the 'QAAMS' Point-of-Care Testing Model for Diabetes Management in Australian Aboriginal Medical Services.

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Abstract
The national Quality Assurance for Aboriginal Medical Services (QAAMS) Program, in which point-of-care testing (POCT) for haemoglobin A_{1c} (HbA_{1c}) and urine albumin:creatinine ratio (ACR) is performed for diabetes management in 65 Australian Aboriginal medical services, is now embedded in the practice of diabetes care across Indigenous Australia. This paper documents the results of a detailed survey to assess levels of satisfaction with the QAAMS HbA_{1c} Program among three key stakeholder groups – doctors, POCT operators and patients with diabetes. Both doctors and patients with diabetes agreed that the immediacy of POCT results contributed positively to patient care, improved the doctor-patient relationship, and made the patient more likely to be both compliant and self-motivated to improve their diabetes control. Both POCT operators and patients with diabetes reported improved satisfaction with their diabetes services after the introduction of POCT. The paper also provides evidence from two participating medical services that POCT has been an effective tool in improving the delivery of pathology services and clinical outcomes for both individuals and groups of patients with diabetes. A statistically significant reduction in HbA_{1c} from 9.3% (± 2.0) to 8.6% (± 2.0) was observed in 74 diabetes patients 12 months after commencing POCT ($p = 0.003$, paired t-test). An improvement in the percentage of patients achieving glycaemic targets and a reduction in the percentage of patients with poor control was also observed in this group. These data provide evidence that the QAAMS POCT model delivers a culturally and clinically effective service for diabetes management in Aboriginal Australia.

Introduction

Type 2 diabetes mellitus and its principal complications, renal disease and retinopathy, are responsible for a significant burden of morbidity, mortality, social and cultural trauma in Australia's Aboriginal people.[1-3] In 1998, Australia's National Diabetes Strategy and Implementation Plan recommended that a trial of POCT for HbA_{1c} on the DCA 2000 analyser (Bayer Diagnostics, Tarrytown, NY, USA) be conducted in Australian Aboriginal Medical Services to assist diabetes management for Indigenous people.[4] The resultant QAAMS Program for HbA_{1c} POCT commenced as a pilot in 45 Aboriginal Medical Services in June 1999. Six years later, the national QAAMS Program has 65 participating medical services, 75% of which are located in rural and remote Australia. The program has now become firmly embedded in the practice of diabetes care for Aboriginal people.[5-7] In 2003, the program was expanded to include urine ACR POCT on the DCA 2000 to monitor microalbuminuria in Aboriginal diabetes patients.[8] The QAAMS Program has been continuously funded by the Australian Government's Department of Health and Ageing since its inception.

The QAAMS model provides continuing education, training, competency assessment and support services for Aboriginal health workers and allied health professionals in their role as in-service POCT operators. The program also has a unique quality management framework involving both internal quality control and external quality assurance testing. These features set QAAMS apart from any other model of primary health care delivery for Indigenous communities world-wide. The ability of Aboriginal health workers to conduct POCT in the field to an analytical standard that meets current

laboratory-based goals has been verified for both HbA_{1c} and, more recently, urine ACR testing.[5-6,8]

However, two key research questions for the QAAMS Program remained unanswered. Firstly, how well had the program been accepted by clinical staff (utilising POCT results for patient management), by Aboriginal health workers and allied health professional staff (as POCT field operators) and by patients with diabetes (the consumers of the POCT service)? Secondly, had POCT been an effective tool in improving clinical outcomes for both individuals and groups of patients with diabetes?

This paper provides the evidence base to answer these questions. It documents the results of a detailed questionnaire to assess levels of acceptance with the QAAMS HbA_{1c} Program among its three key stakeholder groups – doctors, POCT operators and patients with diabetes. The paper also reports improvements in glycaemic control among diabetes patients at two rural and remote Aboriginal medical services in the QAAMS Program following the introduction of POCT.

Methods

Questionnaire for Key Stakeholders in the QAAMS Program

During mid-2004 the QAAMS Program Manager, in collaboration with the Flinders University Centre for Biostatistics and Epidemiology, prepared three questionnaires for dissemination to all Aboriginal medical services participating in the QAAMS Program. A small group of Aboriginal health workers from selected medical services assessed the questionnaires for their cultural appropriateness in their development phase.

The questionnaires were specifically designed to determine satisfaction levels with the QAAMS HbA_{1c} Program among three key stakeholder groups; namely doctors, Aboriginal health workers and allied health professionals, and patients with established diabetes.

Each questionnaire contained a series of short statements or questions, with respondents rating their level of agreement or disagreement with the statement or question posed according to a five-point Likert scale.[9] Participants were given equal opportunity to agree or disagree with each statement or question. The questionnaire also listed other open questions where a more detailed written response was requested or selections could be made from a series of options provided. In relation to the patient questionnaire, Aboriginal health workers were invited to work with and assist as many diabetes patients as possible to complete this questionnaire. All respondents completed the questionnaires anonymously.

Distribution of the questionnaires commenced in mid-July 2004. The Chief Executive Officer of each Aboriginal medical service was also sent an accompanying letter, explaining the purpose of the questionnaires. Services were asked to return their completed questionnaires by fax or post by mid-October 2004.

The results of the questionnaires were analysed by the QAAMS Program Manager, in collaboration with an epidemiologist (Dr Kristin McLaughlin) from the Flinders Centre for Biostatistics and Epidemiology using the Epidata software program (www.epidata.dk).

Impact of POCT on Delivery of Pathology Services and Clinical Outcomes

For the past two years, the QAAMS Program Manager and his supporting scientific team have worked closely with two Aboriginal health services in rural and remote Australia to collect information concerning the impact of POCT on the delivery of pathology services and on clinical outcomes among individuals and groups of patients with diabetes. These studies have been conducted at the request of the health services concerned and have been undertaken since full DCA 2000 POCT services for diabetes management were introduced at each site.

Information was initially obtained on the number of HbA_{1c} test requests from patients with diabetes who attended their clinics for set periods immediately preceding and following the introduction of POCT; these periods were one year for service 1 and two years for service 2, respectively.

POCT HbA_{1c} results on patients with diabetes who attended the clinics at both services were monitored across a 12-month period to assess the change in glycaemic control following the introduction of POCT. All POCT HbA_{1c} tests were performed on-site by the principal Aboriginal POCT operator at each site.

Results

Questionnaire for Key Stakeholders in the QAAMS Program

(i) Questionnaire for Doctors

41 doctors completed the clinician questionnaire. A summary of their responses is shown in Table 1. Greater than 95% of doctors agreed that POCT provided a convenient service for them. Approximately 90% felt confident with the accuracy and reliability of the POCT result and that POCT was an acceptable alternative to the laboratory. More than 90% of doctors stated that the immediacy of the POCT result contributed positively to patient care, they were comfortable in continuing to use POCT for patient management, and they would like to see POCT available to all patients with diabetes

Table 1. Results of satisfaction questionnaire for doctors (n=41)

Synopsis of Statement	DISAGREE Strongly Disagree or Disagree		UNSURE		AGREE Agree or Strongly Agree	
	n	%	n	%	n	%
Section 1. Specific Questions						
Convenience						
Satisfied with POCT results immediately available	1	2%	1	2%	39	96%
Advantage discussing results immediately with patient	1	2%	0	0%	40	98%
Analytical Quality						
Confident in accuracy and reliability of POCT result	1	2%	4	10%	36	88%
POCT acceptable alternative to laboratory	2	5%	2	5%	37	90%
Patient Care Issues						
Immediate result contributes positively to patient care	1	2%	1	2%	39	96%
Immediate result contributes positively to patient compliance	2	5%	17	41%	22	54%
Immediate result contributes positively to relationship with patient	2	5%	5	12%	34	83%
Patient more likely to return if POCT available	2	5%	14	34%	25	61%
POC HbA_{1c} testing made positive contribution to patient management	1	2%	1	2%	39	96%
Like POCT for HbA_{1c} to continue for diabetes management	1	2%	0	0%	40	98%
General Issues						
Like to see POCT for HbA_{1c} available for all diabetics in the community	1	2%	3	7%	37	91%
POCT for HbA_{1c} more clinically and culturally effective than laboratory	2	5%	4	10%	34	85%

in their community. More than 80% of doctors agreed that POCT provided a more culturally and clinically effective service for the patient than their laboratory service and that POCT contributed positively to their rapport and relationship with their patients. Over 60% of the doctors felt that patients were more likely to return for a follow-up visit, with more than half believing the immediate availability of results contributed positively to patient compliance with medication.

One doctor responded negatively to all questions asked. This doctor preferred to use the local laboratory service, ordering a complete profile of tests for diabetes management on every patient. The Aboriginal health workers at this site remained keen to use the DCA 2000 but had been progressively discouraged to do so by the doctor.

Selected written comments received from doctors are listed below in response to the question: How did you view the clinical effectiveness of the DCA 2000 point-of-care testing program overall and (could you comment on) whether it had contributed to improved diabetes management in your service? These comments are reflective of the overall views of the 23 doctors who responded to this question.

'This has made a well run Diabetic Clinic to be more effective and impressive to the patient; most of the aboriginal patients are reluctant to come back in a few days for their results. Thus, a well-run point of care test facility gives me a chance to have a bird's eye view of where a patient stands and helps me to readjust their regime.'

'The DCA 2000 POC test adds greatly to the assessment and management of diabetics in our practice by giving a 'real time' picture of the progress, especially after changes have been made to their management. It enhances doctor/diabetic team AND patient satisfaction and most certainly imparts positively on patient outcomes.'

'Many clients of this service do not come for follow-up appointments and so it is very beneficial to have the POC HbA_{1c} result available at the time of that visit rather than hoping they will return. Treatment decisions about need for medication change or need for further diabetic education, weight loss, or diet, etc., can all be made at the one visit. This greatly improves patient care and

> the likelihood of reducing long-term diabetic complications.'
>
> 'The advantages of having this POC testing are incalculable. There are many patients we would otherwise not be able to follow-up or treat appropriately. This is because they are often travelling, they have some reluctance to go to pathology dep[artmen]t. within the hospital, or they do not understand the risks associated with their illness.'
>
> 'HbA_{1c} testing was poorly taken up prior to the POC program. Seeking out people for urine testing was even harder. Now that we can give immediate results and discuss them straight away, clients are happy. They are even happier that the AHWs [Aboriginal health workers] are doing all this. We now are collecting consistent longitudinal data.'

(ii) Questionnaire for POCT Operators (Aboriginal health workers and allied health professionals)

65 respondents completed this questionnaire. Of the 61 who specified their health profession, 51% were Aboriginal health workers and 41% were nurses; the remaining respondents were diabetes educators (2), a community health worker (1) and a primary health care network co-ordinator (1). A summary of their responses is shown in Table 2.

Greater than 90% of POCT operators agreed that the QAAMS educational resources were culturally appropriate, and they understood why the HbA_{1c} test needed to be performed on patients with diabetes and what the result meant in terms of diabetes control. Greater than 90% of respondents were confident in using the DCA 2000, in the accuracy and reliability of the POCT result, and in discussing the result with their patients. POC HbA_{1c} testing on a finger-prick sample was considered an acceptable alternative to laboratory testing on a venous sample. Greater than 90% of respondents understood the need to perform quality assurance testing and felt the frequency of this testing (two samples per month) was appropriate. They also felt the level of support and the training methods of the QAAMS management team were culturally appropriate.

POCT operators agreed that patients were comfortable in having POC HbA_{1c} testing performed as part of their diabetes management. Overall community acceptance of POCT was high, with approximately 80% of POCT operators agreeing that POCT on the DCA 2000 had provided a focus for raising community awareness about diabetes and had enhanced community ownership.

POCT operators were also asked to rate how satisfied they were with the diabetes services for their patients before and after the introduction of POC HbA_{1c} testing on the DCA 2000. Figure 1 shows the satisfaction rating of the 57 POCT operators who responded to this question. The percentage of POCT operators who were unsatisfied with, or unsure about, their diabetes service fell from 30% to 4% and 28% to 7% after the introduction of POCT respectively, while the percentage who were satisfied with their diabetes service increased from 42% to 90% after POCT was introduced (Fishers Exact chi-square = 4.12, p = 0.271). While this result is not statistically significant due to the small sample size, the improvement in satisfaction rating with diabetes services since the QAAMS Program commenced is clearly evident.

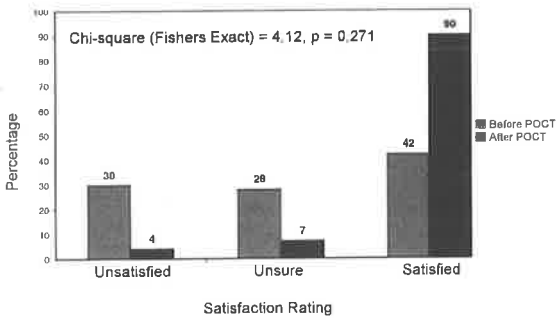

Figure 1. POCT operator satisfaction with services for managing patients with diabetes before and after the introduction of POCT (n=57).

When asked in a series of open questions what the QAAMS Program had meant to them personally, over 90% of POCT operators stated that it had enabled them to know their community members with diabetes better and had given them a greater role in their management, while over 70% indicated it had provided them with a sense of empowerment and had made them better known in their community.

When asked to specify in what ways their diabetes services had improved following the introduction of POCT, over 95% of POCT operators stated that POCT was more convenient than the laboratory service, with patients having their POC test and seeing the doctor during the one visit. 85% of respondents felt POCT had improved patient self-motivation.

POCT operators were also asked to comment on what were the main issues in maintaining the QAAMS Program in the long-term. Over two-thirds felt that neither their current workload nor the number of programs they were responsible for would preclude them from maintaining participation in QAAMS. Nearly three-quarters of respondents felt their

Table 2. Results of satisfaction questionnaire for POCT operators (Aboriginal health workers and allied health professionals) (n=65)

Synopsis of Statement	DISAGREE Strongly Disagree or Disagree		UNSURE		AGREE Agree or Strongly Agree	
	n	%	n	%	n	%
Educational Resources						
Useful and culturally appropriate	0	0%	4	6%	60	94%
Clearly show why POC HbA_{1c} test is needed	0	0%	3	5%	61	95%
Clearly show what POCT result for HbA_{1c} means	2	3%	3	5%	59	92%
DCA 2000 and Testing Procedure						
Confident and comfortable using DCA 2000	2	3%	1	2%	62	95%
Fingerprick blood as reliable as venepuncture for HbA_{1c}	0	0%	4	6%	60	94%
Point-of-Care Results						
Confidence in accuracy and reliability	1	2%	0	0%	62	98%
POCT for HbA_{1c} on DCA 2000 acceptable alternative to lab	0	0%	2	3%	61	97%
Confident to discuss results with client	3	5%	2	3%	58	92%
Quality Management						
Understand need for quality assurance testing	0	0%	1	2%	63	98%
Level of quality assurance testing required is appropriate	1	2%	3	5%	60	94%
QAAMS Team and On-going Support						
QAAMS Team provides appropriate support	0	0%	3	5%	60	95%
Training methods instructive and appropriate	0	0%	6	10%	55	90%
Overall Community Acceptance						
Clients happy with POCT for HbA_{1c} testing	0	0%	1	2%	62	98%
POCT for HbA_{1c} raised awareness about diabetes	1	0%	11	17%	52	83%
DCA 2000 has enhanced community ownership and control	1	2%	12	19%	50	79%

current fridge space was adequate to store program reagents and consumables. Respondents were unanimous in rating the mechanical reliability of the DCA 2000 as good or very good.

POCT operators were invited to provide written comment on: 'What are the 'Positives' and 'Negatives' about the QAAMS Program, and how could the program be improved and made more effective?' A list of selected comments, reflective of the overall views of this group, is listed below.

> 'It is very useful to use opportunistically with clients who are difficult with attending follow-ups on their health care.'
>
> 'Clients are very happy with it saving them a trip to local hospital for blood testing. Clients like to know the result, and what it means.
> Gives me a chance to continue diabetic education.'
>
> 'Well accepted by our health workers and clients and CEO. Visiting specialists, podiatrist know about the DCA machine. Great asset.'
>
> 'The POC testing has greatly improved service delivery particularly with patients who are mobile and are not continuously contactable.'
>
> 'Effective POC, mildly invasive, results in 6-7 minutes instead of 48 hours to 1 week.'
>
> 'The DCA 2000 has given me a time saver in showing community how their diabetes is really going as they can see the results in 6 min and this helps us both to work to a health plan to improve the next reading.'

(iii) Questionnaire for Aboriginal Patients with Diabetes

161 clients with diabetes completed this questionnaire, with the support and assistance of their local Aboriginal health workers. Of the 148 who specified their gender, 58% were females and 42% males. Of the 159 who reported their age,

6% were 25-34 years old, 15% 35-44 years, 24% 45-54 years, 28% 55-64 years and 27% were older than 65.

A summary of their responses is shown in Table 3. Greater than 90% of respondents understood the role of the DCA 2000 machine in managing their diabetes and were comfortable in having their glycaemic control monitored. Patients were very satisfied (97% or greater) with the convenience of POCT and believed a finger-prick collection was less stressful than venipuncture. More than 90% of patients reported regular POCT resulted in improved self-motivation to control their diabetes and they were comfortable in returning for further testing. Over 90% of patients felt the visit to the doctor was more useful and the doctor was able to better manage their diabetes by having the POCT result available at the time of consultation.

In separate questions, greater than 95% of respondents wanted POCT to continue as part of the management of their diabetes and stated they would like POCT to be available to all patients with diabetes in their community.

Patients were also asked to rate how satisfied they were with the diabetes services offered to them before and after the introduction of POC HbA_{1c} testing on the DCA 2000. Figure 2 shows the satisfaction rating of the 159 patients with diabetes who answered this question. The percentage of patients who were unsatisfied with, or unsure about, their diabetes service fell from 11% to 3% and 28% to 6% after the introduction of POCT, respectively, while the percentage who were satisfied with their diabetes service increased from 61% to 91% after POCT was introduced (Fishers Exact chi-square = 12.09, p = 0.007, significant).

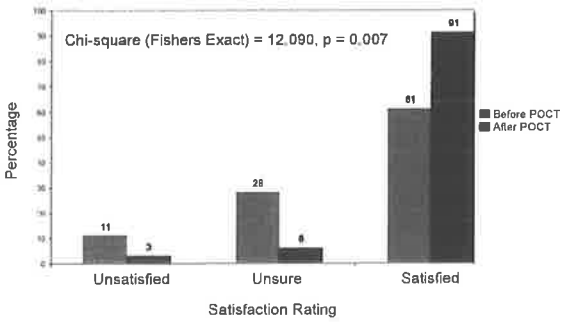

Figure 2. Patient satisfaction with services for managing their diabetes before and after the introduction of POCT (n=159).

Selected written comments by patients with diabetes are listed in response to the question: 'Do you have any other comments on whether POCT has helped you look after your diabetes?'

Table 3. Results of satisfaction questionnaire for patients with diabetes (n=161)

Synopsis of Statement	DISAGREE Strongly Disagree or Disagree		UNSURE		AGREE Agree or Strongly Agree	
	n	%	n	%	n	%
Understanding of POCT						
Understand what POCT machines are used for	0	0%	10	6%	150	94%
Happy to have diabetes checked by POCT rather than lab	0	0%	3	2%	156	98%
Convenience						
Happy with immediate POCT result	1	1%	1	1%	158	98%
Immediate result better than having to come back for lab result	0	0%	1	1%	159	99%
Fingerprick less stressful than venepuncture	1	1%	3	2%	156	97%
Personal Issues						
Regular POCT encourages me to look after my health better	1	1%	10	6%	150	93%
Happy for further POCT to be used for my management	2	1%	2	1%	157	98%
Doctor Patient Issues						
Visit to doctor more useful because POCT results available	2	1%	9	6%	149	93%
Doctor better able to manage my health by having POCT results when seeing the doctor	3	2%	5	3%	152	95%

'This my first time, I'm new about it and I like it. Yes!! I really want to put my head down now, take good care of myself and manage my health.'

'I live 30 kms from the service so it's much better for me.'

'Instant results make management more convenient and efficient.'

'Yes it has helped me to stay positive and not to get too stressed out as I know help is at the door.'

'The health workers explain everything to me and are very helpful. I'm very pleased with this set up.'

Impact of POCT on Delivery of Pathology Services and Clinical Outcomes

At service 1, in the year following the introduction of POCT, there was a 76% increase in both the number of HbA_{1c} tests performed and the number of diabetes patients being monitored for their glycaemic control. Following the introduction of POCT at service 2, there was a 91% increase in the number of HbA_{1c} tests performed (with an average of 3.7 HbA_{1c} tests per patient performed in the two years after POCT compared with 2.0 HbA_{1c} tests per patient performed in the two years before POCT). Across the same period, there was a 3.5-fold increase in the number of urine ACR tests performed (with an average of 1.8 urine ACR tests per patient performed in the two years after POCT compared with 1.1 urine ACR tests per patient performed in the two years before POCT). There was also a doubling of the number of patients tested for urine ACR. Thus, patients with diabetes at this service received closer clinical monitoring of their HbA_{1c} and urine ACR levels (and hence diabetes management) after the introduction of POCT.

Did this increased level of POCT testing at these two services translate into improved glycaemic control for Aboriginal patients with diabetes? A total of 74 patients with diabetes were monitored for their HbA_{1c} levels across both services. There was a statistically significant reduction of 0.7% HbA_{1c} in this group of 74 patients monitored at baseline (when POCT commenced) and at 12 months after the introduction of POCT respectively ($p = 0.003$, 2-tailed paired t-test) (Table 4). This fall in HbA_{1c} indicated that glycaemic control within the group had improved post POCT.

Patients were further categorised into those who achieved optimal glycaemic control (HbA_{1c} <7%), controlled glycaemia (HbA_{1c} <8%) and exhibited poor glycaemic control (HbA_{1c} >10%) before and after the introduction of POCT. Current best practice guidelines for Aboriginal people recommend that the optimal glycaemic goal is an HbA_{1c} of <7%; however, in acknowledging that this will be extremely difficult to achieve in many Indigenous people with diabetes, they also state that an HbA_{1c} of 8% represents a more realistic target for this population.[1,10] HbA_{1c} concentrations of 7% and 8% have been previously recommended by the American Diabetes Association (ADA) as the goal for optimal glycaemic control and a value at which a change of therapy is indicated respectively.[11] More recent recommendations by the ADA suggest that even more stringent goals (for example, an HbA_{1c} as close as possible to 6%) should be considered for individual diabetes patients to further reduce risk of complications at the possible increased risk of hypoglycaemia.[12] The HbA_{1c} value of 10% was selected to represent poor control on both empirical and practical grounds. As can be seen in Table 4, the percentage of diabetes patients who achieved optimal glycaemic control increased by 12%, the percentage who achieved controlled glycaemia increased by 19%, and the percentage exhibiting poor diabetes control fell by 12%. These findings also support the trend towards improved glycaemic control after the introduction of POCT.

Examples of some of the improvements in glycaemic control observed within individual patients are provided in the following brief case histories:

The first case describes a 57-year-old man who was diagnosed with diabetes in 1989. He had not been compliant in taking his diabetes medication and had a past history of heavy alcohol intake. There was a strong family history of diabetes. He visited the health service on average once per year but generally declined blood testing and follow-up. His last laboratory HbA_{1c} was 13.0%. He attended the clinic following the introduction of POCT in the service and his initial POCT results were HbA_{1c} 12.1% and urine ACR 64 mg/mmol (normal ACR <2.5 mg/mmol). His blood pressure was 158/98 mmHg (target for Aboriginal person with diabetes 130/80 mmHg) and weight was 124 kg. His cholesterol was 6.9 mmol/L (target for Aboriginal person with diabetes <4.0 mmol/L), triglyceride 4.2 mmol/L (target <2.0 mmol/L), HDL cholesterol 0.7 mmol/L (target >1.0 mmol/L) and LDL cholesterol 5.1 mmol/L (target <2.5 mmol/L).[10] As a result of his poor glycaemic control, he was placed on selected diabetes medications and referred for dietician, diabetes educator and podiatry review. His HbA_{1c} by POCT was 10.8% at three months and 7.6% at 12 months. His lipids had also improved at 12 months (cholesterol 5.9 mmol/L, triglyceride 2.6 mmol/L, HDL 1.0 mmol/L and LDL 3.8 mmol/L). His weight fell to 110 kg and his blood pressure to 140/90 mmHg. This man's confidence with a local diabetes system was improved considerably by having access to immediate results through

Table 4. Improvement in glycaemic control in Aboriginal patients with diabetes 12 months after the introduction of POCT at two rural and remote Aboriginal medical services (n=74)

Parameter	Baseline POCT	12 Months After POCT
Reduction in HbA_{1c}	**Mean ± SD**	**Mean ± SD**
HbA_{1c}	9.3 ± 2.0	8.6 ± 2.0*
% Patients		
Achieving optimal glycaemic control (HbA_{1c}<7%)	15%	27%
Achieving controlled glycaemia (HbA_{1c}<8%)	28%	47%
Exhibiting poor glycaemic control (HbA_{1c}>10%)	35%	23%

*The observed reduction in HbA_{1c} of 0.7 was statistically significant (p = 0.003, paired t-test)

POCT. The significant improvement in his HbA_{1c} reflected attention to multiple aspects of his diabetes care.

The second case describes a 53-year-old man who was diagnosed with Type 2 diabetes in 1980. In 2001, he was found to have peripheral neuropathy and vascular disease. His initial POCT investigations revealed an HbA_{1c} of 10.9% and a urine ACR of 66 mg/mmol (normal ACR <2.5 mg/mmol). His weight was 126 kg. His poor glycaemic control and macroalbuminuria (ACR >30 mg/mmol) identified by POCT were initially managed with oral hypoglycaemic and ACE inhibitor medications. With aggressive management and regular POCT over the ensuing 18 months, this patient's HbA_{1c} fell from 10.9% to 7.6%, then to 6.7%. His urine ACR levels measured by POCT decreased from 66 mg/mmol to 56 mg/mmol, then to 44 mg/mmol, while his weight was now 106 kg. This case describes substantial improvements in glycaemic control and reductions in albuminuria and weight in a patient with diabetes following intensive management that included regular POCT.

Discussion

The QAAMS Program for diabetes management has recently completed its sixth year of operation. In March 2001, the National Aboriginal Community Controlled Health Organisation (NACCHO), the peak body representing Aboriginal Community Controlled Health Services in Australia, released an independent evaluation on the first 18 months of the QAAMS Program.[13] The Executive Summary of this report viewed the use of the DCA 2000 POC technology as a major opportunity to better care for and manage Aboriginal clients with diabetes within the community setting, while the ability of the POC device to generate rapid results served as a catalyst to enhance patient self-management. The summary also concluded that the DCA 2000's simplicity of use led to high levels of acceptance by Aboriginal health workers nationally, with nearly two-thirds of services expressing the view that it had raised the self-esteem of their health workers. It also concluded that the sense of community control was enhanced as a result of management of diabetes becoming more focused within Aboriginal medical services.

Three years since this initial evaluation and with the approval of the Australian Government's Department of Health and Ageing, a detailed survey of satisfaction levels was undertaken among the three key stakeholder groups involved in the QAAMS HbA_{1c} Program – doctors, POCT operators and patients with diabetes. The results of this survey showed conclusively that the aim of the QAAMS Program to provide a more timely, efficient, and practical diabetes monitoring service using a quality assured framework has been achieved.

From the clinical viewpoint, doctors were comfortable that the POCT result was accurate and reliable. As POCT operators, both Aboriginal health workers and nurses felt the education, training and quality management framework that underpinned the QAAMS Program was culturally appropriate and that the DCA 2000 had proven mechanically sound and reliable in Aboriginal hands. Aboriginal health workers again reported that POCT had provided them with a sense of self-empowerment, an important cultural benefit of the program.[13] Both POCT operators and patients with diabetes reported improved satisfaction with their diabetes services after the introduction of POCT, also reflecting positive acceptance of the QAAMS model. Importantly both doctors and patients felt the immediacy of the POCT result contributed positively to patient care, improved the doctor-patient relationship, and made patients more likely to be both compliant and self-motivated to improve their health.

From a clinical outcome perspective, an improvement in glycaemic control was observed in a group of 74 diabetes patients from two Aboriginal medical services with whom the QAAMS management team worked closely. The UKPDS study has shown that every 1% decline in HbA_{1c} substantially reduced the risk of the microvascular complications of diabetes, particularly retinopathy and nephropathy.[14] Thus the statistically significant fall of 0.7% HbA_{1c} observed in diabetes patients at these two services, together with the improvement in the percentage of patients achieving glycaemic targets and the reduction in the percentage of patients with poor control, augur well for the longer-term outcomes of the patients. The collection of further longitudinal data on these patient groups will continue to be important.

Convenience, acceptability, immediacy of result and improved patient outcomes are often quoted with limited supporting data as 'potential' advantages of POCT. The results documented in this paper confirm, for the first time, the widespread acceptance of the QAAMS POCT model as a culturally and clinically effective service for diabetes management in Aboriginal Australia. This study also verifies that the role of POCT in achieving better clinical outcomes stems mainly from its convenience, the immediacy of result, and an enhanced doctor-patient relationship collectively leading to greater patient self-motivation.

In previously published material, the QAAMS Program has been shown to be analytically sound in Aboriginal hands, with the quality of POCT for both HbA_{1c} (and urine ACR) continuing to improve across time, meeting analytical performance goals and matching equivalent laboratory performance.

Reimbursement of POC HbA_{1c} and urine ACR tests conducted for diabetes management can be obtained through the Australian Government's Medicare rebate system. This rebate system ensures that the QAAMS Program remains cost neutral for participants and is financially sustainable in the long term.

The QAAMS model has also shown its versatility in being adaptable to other health sectors in Australia. For the past three years, the Community Point-of-Care Services unit at Flinders University (from which QAAMS is now managed) have provided specialist POCT services for a novel program called Diabetes Management Along the Mallee Track, which is based at the remote town of Ouyen in north-west Victoria.[15] In this program, POCT is provided through the local hospital and general practice as part of an integrated, multidisciplinary 'one-stop', management service for diabetes patients across the region. POC HbA_{1c}, urine ACR (and lipid) measurements are conducted by nursing staff who participate in on-going education and training sessions and conduct regular quality testing. This model has gained widespread acceptance by the Mallee Track community and also resulted in improved clinical outcomes for diabetes patients from the region.

In summary, there is now a considerable evidence base to show the QAAMS POCT model for diabetes management in Aboriginal Australia is analytically sound, culturally and clinically effective (providing a convenient and accessible service for both doctors and patients with diabetes), results in improved clinical outcomes, is sustainable, and is adaptable and transferable to other POC tests and other non-Indigenous health settings in rural and remote Australia.

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ASSISTING DIABETES MANAGEMENT THROUGH POINT-OF-CARE HbA1c TESTING – THE 'QAAMS' PROGRAM FOR ABORIGINAL HEALTH WORKERS.

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STATEMENT OF AUTHORSHIP

ASSISTING DIABETES MANAGEMENT THROUGH POINT-OF-CARE HbA1c TESTING – THE 'QAAMS' PROGRAM FOR ABORIGINAL HEALTH WORKERS

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Signed .... *Date* 23/11/2006

MUNDRABY, K.

Aboriginal Health Worker, acted as POCT Operator at participating health service and commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed ..... *Date* 23-11-06.

Assisting Diabetes Management Through Point-Of-Care HbA1c Testing – The 'QAAMS' Program For Aboriginal Health Workers.

As for the Umoona Kidney Project, this deliberately descriptive paper provided an opportunity to disseminate information and early results on the QAAMS Program to the Australian Aboriginal Health Worker audience. The paper emphasised the pivotal role of the Aboriginal Health Worker in the program, the cultural fit of POCT in the Indigenous medical service setting and focussed on the excellent analytical performance achieved by Aboriginal Health Workers as POCT operators. The inclusion of Kay Mundraby, one of the program's most senior Aboriginal Health Workers, as co-author on this paper highlighted the desire of the author to engage the health worker profession in the dissemination of information about the program and to further promote the pivotal role the health worker profession in the program.

Assisting Diabetes Management through Point-of-Care HbA1c Testing - The 'QAAMS' Program for Aboriginal Health Workers

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Introduction

Diabetes has had a devastating impact on the health of Indigenous people throughout the world. In Australia, Aboriginal and Torres Strait Islander people suffer between 12 to 17 times more deaths due to diabetes than non-Indigenous people. In many Aboriginal communities rates of Type 2 diabetes range between 15 to 30%. Diabetes itself is a significant risk factor for heart disease and is the major cause of end-stage renal disease in Aboriginal people.

This article describes a national program called QAAMS (or Quality Assurance for Aboriginal Medical Services) that was developed to assist the management of Aboriginal people with diabetes. Aboriginal Health Workers administer the program on a day-to-day basis. The unique feature of the program is that it uses a point-of-care medical instrument (called the DCA 2000) to measure a test for the long-term control of diabetes (called Haemoglobin A1c).

Point-of-care medical instruments are small, portable machines that can measure a range of pathology tests for chronic diseases on just a drop of blood or urine on-site in the community. As well as these advantages, point-of-care testing is particularly suited to the Aboriginal health care setting for the following reasons:

- Through appropriate training, Aboriginal Health Workers can perform point-of-care tests on-site, thereby empowering them to take even greater responsibility for the health of their own community members
- Immediate availability of result means that the client can see the doctor straight away and doesn't have to come back for a follow-up visit
- By conducting the tests on-site, ownership and control of health information remains with the community, a factor crucial to the acceptance and success of health programs for Indigenous people.

The point-of-care instrument used in the QAAMS program, the DCA 2000 (marketed by Bayer Australia), measures Haemoglobin A1c on just a fingerprick of blood and provides an on-site result in only six minutes (Figure 1).

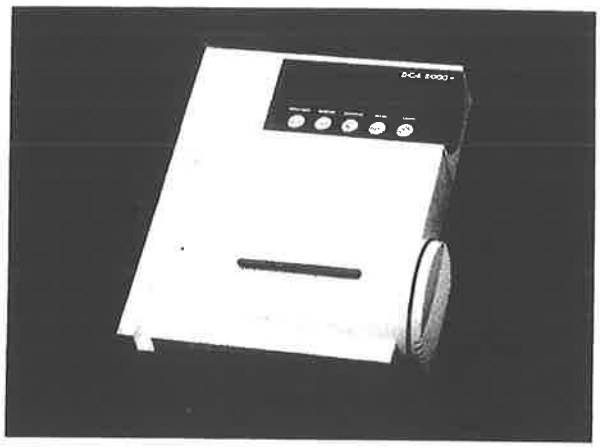

Figure 1: The Bayer DCA 2000 point-of-care medical instrument.

Haemoglobin A1c (also known as HbA1c or sugar-Hb) provides a measure of a person's diabetes control over the preceding three months. HbA1c can be described as sugar that is attached to haemoglobin in the red blood cells of the body. In a person without diabetes, HbA1c makes up around 5-6% of the haemoglobin in red cells. In a person with diabetes, the amount of HbA1c can be much higher. The higher the HbA1c above 7%, the poorer the diabetes control, and the greater the risk of developing the (micro- and macro-vascular) complications of diabetes (such as kidney disease, eye disease, stroke and amputation of limbs). The target for optimal control of diabetes is an HbA1c of 7%. Ideally, every person with diabetes should have his or her HbA1c checked every three months.

The QAAMS program and how it began

The QAAMS program arose from a recommendation of the National Diabetes Strategy, commenced as a pilot in June 1999, and is now fully integrated into mainstream Aboriginal health care in Australia.

The program has been a joint partnership (and very much a team effort) between a number of groups over the years - the National Aboriginal Community

Controlled Health Organisation (NACCHO), the Commonwealth Department of Health and Ageing's Office for Aboriginal and Torres Strait Islander Health (OATSIH) and the Diagnostics and Technology Branch, the RCPA (Royal College of Pathologists of Australasia's) Quality Assurance Programs Pty Ltd and the Community Point-of-Care Centre at Flinders Medical Centre.

The focus of the program is the management of diabetes. Over 2300 Aboriginal patients with diabetes are involved in the program, which is being conducted in 45 Aboriginal Community Controlled Health Services (ACCHS) around Australia covering urban, rural and remote sites and representing every State and Territory (Figure 2).

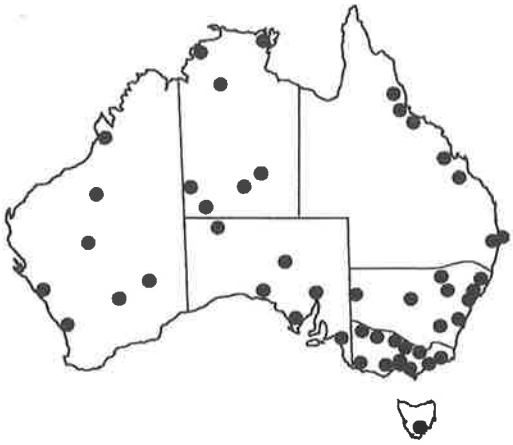

Figure 2: General location of sites participating in the QAAMS program during 2002.

This article has been written on behalf of the Aboriginal Health Workers from those sites, who are using and working the program at the ground level or the 'grassroots'. The ultimate success of this program has been due very much to the goodwill, hard work and commitment of the Aboriginal Health Workers at these sites and the vision of their health services.

Key elements of the QAAMS program

The program is based on the following three key elements:

- The production of an education resource package about diabetes. This comprises a book, video and a series of laminated posters about specific aspects of the program (all of which were developed in collaboration with senior Aboriginal health professionals to ensure they were culturally appropriate) (Figure 3).
- The delivery of formal training for Aboriginal Health Workers (and allied health professionals) from each site about diabetes and its complications, the HbA1c test and control of diabetes, and practical hands-on training in how to perform an HbA1c test on the DCA 2000.
- The development of a quality assurance program to monitor the quality of results generated by the DCA machines in the field, together with a number of other quality management support services for participating sites.

Figure 3: Education resources produced for the QAAMS program.

With 50 DCA machines in the field, it is critical to know that the machines are generating HbA1c results that are acceptable for patient care at all times. A surveillance mechanism was therefore needed to monitor the analytical performance of the machines. To do this, a quality assurance program was developed in partnership with Jan Gill and Lloyd Penberthy from the RCPA Quality Assurance Programs Pty Ltd.

The RCPA Quality Assurance Programs Pty Ltd are internationally renowned for their work with quality assurance in laboratories and run 23 programs for more than 1000 laboratories in Australia, New Zealand and other parts of the world. However, we believe the QAAMS program is the first of its type to be developed for Indigenous people anywhere in the world.

How does the QAAMS program work?

The QAAMS program provides each service with an annual kit of 24 samples with known concentrations of HbA1c. Aboriginal Health Workers from each service test two of these samples (in a blind sense and according to a defined testing schedule) every month. Their results are then faxed to the QAAMS reporting office at Flinders Medical Centre in Adelaide. The performance of each service's DCA 2000 is monitored by comparing their QAAMS results with the pre-set target values for those quality assurance samples and with the results from all other services.

Graphical reports summarising the DCA's short - and long-term performance are then sent to each service.

Table 1. Median precision (CV%) achieved by Aboriginal Community Controlled Health Services and laboratories in parallel Quality Assurance Programs.

Category	Program	Cycle		
		July to Dec 2001	Jan to June 2002	July to Dec 2002
ACCHS	QAAMS	4.1%	3.9%	3.4%
Laboratories	Glycohaemoglobin	4.1%	3.7%	3.5%

By simply eyeballing the report, the service can see where their monthly result lies in relation to the target value and to all other services (that is, their peers). If the result lies within the 'goalposts' or 'limits of acceptability', then their DCA is performing well. The report builds up over time and services can also get graphical information about the long-term performance of their DCA 2000. Services have their own individual code number that ensures confidentiality of their results.

As part of the QAAMS program, other on-going support services, including an immediate telephone 'help hotline' service for sites experiencing technical difficulties or problems with their DCA 2000, is also provided.

Results from the quality assurance testing

Seven (7) six-monthly testing cycles have now been completed over the past three and a half years - from July 1999 to December 2002. The results from the most recently completed testing cycle (Cycle seven, July to December 2002) can be summarised as follows:

- Participation rate: 93%
- Percentage acceptable results: 86% (using limits for acceptable performance set by the program organisers, which are the same as those for the laboratory-based Haemoglobin A1c [Glycohaemoglobin] program run by the RCPA Quality Assurance Programs Pty Ltd)
- Median Precision: 3.4% (coefficient of variation, CV%).

How does this level of precision compare to laboratories?

As mentioned above, the RCPA Quality Assurance Programs Pty Ltd runs a parallel Haemoglobin A1c program for laboratories in Australasia. There are 75 DCA users registered in this program, which uses an identical quality assurance material to that used for QAAMS. It is therefore possible to directly compare the performance of Aboriginal Community Controlled Health Services using the DCA 2000 in the QAAMS program with laboratory users of the DCA 2000 in the Glycohaemoglobin program.

Across the past three testing cycles, the median precision achieved by Aboriginal Community Controlled Health Services in the QAAMS program has more than matched the precision base achieved by laboratories.

This is a quite outstanding achievement by the participating Aboriginal Health Workers. As the table also shows, the precision base achieved by Aboriginal Community Controlled Health Services has been generally trending downwards (improving), again a very pleasing finding.

How is the QAAMS program working in the field?

Participants have used the program in many different ways within the community setting. For example, some services have set up new diabetic clinics as now they can do the test on-site. Others have used the DCA for opportunistic testing in the health service, for home visits for diabetic clients, at community functions and health promotion activities, and during field visits to care for people with diabetes in outstations and distant communities serviced by health services.

Evaluation of the QAAMS program

In March 2001, NACCHO released an independent evaluation on the first 18 months of the QAAMS program (1). The Executive Summary concluded:

- The use of the DCA point-of-care technology provided a major opportunity to better care for and manage Aboriginal clients with diabetes within the community setting.
- The ability of the point-of-care technology to generate rapid results served as a catalyst to enhance patient self-management, while
- The simplicity of use of the DCA led to high levels of acceptance by Aboriginal health workers nationally, with over two-thirds of services expressing the view that it had raised the self-esteem of their health workers.
- Further, the sense of community control was enhanced as a result of diabetic management becoming more focussed within Aboriginal medical services.

Figure 4: Janine Cochrane from Biripi Medical Service, Taree, NSW and Mark Shephard at the DCA 2000 during the 2001 Workshop.

Sustainability of the QAAMS program

In December 2000, the Federal Health Minister (Dr Wooldridge) announced that a Medicare rebate could now be claimed for HbA1c tests conducted for the management of people with established diabetes in Aboriginal Community Controlled Health Services. The rebate has ensured there is a long-term sustainable funding mechanism for the program. The rebate is conditional on services continuing to participate in the QAAMS program.

Figure 5: Cindy Koolmatrie and Louise Dennis from the Central Australian Aboriginal Congress, Alice Springs, with Karan Lavender (QAAMS Assistant) at the 2002 Workshop.

Annual Workshops have been held for participants since 2001 (Figures 4 and 5). The Workshops provide an informal, interactive forum for participants to discuss issues about the program, meet and network with other participants, and set future directions. In addition there are opportunities for everyone to participate in a full training program, particularly new health workers that have not previously had one-on-one training.

Regional Workshops for sites from Cape York, Far North South Australia and country Victoria have also been held as the need has arisen.

Transferability of the QAAMS model

As from January 2003, the program is now available to sites from outside the non-ACCHS sector (that is, State and Territory-funded services), provided they are able to purchase a DCA 2000 and the consumables needed.

In 2003, 10 new sites have been recruited to the QAAMS HbA1c program including our first international participant, the Island of Tonga from the Western Pacific region. There remains considerable interest from other Western Pacific Islands.

The QAAMS model is transferable to other point-of-care tests and instruments. This year, with the further support of the Commonwealth Department of Health and Ageing's Diagnostics and Technology Branch, a new QAAMS program for the measurement of urine albumin:creatinine ratio (ACR) on the DCA 2000 has commenced. There are 30 Aboriginal Community Controlled Health Services enrolled in this program and urine ACR testing will be used to monitor microalbuminuria in Aboriginal patients with diabetes.

Challenges for the QAAMS program

Perhaps the biggest issue confronting the sustainability of the QAAMS programs is maintaining education, training and quality management support services to those sites experiencing high staff turnover. Since the program began, more than 70% of services now have a different health worker responsible for the program, while a further 10% have had more than two staff changes.

Having said this, some services have achieved some quite remarkable performances under very difficult circumstances. One of our services participating in the QAAMS program is located in the southern desert region of Western Australia, 700 kilometres from the nearest town. Despite the tremendous disadvantages of distance, this site has maintained a very high participation rate since the QAAMS program began in June 1999 and is regularly ranked in the top quartile for its analytical performance base.

Other challenges include ensuring the Medicare rebate is accessed maximally, promoting the availability of the program more widely, maximising the

continued page 18

continued from page 15

attendance at, and support for, the annual Workshop, and gathering more quantitative and qualitative data about the program with the help of participating sites - particularly in relation to whether point-of-care DCA 2000 HbA1c testing leads to improved health outcomes for the client.

In conclusion, the QAAMS program places Aboriginal medical services at the leading edge internationally of providing point-of-care technology to assist Indigenous communities with diabetes management and improves the capacity of services to make an impact on the burden of diabetes.

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POINT-OF-CARE TESTING IN ABORIGINAL HANDS – A MODEL FOR CHRONIC DISEASE PREVENTION AND MANAGEMENT IN INDIGENOUS AUSTRALIA.

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Point-Of-Care Testing In Aboriginal Hands – A Model For Chronic Disease Prevention And Management In Indigenous Australia.

In 2001, a new POCT model called Point-of-Care Testing in Aboriginal Hands was developed and introduced into four rural and remote Aboriginal communities in South Australia and Western Australia, each of which varied considerably in their size and infrastructure. This program had a broad chronic disease focus and utilised not only the Bayer DCA 2000 but also the Cholestech LDX lipid device for both risk assessment and management.

This paper reported the chronic disease risk profiles of each community and addressed research questions concerning both the cultural and clinical effectiveness of POCT across the diverse mix of Indigenous medical services.

This research study found similar but disturbing rates of chronic disease risk between communities, with rates of diabetes, microalbuminuria and obesity approximately two to three- times the national average. POCT for HbA1c, urine ACR and lipids was effectively integrated into patient management at two services, where statistically significant reductions in HbA1c were observed in patients with diabetes after the introduction of POCT. At one service, where POCT was introduced concurrently with chronic disease care planning, clinical outcomes were significantly better in patients who self managed well compared to those who had difficulties with self management.

A further significant research finding was the community acceptance of POCT across all stakeholder groups surveyed by questionnaire. Examples of the versatility and adaptability of POCT in the primary care setting were also presented in this paper.

Point-of-Care Testing in Aboriginal Hands—A Model for Chronic Disease Prevention and Management in Indigenous Australia

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Abstract: Point-of-care testing (POCT) has a critical niche in rural and remote indigenous Australia where geographic isolation from laboratory services is common, the resultant turnaround of laboratory results is often slow, and the burden of chronic disease is very high. This paper describes a POCT program called Point-of-Care in Aboriginal Hands, which delivers POCT services for chronic disease prevention and management to 4 rural and remote Aboriginal medical services in Australia. Aboriginal health workers were trained as POCT operators of the DCA 2000 (Bayer Diagnostics, Tarrytown, NY) and the Cholestech LDX lipid analyzer (Cholestech, Hayward, Calif). Prevalence rates in the general community for diabetes (17%), microalbuminuria (20%), and obesity (48%) were between 2 to 3 times the national average. Statistically significant reductions in hemoglobin A1c (HbA1c) of 0.7% and 1.2% (paired *t* test, $P < 0.05$) in type 2 diabetes patients (n = 45 and 24) after the introduction of POCT at 2 services confirmed that POCT had been an effective tool in improving clinical outcomes. Community acceptance of POCT was extremely high among key stakeholder groups (doctors, Aboriginal POCT operators and diabetes patients) interviewed and surveyed in the program. The percentage of patients who were satisfied with their diabetes service after the introduction of POCT rose significantly from 64% to 88%, whereas the percentage unsatisfied or unsure about their diabetes service fell from 8% to 3% and 28% to 9% after POCT (Fisher exact test, $\chi^2_7 = 9.7$; $P = 0.03$). The POCT proved versatile and adaptable in the varied mix of participating communities, which came from widely divergent geographical locations.

Key Words: Aboriginal health, chronic disease, point-of-care testing, prevention and management

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Australia has a total population of 20 million people, 30% of whom live in rural and remote Australia.[1] In these areas, there is greater geographic isolation and an increasingly larger indigenous component of the population. A total of 38% of Aboriginal people live in rural and remote Australia, with the remainder making up only 1% of the urban population.[1] The generally poorer health status of people living in rural and remote Australia is particularly exacerbated in the indigenous community sector.[2–4] In relation to chronic disease, Aboriginal people have approximately 15 times higher mortality rates due to diabetes than non-Aboriginal people, escalating rates of end-stage renal disease in the range 770 to 1300 per million have been recorded in the desert regions of Australia, and rates of cardiovascular mortality in the younger adult Aboriginal population between 25 and 44 years of age are 10 times higher than the national average.[5–9]

During the past 8 years, the Community Point-of-Care Services (CPS) unit within the Flinders University Rural Clinical School has developed and implemented several point-of-care testing (POCT) models for chronic disease in the Australian Aboriginal health sector. The national Quality Assurance for Aboriginal medical services program (QAAMS) focuses on diabetes management, whereas the Umoona Kidney Project investigated the use of POCT for risk assessment and management of renal disease.[10–14] This paper describes a further POCT model for chronic disease called Point-of-Care Testing in Aboriginal Hands. This program is a partnership between the Flinders CPS unit and 4 Aboriginal medical services (AMS) from Port Lincoln, the Riverland, and Meningie in South Australia and Kalgoorlie in Western Australia. Three of the participating AMS are rural, and one is remote according to the Australian government's classification system for rurality (rural remote metropolitan area).[15]

The program has a broad chronic disease focus, with both risk assessment and management arms. There is wider

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use of POCT technology in this program than in our other models, with Aboriginal health workers trained as POCT operators in the use of both the DCA 2000 (Bayer Diagnostics, Tarrytown, NY) and the Cholestech LDX lipid analyzer (Cholestech, Hayward, Calif). There is a strong local community focus, involving teams of health professionals from each service and engaging community members to foster a strong sense of community ownership.

This paper describes the unique features of this model and attempts to answer the following research questions. Can POCT work effectively across Aboriginal medical services with differing sizes and levels of staff? What were the overall chronic disease risk profiles in these Aboriginal communities? Could POCT be integrated into the clinical management of patients with chronic diseases? How well was POCT accepted by doctors, POCT operators, and patients with chronic disease?

METHODS

Participating Communities

Each of the 4 participating Aboriginal medical services was located between 150 and 650 km by road from the nearest capital city. Two were situated in coastal areas, one on a major inland waterway, and the other on the fringe of a large desert region. One site was very small with 1 health worker and 2 doctors servicing a small community. Two sites were well-resourced, servicing communities of several hundred people. The remaining site had a very large infrastructure, delivering health care not only to a large "town" population but also providing outreach services to a number of remote locations. This varied mix of communities provided a challenging environment for POCT.

Ethics Approval

Ethics approval to conduct the program was obtained from the Aboriginal Health Research Ethics Committee of South Australia and the Flinders Medical Centre's Committee on Clinical Investigation.

Community Consultation

Before commencing the program, a series of meetings were held with members of each local Aboriginal community and with each participating medical service to discuss and formulate the aims and objectives of the program. A culturally appropriate information sheet about the program was also developed for each community and disseminated widely to community members.

Organization and Management of POCT Services

Clinical governance for POCT resided with the senior medical officer at each service. The program manager (first author) was responsible for overall supervision and management of POCT services, notably education and training of Aboriginal POCT operators and ensuring compliance with quality management procedures. Where possible, a POCT working group was established comprising the medical officer, program manager, supporting CPS scientist, and practice staff including, for example, the nurse-in-charge, senior Aboriginal health worker, nutritionist, diabetes educator, and information technology personnel. In this way, as many allied health professional staff as possible were aware of the POCT program and could support and encourage the health worker(s) as the on-site POCT operator(s).

With the program manager based at Flinders University, regular on-site visits were critical to maintain rapport with the health professional teams and the broader communities. During field visits, training was delivered, quality management results reviewed, reagent audits conducted, and summaries of results presented to the health team and the service's board of directors. Presentations were also made to the local community, and community functions and health promotion activities were attended. Community posters were also prepared to promote local ownership.

Training for Aboriginal Health Workers in the Use of POCT Instruments

Aboriginal health workers from each health service participated in a series of continuing education and training sessions delivered by the program manager and scientists from the Flinders' CPS unit. Health workers were provided with a culturally appropriate understanding of chronic disease, its burden on Aboriginal Australians, a description of the pathology tests that can be measured by POCT to detect and manage chronic diseases, and basic interpretation of patient POCT results.

Systematic hands-on training and practical instruction in how to conduct patient POCT and quality management testing procedures (internal quality control and, where available, external quality assurance testing) was also provided to health workers from participating services in an on-going sense. A series of color posters providing step-by-step guides to the operation of each POCT instrument and the performance of patient and quality management testing were also produced for each service.

POCT Technology

The 2 POCT instruments used in this program were the Bayer DCA 2000 (Bayer Diagnostics, Tarrytown, NY) and the Cholestech LDX lipid analyzer (Cholestech, Hayward, Calif). The Bayer DCA 2000 measured hemoglobin A1c (HbA1c) on a capillary whole blood sample in 6 minutes and urine albumin:creatinine ratio (ACR) on 40 μL of first morning urine in 7 minutes. HbA1c is an established marker of long-term diabetes control in patients with diabetes. Urine ACR is not only a sensitive marker for early renal disease that can be used for risk assessment and management but also predicts cardiovascular disease.[16] The Cholestech lipid analyzer measures a full lipid profile (total cholesterol, triglyceride, high-density lipoprotein [HDL] cholesterol, and calculated low-density lipoprotein [LDL] cholesterol) and glucose on 35 μL of whole blood in approximately 5 minutes. The analytical performance of both these POCT instruments has been previously validated by the Flinders CPS unit.[17,18]

Community Risk Assessment

Chronic disease risk assessment was conducted on a voluntary basis for adult community members, after their

prior informed consent. A risk assessment algorithm was developed, based on current best practice guidelines, and included urine ACR, lipid and glucose measurements by POCT as well as blood pressure, age, body mass index, personal and family history, smoking status, and alcohol consumption.[5,6,19–21] With specific regard to POCT measurements, each patient was asked to provide a first morning urine sample to be tested by an Aboriginal health worker for urinalysis (by dipstick) and urine ACR (on the DCA 2000). The Aboriginal health worker also took a capillary (finger-prick) whole blood sample for measurement of HbA1c (on the DCA 2000) and fasting lipids and glucose (on the Cholestech). All risk assessment results were recorded by the health worker on a single-page pro forma, which the patient then took to the doctor. Results were also entered into the service's patient management system and faxed to the CPS unit where subsequent community risk profiling was conducted.

Whereas most risk assessments were conducted in the service's clinic, the opportunity was taken wherever possible to conduct POCT in the community setting.

Management of Chronic Disease

Patients identified at risk for chronic disease were managed locally, with POCT being an integral component of their management strategy and conducted at a frequency consistent with best practice management guidelines.[5,6,19–21] With the permission of 2 services, the Flinders CPS unit tracked the management of selected patients with type 2 diabetes to assess the impact of POCT on clinical outcomes among individuals and groups of patients with chronic disease. At the first service, HbA1c POCT results were recorded on type 2 diabetes patients who attended their clinic across a 12-month period from 2003 to 2004. At the second service, POCT was linked to chronic condition self-management care planning, and selected POCT results were monitored on these patients from 2003 to 2005, as they entered the care planning process.[22] Care planning provided a structured program for the patient to set personal, behavioral, lifestyle, and medication goals in conjunction with the doctor and health workers.

Community Acceptance of POCT

Community acceptance was assessed by 3 stakeholder groups, namely doctors, Aboriginal health workers (as POCT operators), and patients with chronic disease (specifically those with type 2 diabetes). The principal doctor and Aboriginal POCT operator from each participating service were interviewed during the production of a CD-ROM for the program. More broadly, all stakeholder groups were invited to complete separate questionnaires developed by the program manager, in conjunction with the Flinders University Centre for Biostatistics and Epidemiology. The questionnaires, which were also part of a larger survey for the national QAAMS HbA1c program, contained a series of short statements or questions, based on the 5-point Likert scale.[23] Respondents were asked to rate their level of agreement or disagreement with the statement or question posed. The results of the questionnaires were analyzed by the program manager and an epidemiologist from the Flinders University Centre for Biostatistics and Epidemiology using the Epidata software (www.epidata.dk).

Quality Management for POCT

To oversee the analytical performance of POCT in the field and to ensure the highest standards of methodological rigor were maintained, POCT operators were required to conduct both internal quality control testing (on both the DCA 2000 and Cholestech) and participate in external quality assurance testing (on the DCA 2000) as part of the national QAAMS Program for HbA1c and urine ACR testing. All 4 services had been active members of the QAAMS Program since 2001. A quality assurance program for POCT lipid testing in Aboriginal medical services is not currently available.

RESULTS

Community Risk Assessment

Six hundred and twenty-six risk assessments were carried out across the 4 AMSs from 2002 to 2004. The overall prevalence of individual risk factors found in the general adult population in 3 of the communities, together with age and sex profiles, is shown in Table 1. Risk assessments at service 4 (n = 246) were conducted on persons specifically referred to the service's chronic disease clinic. Prevalence rates at this service were thus overestimated in this more selected population and have been excluded from this table.

The prevalence of type 2 diabetes (self-reported and/or capillary glucose, >11 mmol/L) in communities 1 to 3

TABLE 1. Prevalence of Chronic Disease Risk Factors in 3 Aboriginal Communities

Parameter	Community 1	Community 2	Community 3
No. risk assessments	162	117	101
Age (years)			
Mean ± SE	41 ± 1.1	43 ± 1.3	43 ± 1.4
Range	16–80	15–83	17–74
Aged 15–29, %	37	20	24
Aged 30–44, %	66	40	33
Aged older than 45, %	59	57	44
Sex			
Male:Female ratio, %	47:53	30:70	42:58
Risk Factor Prevalence (%)			
Diabetes	15	15	18
Microalbuminuria	19	20	24
Macroalbuminuria	4	2	6
Lipids	35	44	31
Hypertension	29	20	34
Smoking	55	63	56
Obesity	40	46	59

Risk assessments at service 4 (n = 246) were conducted on persons who were specifically referred to the service's chronic disease clinic, and therefore, prevalence rates do not reflect those of the general community. They were therefore excluded from this table.

TABLE 2. Improvement in Glycemic Control in a Group of 45 Type 2 Diabetes Patients After the Introduction of POCT in Service 1

Observation	Baseline POCT (n = 45)	12 Months After POCT (n = 45)	Paired Difference
Reduction in HbA1c (mean ± SD)			
HbA1c	9.5% ± 2.1%	8.8% ± 1.9%	0.7%*
Patients (%)			
Achieving target glycemia (HbA1c, <7%)	18	24	6
Achieving controlled glycemia (HbA1c, <8%)	24	42	18
Exhibiting poor glycemic control (HbA1c, >10%)	40	27	−13

*Statistically significant change ($P = 0.02$, paired t test).

ranged from 15% to 18%. Microalbuminuria (urine ACR between 3.4 and 34 mg/mmol measured by POCT) was detected in approximately 20% of people assessed. Abnormal lipids (total cholesterol, >5.5 mmol/L measured by POCT) were found in over one third of people, whereas rates of hypertension (blood pressure, >140/>90 mm Hg or >130/85 mm Hg for diabetic patients) were approximately 30%. Almost half of all persons assessed were obese (body mass index, >30 kg/m^2). More than 50% were current smokers. Significant sex differences in prevalence rates were observed at 2 services for cholesterol (service 1, men 45% and women 28%; service 2, men 59% and women 32%) and obesity (service 1, men 30% and women 49%; service 2, men 19% and women 53%) (χ^2 test, $P < 0.05$ in each case).

Community risk assessments were carried out at a range of different locations outside the main service clinic, including at a local ecotourism center, an adult education college, an adult women's center (as part of a nutrition health promotion activity), the local community fair and home visits. At 1 service, a bus was renovated to accommodate the POCT instruments and provide a mobile POCT testing service for community members throughout the region. An eye check for diabetes patients was also available on the bus. The local Aboriginal POCT operator and doctor traveled on the bus to provide this mobile service.

Management of Chronic Disease

At service 1, a group of 45 Aboriginal patients with type 2 diabetes had POCT performed at baseline (when POCT commenced) and at 12 months after the introduction of POCT. There was a statistically significant reduction in HbA1c across this period (Table 2). Categorization of patients into those who achieved target or controlled glycemia (HbA1c, <7% and <8%, respectively) and those exhibiting poor diabetes control (HbA1c, >10%) also revealed a trend toward better glycemic control after POCT, although these trends did not reach statistical significance due to small patient sample size (χ^2 test, $P > 0.05$).

At the second service, 36 patients with type 2 diabetes participated in chronic condition self-management care planning. Twenty-four patients were clinically assessed by the service's doctor and chronic disease coordinator as "self-managing well" (SMW); that is, they attended their clinic appointments, had regular POCT, and were compliant in taking medication. They were managed on care plans for a median of 18 months (up to a maximum of 33 months). The remaining 12 patients were classed as "having difficulties with self-management" (SMD) because they were unable to regularly attend the clinic and have POCT, they were generally noncompliant in taking medication or they had other associated illnesses or social and emotional issues that impinged negatively on their ability to participate in care planning. This group had been on care plans for a median of 15 months (up to a maximum of 30 months). Selected clinical outcome measures in the SMW and SMD groups are compared in Table 3. The mean HbA1c of the SMW group fell significantly by 1.2% ($P = 0.0001$; paired t test), whereas the mean of the SMD group rose by 0.9% ($P = 0.097$; paired t test). The renal profiles of the 2 groups, as assessed by their urine ACR status, were very different with the high rate of macroalbuminuria in the SMD patients of particular concern. There was a statistically significant reduction in mean total and LDL cholesterol (as measured by POCT) of 1.0 and 0.7 mol/L ($P = 0.02$ and 0.03, paired t test),

TABLE 3. Comparison of Clinical Outcome Measures in the Group of Type 2 Diabetes Patients Who Were SMW (n = 24) or SMD (n = 12)

		Group			
		SMW		SMD	
Test	Units	Baseline POCT	Most Recent POCT	Baseline POCT	Most Recent POCT
HbA1c	%	8.7 ± 2.0	7.5 ± 1.5*	9.4 ± 1.9	10.3 ± 1.2
Total cholesterol	mmol/L	5.92 ± 1.5	4.93 ± 1.1*	5.14 ± 0.9	5.34 ± 0.9
LDL cholesterol	mmol/L	3.24 ± 1.2	2.52 ± 0.7*	2.63 ± 0.9	3.03 ± 0.6
Weight	kg	83.3 ± 13.5	83.2 ± 13.2	98.9 ± 24.8	108.8 ± 2.0
Albuminuria (ACR)	% Normal		58		36
	% Microalbuminuria		37		14
	% Macroalbuminuria		4		43

*Statistically significant change ($P < 0.05$, paired t test).

respectively, in the SMW group. In contrast, the mean of these lipid fractions were slightly higher (by 0.2 and 0.4 mmol/L) in the SMD group. Although the changes in the SMD group did not reach statistical significance due to the small sample size, the contrasting trends in the 2 patient groups are apparent. Patients who self-managed well benefited from care planning and regular POCT, whereas those patients unable to take advantage of these services exhibited poorer health and were at higher risk of developing diabetic complications.

The clinical usefulness of POCT is also illustrated in the following brief case studies.

The first case describes a middle-aged man with type 2 diabetes, obesity, and ischemic heart disease. He had not visited the health service clinic for more than 2 years but had become aware of the availability of the new POCT service. His initial POCT results were HbA1c 10.5%, urine ACR 2.8 mg/mmol, blood pressure 150/90 mm Hg, and weight 124 kg. His poor glycemic control was immediately treated. During the next year, the patient had regular POCT, with his HbA1c falling to 9.7%, 8.8%, and 8.4%. Across this period, he received on-going dietary, podiatry, and retinopathy review. He commented that regular POCT has helped motivate him to achieve improved diabetes control. He also began undertaking bush trips and consuming more traditional bush foods.

The second case describes a young man from a remote Aboriginal community who presented at the local health service complaining of severe headaches. His POCT results were HbA1c 10.6%, urine ACR 22.7 mg/mmol, cholesterol 12.0 mmol/L, nonfasting triglyceride more than 7.3 mmol/L, and blood pressure 156/ 115 mm Hg. The patient's blood sample was also left standing on the bench, allowing the red blood cells to settle and revealing a plasma that was strawberry milk in color. Opportunistic POCT led to the patient being identified as diabetic with poor glycemic control, microalbuminuria and severe hyperlipidemia (as well as hypertension). Treatment was initiated immediately, and the patient is now managed in his own community by the visiting Royal Flying Doctor Air Service. Visualization of the milky plasma led to valuable education for Aboriginal health worker team about heart disease and raised community awareness about blood fats.

The third case describes a grossly overweight middle-aged women whose initial POCT results were urine ACR 8.7 mg/mmol, HbA1c 5.0%, blood glucose 6.1 mmol/L, blood pressure 135/85 mm Hg, and weight 97 kg. Medications were commenced to treat microalbuminuria and assist weight loss. A visiting renal specialist, podiatrist, and dietician subsequently reviewed the client. Follow-up urine ACR measurements performed by POCT over the next year (7.5 and 3.5 mg/mmol) indicated an improvement in microalbuminuria. The patient also showed increased motivation to lose weight, exercise, and adhere to medication. This case describes how opportunistic POCT helped identify and improve obesity-related microalbuminuria in a patient who did not have diabetes or hypertension.

The final case describes an elderly woman with cardiovascular disease who was placed on a care plan. Her initial lipids by POCT were extremely high (total cholesterol, 11.1 mmol/L and triglyceride, 7.3 mmol/L). She was placed on lipid lowering medication, and her lipid profile improved significantly (cholesterol 5.0 mmol/L and triglyceride 3.3 mmol/L). However, severe muscular pain developed, and the patient could no longer tolerate this medication. Her lipid profile subsequently worsened necessitating a further change in medication. Her most recent POCT lipids were total cholesterol, 4.7 mmol/L; triglyceride, 2.1 mmol/L; HDL cholesterol, 1.1 mmol/L; and LDL cholesterol, 2.7 mmol/L. Close monitoring through care planning and POCT during the past 18 months have now stabilized her cardiovascular risk.

Community Acceptance of POCT

The 12 clinical staff responsible for managing patients with diabetes across the 4 participating AMSs unanimously agreed that the availability of the POCT results at the time of consultation was convenient for them, the opportunity to discuss the POCT results immediately with the patient was advantageous, and they had confidence in the accuracy and reliability of the POCT result. More than 90% believed POCT was an acceptable alternative to the laboratory, contributed positively to overall patient care and management and provided a more clinically and culturally effective service for patients with diabetes than the laboratory.

Specific comments by doctors during interview included the following:

"The program has been very successful so far and the ability to perform analyses opportunistically by point-of-care has been critical. Being able to give results to people immediately is a powerful tool in recruiting and retaining patients on disease registers. Local acceptance of point-of-care testing has been good so far. The ability for Aboriginal health workers to perform the testing has however proven its greatest success. Lastly, the doctors have not had to change their practice very much and have found immediate discussion of results very helpful. It may mean that treatment is not delayed, or patients lost in uncertain follow-up."

"POC testing has greatly improved the efficiency and effectiveness of the chronic disease services we provide. We are now able to offer a full range of risk assessment and monitoring tests for common chronic diseases with instant results. This means doctors and health workers are able to make management decisions for our diabetic and renal clients on the spot instead of having them come back for results. Clients get quick feedback on how they are progressing."

There was unanimous agreement among the 13 Aboriginal POCT operators across all participating services that they were confident in the accuracy and reliability of the POCT result, were satisfied with the level of support services provided by the Flinders' team, and believed that the patients with diabetes were pleased to have POCT as part of their management. More than 90% of health workers felt confident in discussing the POCT result with the patient and agreed that the training methods used by the Flinders' team were instructive and culturally appropriate.

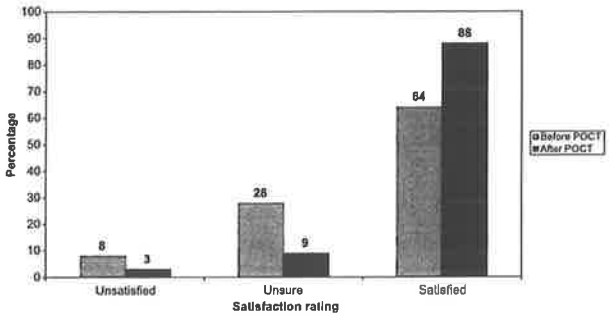

FIGURE 1. Patient satisfaction with services for managing their diabetes before and after the introduction of POCT (n = 58). Difference between satisfaction ratings (unsatisfied, unsure, and satisfied) before and after POCT (Fisher exact test, $\chi^2_7 = 9.7$; $P = 0.02$).

Specific comments from Aboriginal health workers during interview included the following:

"All the health workers at our service think the program is good because it empowers us to do the testing and to have an important role in chronic disease management. We've already picked up a lot of people with problems. All the clients are now really keen on the program. The availability of the program is now spreading rapidly by word-of-mouth through the community. People want to come and get tested. They are asking questions about the machines and what they can tell us about chronic diseases."

"The program has been received well by the community. Clients are interested to know what their results mean. Those with diabetes are keen to see how their control is. They know if they're not looking after themselves that we can help them. From my perspective as a health worker, the program has been very educational."

"We all feel confident in using the machines. The program is well worth it and great for the community. The program has good health promotional benefits because the program has shown people that they must take greater responsibility for their own health."

Fifty-eight Aboriginal patients with type 2 diabetes across the 4 services completed the patient questionnaire. They were unanimous that regular POCT encouraged them to "look after their health better" and that obtaining their POCT result while they waited was more convenient than having to come back for a follow-up visit. More than 90% understood the purpose of using POCT instruments and believed that the doctor was better able to manage their chronic condition by having their POCT results available at the time of consultation. Fingerprick testing was considered less stressful than venipuncture by 98% of respondents.

Patients were specifically asked to rate how satisfied they were with their diabetes service before and after the introduction of POCT (Fig. 1). The percentage of patients who were satisfied with their diabetes service after the introduction of POCT rose significantly from 64% to 88%, whereas the percentage who were either unsatisfied or unsure about their diabetes service fell from 8% to 3% and 28% to 9% after POCT had commenced for their management (Fisher exact test, $\chi^2_7 = 9.7$; $P = 0.03$).

Quality Management for POCT

The average within-site imprecision (coefficient of variation, CV%) achieved for external quality assurance HbA1c and urine ACR POCT in the national QAAMS program by all 4 participating services for each 6-month testing cycle over the past 3 years is shown in Figure 2. The performance for urine ACR quality assurance testing continued to improve across time. Apart from one time point (HbA1c, first cycle in 2004), the level of imprecision readily met the minimum precision goals of 4% and 12% recommended for these 2 analytes by the Australian Government's Interim Standards for Point-of-Care Testing.[24]

For POCT lipid testing on the Cholestech, an external quality assurance program for lipids was not available. In addition lot numbers of commercial quality control material changed between and within participating services every

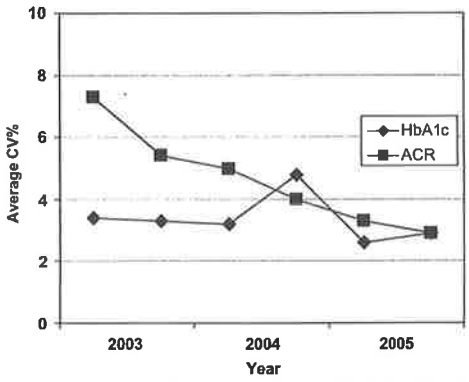

FIGURE 2. Average within-site imprecision (CV%) achieved for external quality assurance HbA1c and urine ACR POCT in the national QAAMS program by all 4 participating services over the past 3 years.

3 to 6 months, making detailed analysis of imprecision difficult. However, the average imprecision for quality control testing across participating services has been calculated using control lot numbers for which the highest number of quality control results have been documented (n = 36 and 33 for low and high controls, respectively). Imprecision averaged 4.2% and 4.0% for total cholesterol, 4.7% and 4.7% for triglyceride, and 6.9% and 4.1% for HDL cholesterol (for low and high controls, respectively). This level of imprecision meets the minimum precision goals of 5.0% for cholesterol, 7.5% for triglyceride and 6.0% for HDL cholesterol recommended for these analytes by the Australian Government's Interim Standards for Point-of-Care Testing, except for the low HDL cholesterol control.[24]

DISCUSSION

In rural and remote Australia, many Aboriginal medical services (AMS) are often hundreds of kilometers from their local laboratory service provider and the turnaround of laboratory results can take several days often weeks in some areas. It can also be very difficult for Aboriginal people to attend a follow-up clinical appointment to discuss their pathology results with the doctor due to other family and cultural priorities. POCT, where results are immediately available for both the doctor and the patient, offers a practical and more efficient solution to the delivery of pathology services in the rural and remote environment. With appropriate training, Aboriginal health workers (Aboriginal people living and working in the community and trained in primary health care) can perform POCT on-site, empowering them to have a significant role in the care of their community members with chronic disease and ensuring ownership and control of patient information is retained within the medical service. Both these factors are crucial advantages of POCT in the cultural context.

This paper describes the results from a POCT model for chronic disease risk assessment and management conducted in the challenging environment of rural and remote indigenous Australia, where poor accessibility to goods and services, limited employment opportunities, low income and poor access to housing and education all contribute to excessively high morbidity and mortality rates for chronic disease in this health sector.[4]

The paper reports the results of community risk assessments for chronic disease, which used POCT as its centerpiece. Chronic disease risk profiles between communities were generally similar. However, comparisons with national averages, as reported in the recent Australian Diabetes, Obesity and Lifestyle study, show disturbing trends.[25] The prevalence of diabetes found in Aboriginal communities participating in the POCT in Aboriginal Hands program was between 2 to 3 times the national average and consistent with rates reported in other indigenous studies.[5] Rates of microalbuminuria of the order of 20% were 3 times the national average.[26] As for diabetes, these high rates of early renal disease were consistent with those found in previous studies by our group and other independent studies in Aboriginal Australia.[14,27–29] Rates of hypertension were approximately the same as the national average of 29%, whereas prevalence of abnormal lipids (cholesterol, >5.5 mmol/L) were lower than the national average of 51%. Rates of smoking and obesity were 3 to 4 times and 2 to 3 times the national averages, respectively.[25] In May 2004, the Australian Government introduced the Adult Health Check for all Aboriginal people aged between 15 and 54 years of age.[30] The aim of this national initiative was to encourage early detection, diagnosis and intervention for common chronic conditions (such as diabetes, renal and heart disease) that cause significant morbidity and early mortality. POCT dovetails neatly into this initiative, which should result in the wider use and uptake of POCT across Aboriginal Australia.

For management of chronic disease, POCT has a crucial role in reducing the burden of diabetes and end-stage renal disease in Aboriginal Australia. Glucose meters have not been accepted well by Aboriginal people with diabetes for a number of cultural and financial reasons, and alternative programs have been needed. Regular monitoring of HbA1c concentrations (to track glycemic control) and urine ACR levels (to target albuminuria and reduce renal complications from diabetes) are now becoming an integral component of the national QAAMS POCT program to assist diabetes management. Increased testing of lipids by POCT should further enhance management for both diabetes and cardiovascular patients. Data presented in this paper confirm that POCT can be effectively integrated into the management of patients with chronic disease and assist in improving clinical outcomes. However, the high mean HbA1c concentrations found in Aboriginal patients with diabetes when POCT was first introduced at the 2 services studied (approximately 9%–9.5%) indicates the extent of poorly controlled diabetes in indigenous Australians and highlights the magnitude of the task ahead for clinical and allied health professional staff managing these patients.

Community acceptance of POCT was extremely high in all stakeholder groups surveyed in the POCT in Aboriginal Hands program. POCT played a vital role in improving patient self-motivation due its convenience, the immediacy of result and a belief by patients that the doctor was better able to manage their diabetes by having their results available at the time of consultation. POCT proved clinically and culturally effective across the diverse mix of participating Aboriginal medical services with small, medium, and large infrastructures and widely divergent geographical locations. In addition, the versatility and adaptability of POCT in the rural and remote Aboriginal community setting was confirmed by the variety of different locations and community contexts in which POCT was used during this program.

Many challenges nonetheless remain for POCT in the indigenous rural and remote environment. In this program, a government-funded medical rebate was available for POCT HbA1c testing conducted for managing patients with established diabetes. This rebate for POCT HbA1c testing is available to all services who are members of the national QAAMS Program. For risk assessment, the costs of selected POCT were absorbed as part of the rebate available for the

adult health check. The remainder of the costs for reagent and consumable supplies were borne by the goodwill of the participating POCT diagnostic companies. Cost effectiveness of POCT will continue to be an important element for sustainability of POCT programs in rural and remote Australia.

The POCT in Aboriginal Hands program has been successful because there has been excellent commitment to this program from the management and clinical staff of participating services. Furthermore, each service has provided strong support and encouragement for the Aboriginal health worker teams in their role as POCT operators, and there have been minimal health worker staff changes across the lifetime of the program. However, it should be noted that many Aboriginal medical services continue to have excessive rates of staff turnover that make health programs, including POCT, difficult to sustain. Innovative means to maintain "by distance" education and training for POCT operators in the face of ever-changing staff patterns will be a crucial factor for POCT programs as the use and application of POCT continues to expand and evolve in rural and remote Australia.

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All members of the participating Aboriginal communities are sincerely thanked for their long-term interest in the program. In particular, the dedicated and committed team of Aboriginal health workers across participating sites were pivotal to the success of the program; they include Richard Jones, Jeremy Coaby, Judith Borg, Sandy Wilson, Denise Pompey, Naomie Winters, Ray Coleman, Albert Doughty, Cyril Yarran, Peggy Giles, Muriel Fewquandie, and Regina Williams. Clinicians and allied health professional staff deserving of specific acknowledgment for their significant input to the program include Drs Sue Nettlefold, Wayne Hayter, Torome, Anne Stephens, Ben Ansell, Andrew Knight, Kathy Mallory, Michael Kerrigan, and Katrina Allen, as well as Lynette Lemmey, Donna Sellen, Heather Collins, Bev McCurry, Louis Szema, Elize Willemse, and Steve Pratt.

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POINT-OF-CARE IN ABORIGINAL HANDS.

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STATEMENT OF AUTHORSHIP

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Conceived research and study design; initiated, implemented and managed study, analysed and interpreted data, wrote manuscript and acted as corresponding author.

Signed .... *Date* 18/12/2006

JONES, R.

Aboriginal Health Worker, provided community and clinical services including acting as POCT Operator at Aboriginal health service, and commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed .... *Date* 18.12.06

MAZZACHI, B.

Assisted with POCT training at community level, assisted with data analysis, and commented on initial draft of manuscript.

I give consent for M.D.S. Shephard to present this paper for examination toward the Doctor of Philosophy

Signed .... *Date* 18/12/06

Point-of-Care in Aboriginal Hands.

This descriptive paper, published specifically for the Australian Aboriginal Health Worker audience, provided a narrative about the Point-of-Care Testing in Aboriginal Hands Program and reported early results from the study. The inclusion of Richard Jones, the principal Indigenous POCT operator at the Port Lincoln Aboriginal Health Service, as co-author on the paper further demonstrated the collaborative nature between my research team and the Indigenous health service in this program.

Point-of-Care in Aboriginal Hands

RICHARD JONES#, BERYL MAZZACHI* AND MARK SHEPHARD*

Introduction

Diabetes, kidney disease and heart disease (which are all called chronic diseases) are among the most serious health problems facing Aboriginal people today. Aboriginal people suffer between 12 to 17 times more deaths due to diabetes than non-Aboriginal people. In many Aboriginal communities, between 15 and 25% of adults have diabetes. Across Australia, the number of Aboriginal people who have serious kidney disease and are on kidney machines (dialysis) is nine times that of non-Aboriginal people. We've all heard about the situation in the Tiwi Islands off the coast of Darwin where rates of renal disease are the highest in the world. Looking at cardiovascular disease, the number of Aboriginal people between 25 and 44 who have severe heart disease is now ten times that of non-Aboriginal people.

The problem with these chronic diseases is that a person may feel relatively well and not know they have the disease until it's too late. One of the keys to preventing these diseases is to identify them early through regular health checkups even when a person feels well. Early identification, with follow-up management, can slow and in some cases even prevent the diseases from becoming serious. This allows people to live longer and more healthily, without getting the serious complications these diseases cause (like blindness from diabetes, being on the kidney machine, and strokes or heart attacks).

What's our Program About?

Through a partnership between the Port Lincoln Aboriginal Health Service (PLAHS) at Port Lincoln and the Community Point-of-Care Centre at Flinders Medical Centre (FMC) in Adelaide, we have been running a new comprehensive health program for the past year called 'Point-of-Care in Aboriginal Hands'. The program has a broad chronic disease focus that **(a)** looks for early signs of diabetes, kidney disease and heart disease collectively and **(b)** provides follow-up management for people identified as being at risk for chronic disease.

The unique feature of the program is that it involves the use of point-of-care (POC) medical instruments. These are small portable machines that can do exactly the same tests for diabetes, kidney disease and heart disease as the large hospital laboratories. However, the specific advantages of these machines in Aboriginal hands is that:

- Aboriginal health workers at PLAHS can do the tests in the Port Lincoln community (thereby empowering them to have greater responsibility for looking after their people's health),
- you only need a fingerprick of blood or a drop of urine to do the tests,
- and the results are available for clients within 10 minutes.

So it's a more convenient and easy service for clients at Port Lincoln. They don't have to have a lot of blood taken from their arm and they don't have to wait several days for their results - results are available on the spot and they can be discussed with the PLAHS Aboriginal health worker team and then with the service's doctor (David Mills) immediately. So the point-of-care instruments provide a real focus for chronic disease in the community and there is a strong sense of community ownership of the program.

Who is involved?

The key people working on the project are Richard Jones (as the main Aboriginal health worker responsible for the program at PLAHS), fellow Aboriginal health workers Tony Burgoyne, Jeremy Coaby, Denise Thomas and Judith Sherry, clinic nurse Angela Dufek, Dr Mills, as well as Mark Shephard, Beryl Mazzachi and Karan Lavender from Flinders. The Flinders team's role is to train the health workers in how to use the instruments, provide a range of ongoing quality management services for the POC machines, and help manage the health information being collected. But, it's important to emphasise that the program is very much community-controlled and community-owned and run by the

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Port Lincoln health worker team. Through a sponsorship agreement secured with the makers of the point-of-care machines, it's also a free service for the Port Lincoln community for the duration of the program (which is a minimum of three years).

The program is also being conducted in a similar way at three other sites, namely the Riverland region in SA, Meningie in the Hills Mallee Southern region of SA and at Bega Garnbirringu Aboriginal Health Service in Kalgoorlie, WA. Each site has a local Aboriginal health worker in charge of the program, with support from a local medical officer or GP. Depending on the site, other support staff may also include further health workers, a clinical nurse, as well as other health professionals like a diabetic educator or nutritionist.

So for example, from the Riverland, health worker Peggy Giles runs the program along with fellow health workers Muriel Fewquandrie and Regina Williams, while Dr Wayne Hayter provides clinical support. Sandy Wilson (from Meningie) is the health worker in charge of the program in the Hills Mallee Southern Mallee region and Sandy receives clinical support from Dr Michael Kerrigan. Denise Pompey is in charge of the program at Bega, with support from nutritionist Steve Pratt, Bega's chief medical officer David Dunn and other health workers Ray Coleman and Cyril Yarran.

How Does the Program Work in the Port Lincoln Community?

The program provides a **screening service for the early detection of chronic diseases** and there is also a **follow-up management arm** of the program for people identified as being at risk.

In relation to the early detection side of the program, clients can simply come to the Port Lincoln Aboriginal Health Service voluntarily and ask for the free screening to be done. If a client is already at the clinic to see Dr Mills for another reason, then Dr Mills may ask that the POC tests be done opportunistically if he thinks the client may be at risk for chronic disease. Because the POC machines are small and portable, they can also be taken out to people's homes or the community to do testing there. For example, community information and screening days for chronic diseases have been run at the Mallee Park Football Club, at the Pt Lincoln Aboriginal Community Council, and at the local TAFE College.

To do the screening, the health

Some members of the Point-of-Care in Aboriginal Hands team at Port Lincoln. Front row (left to right): Denise Thomas, Richard Jones and Angela Dufek. Back row: Jeremy Coaby and mark Shephard.

worker checks the person's blood pressure, records their height and weight (so we can calculate their body mass index, as a measure of obesity) and then takes a fingerprick of blood, which is put onto the point-of-care instruments.

One machine, called the Bayer DCA 2000, does a test called Haemoglobin A1c (or sugar-haemoglobin). This test provides information about diabetes and how well the person's blood sugar has been controlled for the last three months. We're using the test not only for monitoring known diabetics but also to see if we can use it to pick up any new people with diabetes.

Another machine, called the Cholestech LDX Lipid Analyser, measures the lipids (or fats) in a person's blood, especially the different types of cholesterol, as well as glucose. This test therefore gives us information about risk of heart disease.

Each person is also asked to provide a urine sample, with the first morning sample being the best specimen to test. A small drop of urine is put onto the DCA 2000 point-of-care machine to test for albumin:creatinine ratio (or ACR) which looks for very early signs of kidney disease - at a point where kidney disease can be stopped or prevented from becoming serious.

Information is also collected about their personal and family medical history and aspects of lifestyle.

The whole process only takes around 10-15 minutes. The results are written onto a single-page result sheet that is immediately available to the client and to the doctor. Dr Mills takes all the information and uses it to build up a picture of the person's risk for chronic disease. It is explained to clients that, even if something shows up, it's better to know early because Dr Mills can work with them to improve their health. If things are left unchecked, then it may be too late to help once a problem is eventually picked up.

The Flinders team come over to Port Lincoln regularly. They help with community days, assist with screening, provide on-going education and training, keep stocks of testing cartridges up to date, provide on-going quality management services for the POC instruments, and help manage all the results.

Working with the community: Beryl Mazzachi, Richard Jones and a client from Port Lincoln discussing her point-of-care results.

Looking at Some Results So Far

The program commenced in August last year, and will continue for another two years at least. As well as helping individual people, the program is also looking at community trends, which will help identify future health priorities for the Port Lincoln Aboriginal Health Service and highlight areas where we need to raise community awareness.

As at September 2002, 122 people from the community have been tested for their risk for chronic disease (comprising almost equal numbers of males and females). Twenty-eight of those screened were between 15 and 29 years of age, 49 were between 30 and 44, and 45 people were 45 years or over.

The overall chronic disease risk profile of our community currently shows:

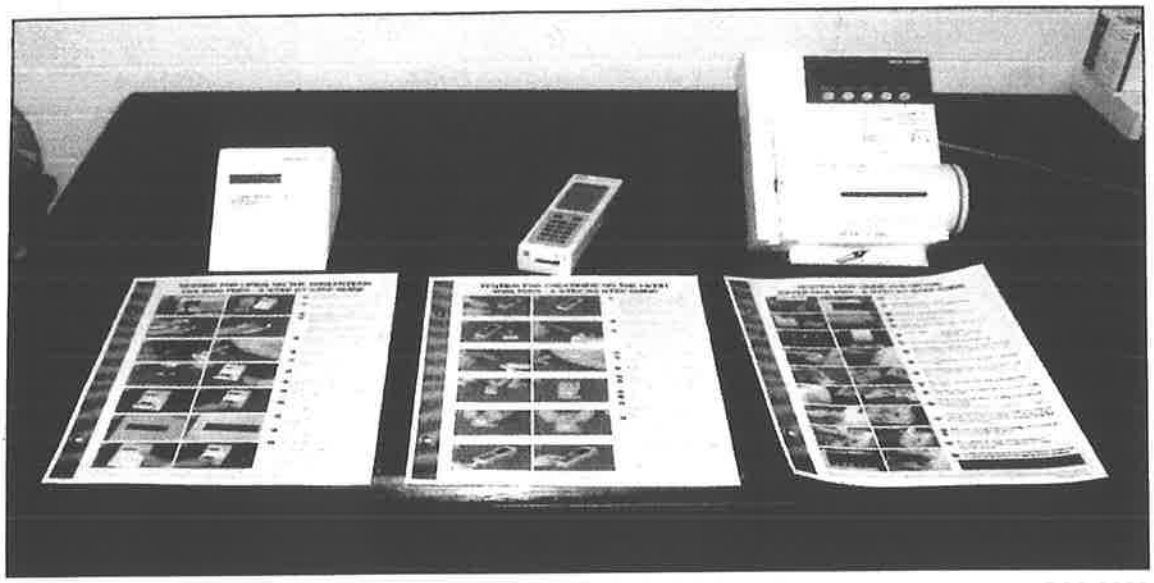
- A quarter of all the people tested have diabetes,
- High levels of total cholesterol were found in nearly 40% of people (with raised levels of other blood fats like triglyceride and LDL cholesterol also being very common),
- One in five people screened had early signs of kidney disease (called microalbuminuria), while a further 5% had established kidney disease (macroalbuminuria),
- Over a third of the people had high blood pressure, while over 40% had a body mass index greater than 30 indicating obesity,
- Rates of smoking, alcohol and family history were also common.

Looking across gender, we have seen that:

- men in the community have much higher total cholesterol levels than women,
- while women had a much higher rate of obesity.

So this information identifies health areas specific to both males and females that PLAHS can target for future health programs.

Looking even more closely at the information the program is generating:



The point-of-care instruments being used at Port Lincoln: Cholestech lipid analyser (left) and the Bayer DCA 2000 (right). The instrument in the middle is the Abbott i-STAT analyser, another POC instrument that may be used at Port Lincoln in the future. Pictured in front of each instrument is a step-by-step guide that shows how to perform a test on each instrument. These guides were produced by the Flinders team as an educational resource to assist the PLAHS health workers.

✦ There is a strong link between age and rates of diabetes, high blood pressure, early and established kidney disease (albuminuria) and blood lipids.

✦ Although, thankfully, the number of people with macroalbuminuria is small, we have also found a link between the degree of albuminuria and HbA1c and glucose, as well as body mass index.

Just a couple of words on the **follow-up or management arm of the program**, which is now starting to gather momentum as the number of people screened is getting larger. As mentioned earlier, a client comes to a health worker and has their point-of-care tests done. The results are written onto a single-page result sheet, which is given to Dr Mills. He then makes an assessment of the person's risk and, using a simple tick-box system at the bottom of the result sheet, records what further point-of-care testing is needed for on-going client management and the frequency of that testing. The result sheet is faxed to Flinders, put into the client's notes, and entered by a health worker into the Ferrett patient management system that is used at Port Lincoln. The Flinders team then sends back regular lists of all tests requested for on-going management of each client (as requested by Dr Mills) including when they need to be done. (The Ferrett system also has a patient recall function that is used to help with patient management). As a further resource for health workers, a series of laminated cards that detail what follow-up tests are needed (and when) for different risk profiles has been produced by the Flinders team.

Across next year, we'll be working with Dr Mills to try to gather information about the relationship between point-of-care testing and improved health outcomes for our clients. We'll be trying to measure the impact that point-of-care testing has had on things like glycaemic control, compliance in taking tablets, turn-around times to get people started on management plans, frequency of follow-up visits by clients, and we'll survey community members at Port Lincoln to see how they feel about having point-of-care testing available as a service in their community.

Concluding Remarks

The program and, in particular the POC instruments, (which are quick and easy to use) has been accepted well within the Port Lincoln Aboriginal Health Service. Clients seem to be happy with the service that's being provided and Dr Mills is pleased with having results immediately available that he can act on.

In the coming years, it's very likely that point-of-care instruments will be used more widely in Aboriginal communities across Australia. Through the Point-of-Care in Aboriginal Hands program and the partnership with Flinders, Port Lincoln Aboriginal Health Service is right at the leading edge of bringing this new technology to help the health of its people. ✦

POINT-OF-CARE TESTING IN THE ABORIGINAL COMMUNITY.

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Australian Journal of Medical Science 2003; 24: 10-16.

Point-Of-Care Testing In The Aboriginal Community.

This paper was written in the early phase of this research program. Its specific aim was to highlight to the broad Australian medical science community some of the unique cultural issues faced by the non-Indigenous researcher in conducting research studies in the Indigenous community setting. It also, at the request of the journal's editor, explored some of the personal issues faced by the author in establishing my POCT research models, having made the decision to leave the laboratory bench to become a community-based researcher with an initially very limited funding base.

Commentary

Point-of-care testing in the Aboriginal community

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Keywords - point-of-care testing, chronic disease, Aboriginal health workers, laboratory concepts, quality assurance

Introduction

This article documents my experiences over the past five years working in the field of Aboriginal health. Since I began this work, I have had to transform myself from a medical scientist working behind the laboratory bench to a manager of people, projects, publications and finances.

During 1996, I left the relative comfort of that laboratory bench to join the Renal Unit at Flinders Medical Centre in the pursuit of becoming involved in Aboriginal health, an area for which I had a long-standing interest and empathy.

Throughout this article, I will focus on a number of fundamental differences between working in the Aboriginal health sector as opposed to the laboratory environment and the western or traditional view of health management.

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The programs

The principle focus of our work is the application of Point-of-Care (POC) technology for the early detection and management of chronic diseases in the Aboriginal community setting. As a medical scientist specialising in clinical biochemistry, I intuitively felt that POC technology might be useful in the Aboriginal health sector. It was only when our work started in earnest that I realised just how exquisite was the fit. Apart from the well-acknowledged advantages of using POC technology such as portability and small sample size, there are other advantages specific, and directly applicable, to the Aboriginal health care setting.

Through appropriate training, Aboriginal health workers (Aboriginal people living in the community who are trained in primary health care) can perform POC tests on-site, thereby empowering them to take greater responsibility for the health of their own community members.

Immediate availability of results means that the client does not have to come back for a follow up visit. By conducting the tests on-site, ownership and control of

health information remain with the community, a factor crucial to the acceptance and success of indigenous health programs.

My training as a medical laboratory scientist also provided me with the knowledge and understanding that education, training and quality assurance must underpin the use of POC technology in the field. Having these three elements as our core or fundamental principles has been absolutely pivotal to the successful translation of our work into the community setting.

The chronic diseases diabetes, renal disease and cardiovascular disease account for a huge burden of morbidity and mortality among Aboriginal people. Some of the facts include:

- The mortality rate from diabetes amongst Aboriginal people is twelve to seventeen times that of non-Aboriginal people. Prevalence rates for diabetes in many Aboriginal communities are as high as 25-30%
- Renal disease has reached epidemic proportions in many parts of Australia, notably the Tiwi Islands where rates of end-stage renal disease (ESRD) are sixty times that of non-Aboriginal people and among the highest in the world
- Aboriginal people between the ages of 25 and 44 years suffer ten times more deaths due to coronary heart disease than non-Aboriginal people.

Early detection is the key to slowing (and in some cases preventing) the progression of these chronic diseases and the debilitating complications they cause.

Our work is thus centred on an area of significant disease burden for which there is a biochemical/ technological application to address (in part) the problem. Within this framework, I have been fortunate to work on three major Aboriginal health programs as Program Manager.

The Umoona Kidney Project was a program for the early detection and prevention of renal disease in the 450-strong Umoona Aboriginal Community at Coober Pedy, 850kms north of Adelaide (Shephard *et al* 2003; Shephard and Allen 2001; Shephard *et al* 2000; Shephard 2000; Zeunert *et al* 2002). This project was a partnership between the Renal Units at Flinders Medical Centre and the Women's and Children's Hospital in Adelaide and the Umoona Tjutagku Health Service in Coober Pedy.

The Bayer DCA 2000 POC analyser was used to measure urine albumin:creatinine ratio (ACR) as the cornerstone of the renal screening program. The overall risk factor profile for chronic disease among the 158 adults screened was very disturbing, with 42% of people being hypertensive, a quarter having diabetes, and there was a large incipient pool of renal disease with 19% of people having microalbuminuria and 9% having macroalbuminuria. A strong correlation was observed between the degree of albuminuria and hypertension, obesity, glucose and age.

Thirty-five people were offered the ACE inhibitor medication Coversyl to reduce their blood pressure and stabilise their renal function and a significant improvement in both the cardiovascular and renal disease risk profile of this group has been maintained for over two years. The Umoona Kidney Project was handed over to the community as a self-sustainable program in December 2000.

The Quality Assurance in Aboriginal Medical Services Program (QAAMS) is an on-going national education, training and quality assurance program to support on-site HbA1c testing on the DCA 2000 for over 2300 Aboriginal people with diabetes (Shephard 2000; Brice *et al* 2001). In developing and managing this program, we have worked closely with the Office for Aboriginal and Torres Strait Islander Health (OATSIH), the National Aboriginal Community Controlled Health Organisation (NACCHO) and the RCPA Quality Assurance Programs Pty Ltd. Over 40 Aboriginal Community Controlled Health Services around Australia participate in the program, with their Aboriginal health workers conducting the HbA1c testing. The quality assurance arm of the program is believed to be a world-first for indigenous people.

The program has achieved a number of key milestones. For example, a participation rate of 86% has been maintained across the first three years of the program, despite a significant number of health worker staff changes. Aboriginal health workers, with culturally appropriate continuing education and training have been

able to achieve a standard of analytical performance for quality assurance testing that is consistently close, or equivalent, to that of trained laboratory personnel.

Through a directive of the Federal Health Minister, a Medicare rebate is now available for on-site HbA1c testing on the DCA 2000 conducted in participating Aboriginal Community Controlled Health Services. The rebate, conditional on continued participation in the QAAMS program, will ensure the long-term sustainability of the program.

Further Commonwealth funding has recently been secured to extend the program for another three years. In 2003, our first international site (from the Western Pacific) will join our QAAMS program for HbA1c.

The Point-of-Care in Aboriginal Hands program is a comprehensive screening and management program for diabetes, renal disease and cardiovascular disease (Jones *et al* 2002). The program is supported by the field use of three POC instruments – the DCA 2000 (for HbA1c and urine ACR measurements), the Cholestech LDX lipid analyser (Shephard and Tallis 2002) and the Abbott i-STAT analyser (used for creatinine measurements).

The program is currently being run at Port Lincoln, the Coorong and Riverland regions in South Australia and at Bega Garnbirringu Aboriginal health service at Kalgoorlie in Western Australia. Early results show risk profiles similar to Umoona for diabetes, heart and renal disease.

Across the three programs, our work extends from remote inland desert communities to coastal communities at either end of the country.

In the long term our goals are to:

- Continue to work intensively with individual rural and remote communities on chronic disease prevention and management programs
- Build the scope and breadth of our quality assurance models both within and outside Australia
- Continue to be at the forefront of evaluating new POC technology before or as it hits the Australian diagnostic pathology market
- Integrate all arms of the work together into a centre of excellence for education, training, quality management and evaluative field research using POC technology; a centre that has application and relevance to both Australian and international, rural and remote, indigenous and non-indigenous communities.

People management

One of the great pleasures of our work is the opportunity to work alongside (and learn from) so many different groups of other health professionals. For example, in the Umoona Kidney Project, at one point, there were 15 people from various disciplines across three sites to work with – these included the Chairman of the Board of the health service, the Director of the health service, its clinical nurse, four Aboriginal health workers, three renal specialists and a medical practitioner, two nutritionists, a medical student, two medical laboratory scientists, and two sports physiologists from the University of South Australia.

In the QAAMS program, we have been fortunate to have the opportunity to work with, in a one-on-one sense, nearly 100 Aboriginal health workers (and allied health professionals).

As mentioned earlier, with appropriate education and training, these health workers are consistently achieving an analytical performance standard for quality assurance testing that is close, or equivalent, to that of trained laboratory personnel.

Through this program, there has also been the opportunity to work closely with two medical laboratory scientists from the RCPA Quality Assurance Programs Pty Ltd, Janice Gill and Lloyd Penberthy.

With the Point-of-Care in Aboriginal Hands program, we have worked with rural doctors at each site, local nurses, diabetic educators and nutritionists and, collectively, more than 10 Aboriginal health workers.

There has also been the opportunity to develop and foster productive working relationships with government officials at State and Commonwealth levels (notably from within the Commonwealth Department of Health and Ageing), and industry representatives across Australia.

Finally there is my work team, comprising a medical laboratory scientist (Beryl Mazzachi), a research assistant and an administrative assistant, at our newly created home base, the Community Point-of-Care Centre at Flinders Medical Centre. Glen Allen, a senior medical laboratory scientist with the Renal Unit, also has significant input with the information technology and data management side of our work.

Working with all the above groups from so many diverse medical and health backgrounds, good communication skills and, more importantly, the ability to adapt those skills to suit the particular situation and environment have been crucial to ensure the on-going (community-based and financial) viability of the work.

Cultural skills and cultural awareness

The fundamental principle in working on any Aboriginal health project is that the community involved must have a sense of ownership and control of the program. Partnerships based on equal standing, mutual trust and respect are paramount. Otherwise the project will be doomed to failure and will not get past first base. With the Umoona Kidney Project for example, we spent six months liaising with the community, listening to the community's aspirations and developing project aims and objectives before the project commenced in earnest. This proved crucial in both getting the project off the ground and maintaining its success. On the first day we commenced renal screening, seventy community members voluntarily presented at the clinic. The Director of the health service said she had never before seen such a positive response to a community project – all because the community were fully informed and understood what the project was about, and they knew what the program meant for them individually and collectively.

There is a real challenge for the non-Aboriginal health professional to translate complex scientific, medical or laboratory concepts into culturally appropriate images as transfer of information in Aboriginal culture is based on the spoken word and visual images. Using some examples from our work, the relationship between HbA1c and diabetic control has been portrayed by using spoonfuls and wheelbarrows of sugar. HbA1c has been described simply as sugar that is attached to haemoglobin in the red cells of the body. In discussing the concept of accuracy and precision, the analogy of an AFL footballer having kicks for goal has been used.

In another example, from the Point-of-Care in Aboriginal Hands program, we were helping an Aboriginal health worker screen a young man in the service's clinic. The man's blood was left standing temporarily on the bench while we attended another client. When we returned, the red blood cells had begun to settle out, and the plasma was very milky. We explained to the health worker that this milky colour was due to fat in the plasma and that this fat could potentially deposit in a person's arteries and cause a heart attack. This had been discussed previously in detail in an education session given to the health workers. However that instant visual image of the milky fat provided a stronger and more powerful message about heart disease than the ten minute talk I had given about the same topic.

Within an hour, everyone at the health service had seen that lipaemic sample and it was shown to every client in the waiting room with the explanation about how too much fat in the diet can make your blood go this colour and potentially kill you. The blood sample was later photographed and is still used to talk about heart disease.

It is important to be respectful of Aboriginal time, space and cultural priorities. Aboriginal people have a different concept of time to non-Aboriginal people. Their culture is based on time being circular (linking present experiences with their ancestral past), rather than linear (as non-Aboriginal people perceive it, for example, with the working day starting at a set time of 9 am and ending at another set time of 5 pm).

Even though an Aboriginal person may have a known serious health problem, that person may give other family-related issues a much higher priority than his/her own failing health. This is why it may sometimes be difficult for an Aboriginal person to keep to a health appointment or a follow up visit. Further, a community funeral assumes a very high priority. During two of our 24 field visits to Umoona (each a 20-hour, 1600-km round trip), a community funeral occurred on the day of our arrival. There was no-one in town. We accepted this as we understood and appreciated just how culturally important these sad events were for the community.

Even simple things are important. Casual jeans and an open-necked shirt are our standard uniform during

field visits. It is important to blend in rather than stand out in the community because we are coming to work on Aboriginal land and in their environment.

In the laboratory, expensive equipment, computers and other resources surround us and (generally, although perhaps not necessarily in this day and age) we have adequate staff numbers. As a non-Aboriginal health professional, it is important to understand and appreciate the extreme difficulties most Aboriginal health services (particularly those in rural and remote locations) have in relation to staff turnover, or access to even the most basic resources.

The best example I can give is to describe the working conditions at one of the sites in the QAAMS program. It is located in a very remote desert region of outback Australia and receives mail delivery by plane once a week. (The plane actually lands at the nearest town some 700 kilometres away and a service representative then collects the mail). The service experiences regular power fluctuations, is connected to the outside world by a satellite phone link that regularly breaks down stranding the service from outside communication for days at a time, and only one Aboriginal health worker is employed at the service. Despite these difficulties the service has maintained a 90% participation rate in the QAAMS program over three years and has regularly been ranked in the top 25% of services for its accuracy and precision base for HbA1c testing on the DCA 2000.

Ethics

Most clinically based health programs involving human subjects need institutional ethics approval before they can be conducted.

In Aboriginal health, there are additional ethical requirements. For example, in South Australia, there is an over-riding body called the Aboriginal Health Research Ethics Committee (AHREC) of South Australia. Every health project involving Aboriginal people must receive ethics clearance from this body before commencing.

Grant writing – and the connection with time and resource management

One of the conditions of my move from medical biochemistry to Aboriginal health was that the work would need to be funded entirely from external grants. So one could say, with good justification, that we have very much been living on the edge for survival.

One of the downsides of being successful in securing a grant, however, is that most granting bodies now have very rigid and frequent reporting deadlines.

There is a vicious cycle occurring here too. Spending 25-30% of my time writing grants means there is less time to spend actually doing the work. Productivity therefore suffers potentially. But you must continue to be productive, because when the time arrives to go back to funding bodies to seek the next extension of your grant, they want to know how productive you have already been.

With the way in which our workload has expanded over the past two years in particular, additional staff have been employed to maintain our productivity. Extra staff means further salary money is required and therefore extra grant writing ... and so the cycle continues.

Financial management

When I first started this work, a colleague told me: "you'll be right, there's plenty of money in Aboriginal health." Yes, there is funding to support Aboriginal health – but, quite appropriately, funding bodies prefer to direct available funding to the Aboriginal community itself, rather than to non-Aboriginal, metropolitan-based health professionals.

A breakdown of the source of the funds we have been able to attract over the past 5 years is as follows: Commonwealth government 62%, State government 13%, Industry 19% and Private Enterprise 6%. The level of funding secured on a year-by-year basis since we started this work is thankfully trending upwards.

Our main budget lines are salary, travel, rent (for our new centre), quality assurance materials, information technology, and production of education and training materials. Around 5% of my time goes towards administration of these funds.

There is a hidden story in these figures, in that the flow of funds has tended to be very cyclical in nature.

Therefore it has been very important to have reserve funds in hand for the periods of drought, and this is where support from industry has been so vital.

We have been fortunate to be able to forge good collaborative working relationships with senior researchers in Aboriginal health, who have been at the forefront of research into Aboriginal renal disease and diabetes respectively for many years. There will be major opportunities to build on these collaborative links in the coming years.

Publish or perish

In the cut-throat world of research today, the philosophy of publish or perish is very strong, and researchers are often judged by the number of papers they write. However, when working in Aboriginal health, it is not just a matter of completing the work, writing it up and sending it off.

Permission to publish must be given by the Aboriginal community and/or the health service with which you have been working, while the manuscript must be reviewed and approved at the community level before sending it for publication.

With the Umoona Kidney Project for example, published papers or abstracts we have prepared have generally been co-authored by at least the Director of the Health Service, while Aboriginal health workers have been included regularly as co-authors.

One of the pleasing things about the projects that we have worked on is that we have been able to publish in a diverse range of journals - medical, scientific, nutrition and Aboriginal-based.

Conclusion

I would like to finish by briefly addressing several questions.

Has the vision of taking POC technology to the Aboriginal community worked? An independent report (Brice *et al* 2001) prepared on the first eighteen months of the QAAMS program by the National Aboriginal Community Controlled Health Organisation (NACCHO), the peak Aboriginal body representing the health of its people in Australia, concluded in its Executive Summary that:

- The use of [the DCA] POC technology presented a major opportunity to assist communities to better care for and manage Aboriginal clients with diabetes within the community setting
- The ability of the POC technology to generate rapid results served as a catalyst to enhance patient self-management
- The simplicity of use of [the DCA] POC technology generally led to high levels of acceptance by Aboriginal health workers nationally, with two-thirds of services expressing the view that it had raised the self-esteem of Aboriginal health workers in the community context
- The sense of community control was enhanced as a result of diabetic management becoming more focussed within Aboriginal medical services.

Finally, have we, as a group, been successful? As mentioned previously, success is not judged by western standards of number of publications, the volume of medical/scientific results or the complexity of statistical analyses. It is judged by how well your programs are accepted within and by the community, and it takes time and patience to establish yourself and your credentials.

I will conclude this article with a quote from the inaugural Director of the Umoona Tjutagku Health Service, who wrote to us in late 1998:

> *"The [renal] team has built up a feeling of trust amongst community members and has made many friends. The team's willingness to listen and involve the community has provided a good model for future projects."*

Acknowledgement

I wish to acknowledge Barry Young from Servier Laboratories (Australia) Pty Ltd in Melbourne, who provided crucial start up assistance to our work in 1997.

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POINT-OF-CARE TESTING IN THE INDIGENOUS RURAL ENVIRONMENT – THE AUSTRALASIAN EXPERIENCE.

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Point-Of-Care Testing In The Indigenous Rural Environment – The Australasian Experience.

This invited book chapter described my three main Indigenous POCT models and some of the early research findings from these programs. The book chapter discussed both the general application of POCT in the rural health environment in Australia and the specific context of rural Indigenous medical service, outlining both the potential benefits and challenges faced by POCT in this primary care setting.

As mentioned previously, the book in which this chapter was written, is now considered the definitive global text book in the field of POCT.

Erratum:

The examiners should note two minor discrepancies in the results presented in this chapter.

In the section on the Umoona Kidney Project, the reduction in urine ACR among the 35 patients receiving specialist management is stated as falling from a mean of 17 to 12 mg/mmol. Specialist statistical advice received post publication suggested that urine ACR reduction would be better expressed as a median rather than mean due to the non-Gaussian distribution of the urine ACR values. This correction was made in the main paper on the management arm of the Umoona Kidney Project published in *Rural and Remote Health* 2006 and presented earlier in this Chapter.

Table 29.2 documents the comparative precision base achieved by QAAMS services and laboratory users of the DCA 2000 for HbA1c POCT. The imprecision for laboratories in the period July-December 2003 was quoted as 3.0. This figure, which was correct at the time of publication, was later updated by the RCPA Quality Assurance Programs Pty Ltd to 3.3. This revised figure is presented in the Table in the most recent paper on the analytical quality of the QAAMS Program published in the *Clinical Biochemist Reviews* in 2006 and presented earlier in this chapter.

Chapter 29

Point-of-Care Testing in the Indigenous Rural Environment—The Australian Experience

Mark D. S. Shephard

The characteristics of rural health and the issues driving the delivery of healthcare services to the rural environment are very different from those of metropolitan centers. Geographical isolation and its effect on access to health services is the defining element of rural health (1). In addition, the differing social, lifestyle, and environmental determinants of health in the rural population, including a greater degree of cultural diversity; lack of employment opportunities; lower income levels; and poorer access to housing, education, and transport, significantly influence the mode of healthcare delivery, health status, and patterns of disease (2). Overall, the rural sector experiences higher mortality rates and poorer health status than metropolitan regions, a trend that becomes more apparent with increasing remoteness (3). Prevalence rates for both acute and chronic conditions and communicable and noncommunicable diseases are generally higher in rural than in metropolitan environments, and greatest in remote regions (4).

The challenge of reducing the health differential between rural and metropolitan environments lies with the development of inventive solutions to specific local health problems (1). The astute and practical application of point-of-care testing (POCT) can unquestionably be one of those inventive solutions in the broader context of improving rural healthcare delivery—in both the acute and chronic clinical context.

POINT-OF-CARE TESTING IN THE RURAL HEALTH ENVIRONMENT

A recent review of the role and value of POCT in general practice in Australia concluded that rural and remote health practices in particular could be major beneficiaries from the adoption of POCT (5).

There are a number of clinical conditions for which POCT represents a practical and viable option for the rural health practitioner. For acute trauma and/or emergency surgery where retrieval may be necessary, POCT for tests such as potassium and blood gases are of particular clinical relevance. Point-of-care (POC) measurement of cardiac markers such as the troponins, heart fatty acid binding protein, and ischemic modified albumin can provide important information in the differential diagnosis of chest pain and subsequent early initiation of thrombolytic treatment. Timely POC international normalized ratio (INR) monitoring is important in preventing thrombosis and avoiding excessive bleeding during surgical procedures. INR is also of use in monitoring of Coumadin® (warfarin) therapy.

There are several examples of innovative and effective rural hospital-based POCT models for some of these acute care tests being used in Australia. Queensland Health Pathology Service has developed an integrated state-wide network of approximately 50 rural and remote hospital sites that are all using the i-STAT® analyzer (i-STAT, East Windsor, NJ, USA) for onsite measurement of electrolytes and blood gases. All patient results and quality control data are captured following analysis and sent to a central data station, located at the Prince Charles Hospital in Brisbane, via a network downloader. Results with correct patient data entry are then forwarded to the hospital's laboratory information system (6).

In South Australia, the *i*CAR*net* group (Integrated Cardiac Assessment Regional Network) was established in 2001 to support rural general practitioners in the delivery of up-to-date evidence-based management of patients presenting with chest pain, or other symptoms suggestive of acute coronary syndrome. The network provides POC Troponin T testing using a cardiac reader (Roche Diagnostics, Mannheim, Germany), evidence-based triage, risk stratification and management guidelines, and 24-h on-call cardiologists (7).

In addition, many POC tests for the management and/or risk assessment of patients with chronic illnesses are being used in the rural environment. Hemoglobin A1c (HbA1c), glucose, and urine microalbumin or albumin:creatinine ratio (ACR) are key tests for the management of patients with diabetes that can be performed at the point of care (8, 9). Urine ACR is also a particularly useful test in the detection of early renal disease (8), and blood urea and creatinine can be monitored for the management of established renal disease. Blood lipids can be conveniently measured by POC technology as part of heart disease risk assessment and management (10), while urine ACR has also been shown to predict cardiovascular risk (11, 12). Whole blood hemoglobin can be measured at the point of care for assessment of anemia status, which may be of significant clinical benefit because anemia is very prevalent in rural tropical environments, particularly among indigenous women and young children (13, 14). There are now many POC tests for tumor makers such as prostate-specific antigen (PSA) and carcinoembryonic antigen. Working POCT models for some of these chronic disease tests are described later.

INDIGENOUS RURAL HEALTH ENVIRONMENT IN AUSTRALIA

Nowhere is the health differential between rural and metropolitan environments more profound than for indigenous peoples living in rural and remote regions. Regardless of which health indicator is used, the health status of Aboriginal people in Australia is worse than that of non-Aboriginal people (15, 16). The chronic diseases—diabetes, renal disease, and cardiovascular disease—typify the health disadvantage of Aboriginal people and collectively pose one of the most significant health issues for contemporary Australian Aboriginal society. For example, Aboriginal people suffer between 12 and 17 times more deaths attributable to non–insulin-dependent diabetes (NIDDM) than nonindigenous Australians. Overall prevalence rates of diabetes are generally within the range of 10% to 30%, and at least two to four times that of the non-Aboriginal population (16, 17). In some communities, nearly half of the entire adult indigenous population has diabetes.

During the 1990s there was a rapid escalation in the number of Aboriginal Australians with end-stage renal disease. Recent age- and sex-adjusted figures indicate Aboriginal people have ~9 times greater risk of developing end-stage renal disease than all other Australians. In some parts of Australia, notably the Tiwi Islands, rates of renal disease are among the highest in the world (18–21). In the Northern Territory, Aboriginal people comprise just over 20% of the population, but represent 95% of people on hemodialysis (22). Cardiovascular disease is the leading cause of mortality in Aboriginal Australians, with mortality rates attributable to coronary heart disease and stroke being twice those of non-Aboriginal Australians (23, 24). Of particular concern are the high death rates from coronary heart disease among young and middle-aged Aboriginal people, with death rates for people 25 to 44 years of age being more than 10 times those of other Australians (23). The extremely high rates of chronic disease among indigenous Australians are caused by a multitude of interrelated factors such as dispossession from their land, destruction of traditional culture and values, exposure to infectious diseases, poor environmental living conditions, and the effects of alcohol and Western diets that are high in fat and sugar.

These appalling statistics on chronic disease are not unique to Australian Aboriginal communities and are mirrored in many other indigenous populations living in rural parts of the world (25). For the Australian indigenous rural community, there is clearly an urgent clinical need to provide effective services for the monitoring of diabetes control to prevent the long-term complications of this debilitating condition. There is also a need to stem the tide of end-stage renal disease by developing community-controlled risk assessment programs for the early detection of this disease. Given that heart disease is the major cause of Aboriginal mortality, the need to characterize cardiovascular risk profiles, particularly among young Aboriginal people, is also of immediate concern. POCT can have a significant role in fulfilling each of these needs, but in this environment implementation and sustainability of POCT faces major challenges.

AUSTRALIAN ABORIGINAL MEDICAL SERVICE

Aboriginal medical services in Australia are either managed and controlled by local Aboriginal people with funding by the Commonwealth or state governments, or they are controlled and funded by state or territory governments. Aboriginal Community Controlled Health Services (ACCHSs) now represent the principal vehicle for delivering primary healthcare to Aboriginal and Torres Strait Islander peoples. There are more than 125 ACCHSs throughout Australia, more than 90% of which are located in rural and remote areas. A peak body called the National Aboriginal Community Controlled Health Organisation (NACCHO) represents the interests and affairs of ACCHSs nationally.

ACCHSs vary considerably in size, infrastructure, resources, and the number of Aboriginal people they service. Many are located several hundred, up to a thousand kilometers, from the nearest hospital or laboratory service. Staffing levels also vary widely, but most services generally have a medical doctor, a clinic nurse, and one or more Aboriginal health workers. The Aboriginal health worker is an Aboriginal person who lives and works in the local community and who has attained a primary healthcare qualification. The health worker provides the pivotal communication link between the community and non-Aboriginal professional staff at the health service.

POTENTIAL BENEFITS AND CHALLENGES OF POCT IN THE INDIGENOUS RURAL ENVIRONMENT

The most significant barrier to effective clinical services in rural and remote Aboriginal communities is limited access to pathology laboratories. As stated above, Aboriginal health services may be several hundred, even thousands, of kilometers from the nearest pathology service, and it may take up to several days for blood samples to reach that service, particularly if air transport is limited or unavailable. The return of results to the community and then to the individual patient incurs further delays. Conventional means of delivery of pathology services are time consuming and of less relevance to the patient, while clinical management is delayed. POCT services overcome these problems of "disadvantage by distance" and do not incur the additional costs associated with transport of pathology samples. Furthermore, distance, in either a temporal or geographical context, can also be associated with poor compliance, e.g., with reattendance at clinics, follow-up of results, and treatment changes. The benefits of POCT in relation to improved compliance have been demonstrated for diabetes and anticoagulation therapy in other communities (see Chapters 31 and 41).

POCT has other advantages specific to the Aboriginal healthcare setting. Through appropriate training, Aboriginal

health workers can perform POCT, thereby empowering them to take greater responsibility for the health of their own community members. Immediate availability of results provides a more convenient and timely service for the patient. It also means that the Aboriginal patient does not have to come back for a follow-up visit, which may often be very difficult to organize in the Aboriginal community setting because other social and cultural priorities sometimes take precedence over health matters. By conducting the tests onsite, ownership and control of health information remains with the community, a factor crucial to the acceptance and success of indigenous health programs worldwide.

The challenges faced in providing an effective POCT service in the indigenous rural environment are considerable. Many rural Aboriginal medical services experience difficult working conditions such as dust, excessive heat and/or humidity, power fluctuations, and inadequate lighting and refrigerator space. High rates of staff turnover are a constant problem in many services, making health programs (including POCT services) difficult to sustain. This applies not only to administrative and clinical staff where health service priorities may change with new appointments, but also at the Aboriginal health worker level—the person generally responsible for daily operation and maintenance of POCT. POCT services need to be robust in the face of such change and, as described later, the ongoing delivery of education, training, and support services is critical for sustainability.

Specifically in relation to education and training, there is a real challenge for the non-Aboriginal health professional to translate complex scientific, medical, or laboratory concepts into culturally appropriate images that can be readily understood by an Aboriginal health worker team. This translation is even more important given that the transfer of information in Aboriginal culture is based on the spoken word and visual images. Highly visual laminated posters with simple step-by-step instructions showing how to perform POCT and how to conduct quality assurance testing procedures that consolidate detailed information into a practical, workable format have proven useful in our hands.

EFFECTIVE AND SUSTAINABLE POCT MODELS IN THE INDIGENOUS RURAL ENVIRONMENT

Three health models utilizing POCT for chronic disease prevention and management, which have proven successful in the rural Australian Aboriginal environment, are now described. They are the Umoona Kidney Project, the national Quality Assurance for Aboriginal Medical Services (QAAMS) Program for POC HbA1c testing, and the Point-of-Care in Aboriginal Hands Program (26). Each model is based on four fundamental elements: continuing education, training, quality management, and ongoing support for POCT. It is important to reemphasize that these models function outside the comfort zone of the hospital base, with the Aboriginal community and their associated health service driving the model (not the laboratory). The POCT challenge has been to develop quality-assured, robust, sustainable, and clinically effective models for the community setting. Each model is discussed in turn under common themes of background, chronic disease focus, POCT instrumentation and markers used, principal activities and results, evaluation, sustainability, and transferability.

Umoona Kidney Project

The Umoona Kidney Project was a partnership between the Umoona Aboriginal community at Coober Pedy in South Australia's far north (850 km from Adelaide) and the Renal Units at Flinders Medical Centre and Women's and Children's Hospital, Adelaide, South Australia (27–31). The program involved a number of people and health professional groups. From the Umoona community, the board, the director, the clinical nurse, four Aboriginal health workers, and community members participated in the program. From the Flinders' and Women's and Children's Hospital teams, there were two nephrologists, two scientists, and one nutritionist from each site together with a medical student who worked under a National Health and Medical Research Council (NHMRC) Training Scholarship.

The primary focus of the Umoona Kidney Project was a voluntary (or opportunistic) renal disease risk assessment program for the >400 adults and children in the community. There was also a voluntary clinical management program for adults identified as being at risk for renal disease.

The DCA 2000 (Bayer Diagnostics, Tarrytown, NY, USA) was the cornerstone of both the renal risk assessment program and the clinical management arm. The device measures urine albumin:creatinine ratio (ACR) on 40 μL of a first morning urine, as a marker for early renal disease or microalbuminuria. Prior to the commencement of the program, the Adelaide team spent 6 months of groundwork speaking to the community, holding information forums, showing the POCT technology and discussing the ACR test, and educating and training the Aboriginal health worker team in the use of the technology and quality management practices. This groundwork unquestionably contributed to the successful use of the DCA 2000 and the program overall. In addition to the ACR test, risk assessment also involved the measurement of blood pressure, blood glucose, body mass index, and dipstick urinalysis, while a full medical examination and history was taken for each person.

The overall risk factor profile of the 158 adults assessed (which represented ~65% of the adults in the community) showed 42% of the people had high blood pressure, 24% had diabetes, and there was a large pool of incipient renal disease, with 19% of adults having persistent microalbuminuria and 9% macroalbuminuria. A significant association was observed between blood pressure, blood glucose, and body mass index and the progression of albuminuria (as measured by the DCA 2000). A strong association was also found between albuminuria and an increasing number of coexisting risk factors, with only 20% of people having a normal urine ACR in the presence of three or more risk factors (27).

In relation to clinical management, 35 people were identified as being at risk for renal disease. All were either overtly hypertensive, hypertensive with other risk factors, or diabetic with microalbuminuria. Each was voluntarily offered the opportunity to take the ACE inhibitor medication Coversyl (Perindopril, Servier Laboratories, Australia) to reduce blood pressure and stabilize renal function. They were monitored according to a management protocol set by the Flinders' renal specialists, who conducted a total of 231 onsite clinical consultations with the patients on medication from 1998 to 2000. A sustained and statistically significant drop in blood pressure to normal levels was observed, as well as a stabilization of renal function, with mean ACR of the group (monitored using the DCA 2000) falling from 17 to 12 mg/mmol (150 to 106 mg/g) ($P = 0.09$, paired t-test). Across this 2-year period, there was no change in the group potassium, urea, creatinine, or glomerular filtration rate (Table 29-1).

Across 2 years of continuous field testing ($n = 46$) the DCA 2000 exhibited a precision base (CV%) of 6.9% and 3.6% for urine albumin (for Bayer quality control samples with concentrations of 36 and 208 mg/L, respectively), 3.2% and 4.1% for creatinine [9 and 36 mmol/L (1018 and 4072 mg/L)] and 6.7% and 5.3% for urine ACR [ratios of 4.1 and 5.8 mg/mmol (36.2 and 51.3 mg/g)] (29). These are well within precision goals of 10%, 6%, and 12% for urine albumin, creatinine, and ACR that are derived from biological variation and other international consensus data on performance criteria (8, 32).

Members of the Umoona community evaluated the program internally through a survey conducted by community elders, supported by the NHMRC medical student. By all criteria, the community expressed a high level of satisfaction with the program and the use of POCT technology, with a greater than 90% satisfaction rating recorded for all questions. Education and training initiatives for ACR POCT began in earnest in September 1999. Over the next 15 months Umoona's Aboriginal health workers took an increasingly greater responsibility for performing onsite blood pressure measurements and urine ACR testing on the DCA 2000. In December 2000, the program was handed over to the Umoona Community as a self-sustaining activity fully integrated into the health service infrastructure. Both the South Australian Government's Department of Human Services Renal and Urology Services Implementation Plan 2000–2011 and the Statewide Iga Warta Aboriginal Renal Disease Summit, 1999 endorsed the Umoona model for expansion to other Aboriginal communities in rural and remote South Australia.

One of the most pleasing aspects of the Umoona Kidney Project was that POCT became a focal point for raising community awareness about renal disease. Through the trust and respect gained from the renal program, a number of other community activities (for both adults and children) around related health issues and health promotion were conducted. These included developing a nutrition training program for Umoona's Aboriginal health workers at their request (28), staging a poster competition for the children at the local area school about healthy foods, and holding education days at the school about kidney health and the importance of good nutrition (sponsored by the Australian Kidney Foundation). A bush tucker trip was also conducted with the Umoona community elders for the school children, where the children were taught how to dig for witchetty grubs, collect other bush foods, and cook kangaroo.

National QAAMS Program for Point-of-Care HbA1c Testing

The QAAMS Program arose from a recommendation of the Australian National Diabetes Strategy in 1998 (33), commenced as a pilot program in June 1999, and is now fully integrated into mainstream Aboriginal healthcare in Australia (34, 35). Since its inception, the program has been a collaborative partnership between a number of groups including the Office for Aboriginal and Torres Strait Islander Health and the Diagnostics and Technology Branch within the Australian Government's Department of Health and Ageing, NACCHO,

Table 29-1 Reduction in Renal and Cardiovascular Risk Two Years after Commencing Coversyl

Marker	Measure/matrix	Units	Pre-Coversyl baseline, mean ± SEM	Post-Coversyl 2 years, mean ± SEM	*P*-value[a]
Blood pressure					
Standing	Systolic	mmHg	151 ± 3	137 ± 3	<0.0001
	Diastolic	mmHg	92 ± 2	84 ± 2	<0.0001
Lying	Systolic	mmHg	147 ± 3	131 ± 3	<0.0001
	Diastolic	mmHg	94 ± 2	84 ± 2	<0.0001
Albumin:creatinine ratio (ACR)	Urine	mg/mmol	16.5 ± 3.9	12.0 ± 2.8	NS
Potassium	Plasma	mmol/L	4.0 ± 0.1	4.0 ± 0.1	NS
Urea	Plasma	mmol/L	4.9 ± 0.3	5.1 ± 0.3	NS
Creatinine	Plasma	mmol/L	0.081 ± 0.003	0.077 ± 0.003	NS
Glomerular filtration rate (GFR)[b]		mL/min	110 ± 5	118 ± 8	0.019

[a] Values of $P < 0.05$ are significant; NS, not significant.
[b] Calculated GFR from (44).

the Royal College of Pathologists of Australasia (RCPA)'s Quality Assurance Programs, and the Community Point-of-Care Services unit within the Flinders University Rural Clinical School.

The chronic disease focus of the QAAMS program is the management of Aboriginal people with established diabetes. More than 2300 patients are involved in the program, which is being conducted at 50 commonwealth-, state-, and territory-funded Aboriginal medical services around Australia. These sites encompass every state and territory in Australia, with more than 90% located in rural or remote areas (Figure 29-1). The DCA 2000 was selected for use in this program following the recommendation of the National Diabetes Strategy (33) and all HbA1c tests are performed by Aboriginal health workers. An educational resource package was prepared for each site, which included a laminated A3-size book, video, and supporting posters for specific aspects of the program. Initial training was provided for Aboriginal health workers from every participating site. Health workers were given instruction on how to perform the HbA1c test on the DCA 2000 and on the principles and practice of quality control and quality assurance.

With 50 POCT devices in the field, it was critical that a formal surveillance mechanism was implemented to monitor the performance of results generated by these instruments. Therefore a quality assurance program was developed collaboratively by the Community Point-of-Care Services unit at Flinders University and the RCPA Quality Assurance Programs. The breadth of quality assurance programs available to central laboratories is well known but, to the author's knowledge, the QAAMS program is the first POCT program of this type to be developed for indigenous people anywhere in the world.

The QAAMS program is modeled on the laboratory quality assurance program system used by the RCPA. Each QAAMS participant is provided with an annual kit of quality assurance samples for testing (with two samples to be tested per month), a single-page result sheet, and a monthly summary report with a graphical result format similar to, but more simplified than, that provided for laboratories. Each site has its own code number to ensure confidentiality of results. The government charter in establishing this program has been to provide education, training, and quality management support services and not to collect or analyze patient data. This remains the property of the participating services, under NACCHO's direction.

Figure 29-1 Map showing general location of QAAMS participants in 2003.

At the time of writing, nine 6-month testing cycles have now been completed over the past 4.5 years from July 1999 to December 2003. Some of the key performance indicators are as follows. Participation rate has averaged 86% (range 73% to 93%) across all nine testing cycles, with almost 4000 quality assurance results returned during this time. The percentage of results considered acceptable has averaged 83% (range 81% to 86%), using limits for acceptable performance that are the same as those for the laboratory-based glycohemoglobin program conducted by the RCPA (5%). The median precision (CV%) achieved by the DCA 2000 analyzers across nine cycles has averaged 3.8%, with the precision base consistently improving across time and a CV% of 3.2% being recorded in the most recent testing cycle (Table 29-2).

As mentioned, the RCPA runs a parallel glycohemoglobin program for laboratories in Australasia. Seventy-five laboratory DCA 2000 users are registered in this program, which uses an identical quality assurance material to that of QAAMS. Across the past six testing cycles, the precision base achieved by Aboriginal medical services in the QAAMS program has been equivalent to that achieved by the laboratories (Table 29-2). This reflects the intensive ongoing commitment to continuing education, training, and support for the participating services that the QAAMS program provides.

The importance of precise HbA1c results for serial monitoring of diabetes control is now well recognized following studies such as the Diabetes Control and Complications Trial and the UK Prospective Diabetes Study clinical trials (36, 37). The desirable precision goal (CV%) for HbA1c analysis now recommended by most professional groups is 3% or less (8, 38, 39). In the QAAMS program, the precision base of DCA 2000 is now approaching the 3% goal. In a practical sense, for rural and remote communities where geographical isolation is common and laboratory access is limited, the DCA 2000 analyzer clearly provides a reliable, robust, and timely means of obtaining HbA1c analyses.

In March 2001 NACCHO conducted an independent evaluation of the first 18 months of the QAAMS program (40). The executive summary of this report stated that the use of the DCA 2000 represented a major opportunity to provide better care for and management of Aboriginal clients with diabetes within the community setting, while the ability of POCT to generate rapid results served as a catalyst to enhance patient self-management. The summary also concluded that the DCA 2000's simplicity of use led to high levels of acceptance by Aboriginal

Table 29-2 Comparative Precision Base Over Last Six Testing Cycles[a]
Aboriginal community-controlled health services (ACCHS) versus laboratories using the Bayer DCA 2000

		Cycle period					
Program	Type of service	Jan–June 2001	July–Dec 2001	Jan–June 2002	July–Dec 2002	Jan–June 2003	July–Dec 2003
QAAMS	ACCHS	3.7	4.1	3.9	3.4	3.8	3.2
Glycohemoglobin	Laboratory	3.4	4.1	3.7	3.5	3.6	3.0

[a] Values are CV%, calculated by dividing the SD by the midpoint of the service's range of concentrations, expressed as a percentage. The SD is the error of the estimate $Sy \cdot x$ and represents the mean SD across the range of concentrations analyzed.

health workers nationally, with nearly two-thirds of services expressing the view that it had raised the self-esteem of their health workers. Importantly, the sense of community control was enhanced as a result of diabetes management becoming more focused within Aboriginal medical services.

In December 2000 the Australian Government's Health Minister announced that a Medicare rebate could be claimed for HbA1c testing performed by the DCA 2000 analyzer in Aboriginal Community Controlled Health Services under a separate item number established specifically for the QAAMS program. The rebate, which has ensured a sustainable funding mechanism for the program, is conditional on several factors including continuing participation in and sound analytical performance for quality assurance testing in the QAAMS program.

To enhance the sustainability of the program further, an annual workshop for participants has been held since 2001. These workshops have now become a key feature of the QAAMS calendar. The meetings are very interactive, with significant opportunities for retraining and networking. All participants now undergo competency assessment and certification (in both practical and theoretical elements of the program) at the workshop. In 2003, the island of Tonga from the Western Pacific region was recruited as the program's first international participant. Considerable interest remains from other Western Pacific islands and Canada. The QAAMS model is transferable to other types of POCT. In January 2003 a new QAAMS program commenced for the measurement of urine ACR on the DCA 2000. There are 30 ACCHSs enrolled in the program and ACR testing will be used to monitor microalbuminuria in Aboriginal patients with diabetes.

Point-of-Care in Aboriginal Hands Program

The Point-of-Care in Aboriginal Hands program commenced in mid-2001 (41). It is a partnership between the Community Point-of-Care Services unit at the Flinders University Rural Clinical School and four rural and remote Aboriginal health services at Port Lincoln, the Riverland, and Meningie, rural towns and regions in South Australia, varying from 200 to 650 km from metropolitan Adelaide, and at Kalgoorlie in Western Australia, a rural mining town almost 500 km from metropolitan Perth. Meningie is a small rural community, with one health worker and two doctors servicing the community. The Port Lincoln Aboriginal Health Service and the Riverland Regional Health Service are well-resourced rural health centers, servicing larger population bases. The Bega Garnbirringu Aboriginal health service at Kalgoorlie is by far the largest health center, servicing Aboriginal people from the entire Goldfields region of outback Western Australia and having a very large health worker team and strong clinical and infrastructure support.

Education, training, and quality management of POCT again underpin the program and the local Aboriginal health worker is responsible for the day-to-day operation of the POC technology. The Point-of-Care in Aboriginal Hands program differs from the other models described in several fundamental ways. First, it has a greater local community focus with local medical officers and/or medical directors undertaking all clinical management at each health service, as opposed to the renal specialists associated with the previously described Umoona program. Second, the Point-of-Care in Aboriginal Hands program has a broader chronic disease focus that looks at the early detection and management of diabetes, renal disease, and cardiovascular disease collectively rather than having a single disease focus; for example, renal for the Umoona project or diabetes for the QAAMS HbA1c program. Finally, there is wider use of POCT. Aboriginal Health Workers are trained in how to use the Bayer DCA 2000 for both HbA1c and urine ACR testing and the Cholestech LDX lipid analyzer (Cholestech, Hayward, CA, USA), which provides a full lipid profile and a glucose measurement on a fingerprick of blood in 5 min (42).

The principal activities are education and training for the entire local health professional team and a voluntary (opportunistic) chronic disease risk assessment service for community members at each site with a concomitant chronic disease management arm. Although most of the point-of-care risk assessments are conducted in the clinic setting, the opportunity is taken whenever possible to conduct field-testing outside the clinic. For example, testing has been carried out at such diverse locations as a local ecotourism center, a local adult education college, and in a tin shed at the Port Lincoln Aboriginal Women's Centre (an event that was also linked with a nutrition health promotion activity). In the Riverland, a bus has been purchased and renovated to provide a mobile POCT service throughout the Riverland region (with risk assessment also

linked to an eye examination for people with diabetes through a separate program). These examples highlight the flexibility and versatility of POCT in the community setting.

More than 600 chronic disease risk assessments have been performed by POCT across all four participating sites. A number of common trends relating to chronic disease risk between participating communities have been identified. Diabetes is extremely prevalent (ranging from 15% to 26% in the general community). Again, there is a large incipient pool of renal disease, with rates of microalbuminuria ranging from 19% to 26% in the general community. Elevated lipids are very common (35% to 44%), particularly in males and the younger age group (where increased lipids were found in 24% to 28% of people assessed). Obesity is extremely prevalent in females (ranging from 47% to 59%). An example of the risk assessment profile found in one community is shown in Figure 29-2.

For clinical management, flow charts for POCT processes have been developed in collaboration with each community, based on best practice evidence and input of the local clinicians. The frequency of follow-up testing is determined by diabetes, blood pressure, microalbumin, and lipid status. A well-defined niche for the use of POCT in chronic disease management has been identified, namely integration of POCT with the Australian government's Chronic Disease Self Management Care Plan initiative (43). At Port Lincoln, for example, a subset of 29 patients in the Point-of-Care in Aboriginal Hands program were entered into the Chronic Disease Self-Management Care Plan program during 2002. Their HbA1c (as performed by POCT on the DCA 2000) was measured at baseline and at 12 months. The mean HbA1c of the group improved from 7.8% at baseline to 7.4% after a year (43).

A number of case studies have also been identified across the program that clearly demonstrate the benefits of POCT in the early detection and diagnosis of chronic disease, more expedient initiation of treatment, improved clinical effectiveness, and greater patient satisfaction and motivation. Two case examples are described in the following.

The first case describes a 57-year-old man with NIDDM, obesity, and ischemic heart disease. He had been "lost to the health system" in the community for more than 2 years until he re-presented at clinic in December 2001. His POC results on presentation were: HbA1c, 10.5%; blood glucose, 11.6 mmol/L (209 mg/dL); urine ACR, 2.8 mg/mmol (24.8 mg/g); blood pressure, 150/90 mmHg; and weight, 124 kg (273 lb). Insulin was resumed immediately to treat his poor glycemic control. During the next year, regular HbA1c tests were performed using POCT, and the patient's HbA1c fell to 9.7% (February 2002), 8.8% (August 2002), and 8.4% (December 2002). Across this period, he received ongoing dietary, podiatry, and retinopathy review. He commented that regular POCT has helped motivate him to achieve improved diabetes control. He has also initiated lifestyle changes including taking bush trips every second day and consuming more bush foods and fish.

The second case describes a 32-year-old male student from a very remote Aboriginal community who was visiting "town" to attend a training course. He presented at the local health service complaining of headaches after drinking heavily the previous night. His POCT results were: HbA1c, 10.6%; blood glucose, 19.0 mmol/L (342 mg/dL); urine ACR 22.7, mg/mmol (200 mg/g); cholesterol, 12.0 mmol/L (463 mg/dL); nonfasting triglyceride >7.3 mmol/L (>650 mg/dL) (the upper measuring limit of the Cholestech LDX analyzer), and blood pressure, 156/115 mmHg. The patient's blood sample was also left standing on the bench, allowing the red blood cells to settle and reveal plasma that was strawberry milk in color. Opportunistic POCT led to the patient being identified as diabetic with poor glycemic control, microalbuminuria, and severe hyperlipidemia (as well as hypertension). Treatment was initiated immediately and the patient returned home and is now managed by the visiting Royal Flying Doctor Air Service. Visualization of the milky plasma also led to valuable education for the health worker team about heart disease and raised community awareness about blood fats, as this sample was photo-

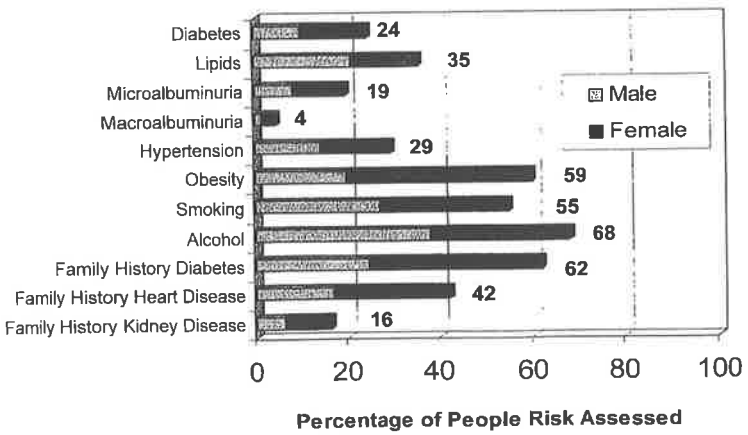

Figure 29-2 Chronic disease risk assessment profile in one community in the Point-of-Care in Aboriginal Hands program.

Table 29-3 Median Precision of QAAMS HbA1c and Urine ACR Testing by Four Sites in the Point-of-Care in Aboriginal Hands Program[a]

	HbA1c		Urine ACR	
Site	Median precision	Precision goal	Median precision	Precision goal
1	3.2	3	4.3	12
2	3.1	—	5.1	—
3	3.1	—	NA[b]	—
4	2.9	—	5.0	—

[a] Values are CV%.
[b] Data unavailable.

graphed and is now used as a teaching aid at community health promotion functions.

For quality management purposes, all sites are now enrolled in both national QAAMS programs for HbA1c and urine ACR. In addition, they conduct onsite internal quality control testing, the results of which are immediately faxed to and managed by the Flinders' Community Point-of-Care Services unit. There is also monthly communication between the unit and each participating site around a quality management checklist. Table 29-3 details the analytical performance achieved by each site for QAAMS testing in the most recent cycle. These results again clearly demonstrate that POCT can be carried out to a high level of analytical competency by Aboriginal health workers, provided they are supported by a quality management framework comprising ongoing education, training, and participation in structured quality management programs.

The Point-of-Care in Aboriginal Hands program has been well accepted by the participating Aboriginal communities, Aboriginal health workers, and supporting clinical staff. The program has worked effectively in four different rural communities, each with different levels of staff resources, infrastructure support, and clinical agendas.

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CHAPTER 7

ADAPTABILITY AND TRANSFERABILITY OF INDIGENOUS POCT MODELS

THE IMPACT OF POINT OF CARE TESTING ON DIABETES SERVICES ALONG VICTORIA'S MALLEE TRACK. RESULTS OF A COMMUNITY-BASED DIABETES RISK ASSESSMENT AND MANAGEMENT PROGRAM.

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The Impact Of Point Of Care Testing On Diabetes Services Along Victoria's Mallee Track. Results Of A Community-Based Diabetes Risk Assessment And Management Program.

As stated in the conclusion of the literature review, chronic disease is also a serious contemporary health problem for Australia's non-Indigenous people and many patients, particularly in rural and remote Australia, are not able to readily access laboratories services.

My research program had validated the analytical quality and clinical effectiveness of POCT in the Indigenous community, but could the foundation elements of my models be adapted and transferred to the non-Indigenous primary health care setting?

The opportunity to address this research question came with invitation to establish a POCT service for the Mallee Track Health and Community Service at Ouyen in Victoria as part of Government-funded Diabetes Management Along the Mallee Track Program. An education, training and quality surveillance framework for POCT, based on exactly the same principles as that of my Indigenous POCT models, was implemented for both community risk assessment and management of people with diabetes in the rural non-Indigenous setting. The clinical effectiveness of a one-stop management service, which included POCT for HbA1c, urine ACR and lipids, community satisfaction with the new diabetes service and analytical quality, as assessed by quality control testing, were examined as research outcome measures.

The key research findings included significant improvements in glycaemic control, blood pressure and lipids among the community's diabetes patients participating in the management arm of the program, a statistically significant greater level of satisfaction with the new diabetes service, and sound analytical performance for POCT exhibited by the nurse POCT operator. This research study thus confirmed the transferability of my Indigenous POCT models to the rural non-Indigenous primary care setting.

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ORIGINAL RESEARCH

The impact of point of care testing on diabetes services along Victoria's Mallee Track: Results of a community-based diabetes risk assessment and management program

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ABSTRACT

Introduction: In the State of Victoria in Australia, diabetes is considered one of the top 10 health problems for people living in the rural Mallee Track region (which is centred on the town of Ouyen and extends west to the border with South Australia). A project entitled 'Diabetes Management Along the Mallee Track' was conducted through a Rural Chronic Disease Initiative (RCDI) program grant from the Australian Government's Department of Health and Ageing, Canberra, with the aim of improving the delivery of diabetes services in this region. The project's aims were achieved through the implementation of a community risk assessment program and the establishment of an integrated, multidisciplinary 'one-stop' service for the management of people with diabetes. The use of on-site point-of-care (POC) pathology testing equipment was the key component of both arms of the project.

Methods: Community risk assessment sessions were held in seven towns across the Mallee Track region using a local settings approach. Risk assessment included POC pathology testing for glucose and lipids, as well as blood pressure, age, personal and family history of diabetes, smoking status, and self-assessed weight and level of exercise. The multidisciplinary 'one-stop' service for the management of people with diabetes involved having a single appointment with their local GP, during which time they met the local diabetes educator and podiatrist as well as the GP, and on-site POC testing (POCT) performed for haemoglobin A1c (HbA1c),

urine albumin : creatinine ratio (ACR), lipids and glucose. A written survey was conducted among patients with diabetes, local GPs and local health professionals to assess the level of satisfaction with the project and the use of POCT, and to assist policy development for the future planning and development of diabetes services along the Mallee Track region.

Results: Risk assessment: 320 adults were assessed for their risk of diabetes during community sessions (representing approximately 20% of the adult population of the region). Two-thirds of people tested had equivocal random blood glucose levels (5.1-11.0 mmol/L), while hypertension and high cholesterol were found in more than one-third. Management of established diabetes: 49 people with known, established diabetes were initially entered into a Central Diabetes Register (with 5 more joining the register since). These diabetes patients ($n = 54$) have now been monitored by POCT for a mean of 10 months (range 3-18 months). Since the introduction of the 'one-stop shop', the percentage of persons achieving optimal glycaemic control (HbA1c <7%) has increased by 30% (from 33% to 63%), the percentage achieving controlled glycaemia (HbA1c < 8%) has increased by 32% (59% to 91%), while the number exhibiting poor control has reduced by 7% (13% to 6%). The mean HbA1c has fallen from 7.6% at the commencement of the program to 7.1% ($p = 0.03$, paired t-test). Falls in cholesterol and blood pressure were also observed. Satisfaction with new management services for diabetes: 36 patients with diabetes (73% of all known diabetes patients in the region at the time) completed satisfaction questionnaires. There was overwhelming support within this group for the use of POCT as part of their management, because it was convenient, encouraged self-management and enhanced doctor-patient relationships. The proportion of patients with diabetes who were satisfied/very satisfied with the available diabetes services was significantly greater following the introduction of the project (before: $n = 18$ (64%), after: $n = 29$ (91%), $\chi^2 = 6.10$, $p = 0.01$). Doctors agreed that the immediate availability of POCT results at the time of consultation was convenient for them, contributed positively to patient compliance and improved their relationship with the patient. Health professionals felt confident in using the POC analysers and believed the program had raised community awareness about diabetes and enhanced community ownership.

Conclusion: Point-of-care pathology testing has enabled the introduction of a community-friendly risk assessment program for diabetes and provided a convenient and rapid service for monitoring the control of diabetes in people with established disease in the Victorian Mallee Track region. The number of diabetes patients accessing diabetes services has more than doubled since the introduction of the program. All community and health professional groups surveyed agreed that the POC model delivered as part of this project should be available to all people throughout the Mallee Track region. The model, although conducted in a small rural community, has the potential to form a suitable template for the broader introduction of POCT services for diabetes in rural and remote communities across Australia. As an independent measure of the success of the program, the Australian Government's Department of Health and Ageing selected the Diabetes Management Along the Mallee Track project as one of three demonstration projects from the RCDI grants for showcasing to all rural health services in Australia through the production of an education resource called 'Building Healthy Communities'.

Key words: Australia, diabetes, Mallee Track, Point-of-Care Testing

Introduction

In 1996, the Federal, State and Territory Governments of Australia identified diabetes mellitus as one of six National Health Priority Areas. The Australian Diabetes, Obesity and Lifestyle Study, which arose from the National Diabetes Strategy and Implementation Plan[1], determined that approximately 940 000 Australians over the age of 25 years had diabetes[2]. Furthermore, the prevalence of diabetes in Australian adults had trebled since 1981 and for every known case of diabetes there was one undiagnosed case[2].

Recently, in the Australian state of Victoria, diabetes was recognised as one of the top 10 health problems for people of all ages in the rural 'Mallee Track' region (centred on the country town of Ouyen, approximately 400 km north-west of Melbourne, the capital of Victoria [Fig. 1])[3]. In an attempt to improve diabetes services in this region, the Mallee Track Health & Community Service (MTH&CS), based in Ouyen, undertook a project entitled 'Diabetes Management Along the Mallee Track'. This project was funded by a Rural Chronic Disease Initiative (RCDI) program grant from the Australian Government's Department Health and Ageing, Canberra, and was based in part on the MAN Model of Health Promotion, piloted and developed by Centre for Advancement of Men's Health across rural Victoria[4].

The primary aims of the Diabetes Management Along the Mallee Track project were:

1. To identify people at risk for diabetes and raise the level of awareness about diabetes in the general community, through the delivery of community-based risk assessment programs across the region.
2. To provide improved services for people with established diabetes across the region, through the establishment of an integrated, multidisciplinary, 'one-stop' service for the management of diabetes.

The novel use of point-of-care (POC) pathology testing was a key component of both the risk assessment and management arms of the project. POC testing (POCT) is a major growth area within community and hospital medicine in Australia, and is soon to be trialled within the general practice sector in Australia[5]. POCT provides the opportunity for pathology tests to be performed on-site in the community by a trained health professional, with results available within 10-15 min.

This article describes the use of POCT for the risk assessment and management arms of the Mallee Track program (focussing particularly on the latter), and reports the level of satisfaction among community members with diabetes, their doctors and allied health professionals with the new POCT services provided as part of this project. An initial assessment on clinical outcome measures for patients with diabetes, one-year post-introduction of the program, is made.

Methods

Description of the Mallee Track Region

The Mallee Track region of north-west Victoria is a classified as a remote area, according to the Australian Government's rural and remote areas (RRMA) classification system[6]. It is more than 350 km from the nearest capital cities (Adelaide and Melbourne) and 100 km from the nearest rural centre, Mildura. Agriculture (wheat and barley) and sheep farming are the region's main local industries. There are three main towns in the region, Ouyen, Underbool and Murrayville, Ouyen having the largest population of approximately 1150 people (690 adults). The region's total population is approximately 2800 (1680 adults).

Description of diabetes services prior to the introduction of the program

Prior to the introduction of the program, diabetes services for patients were disjointed and uncoordinated. Local services provided by two GPs were used sporadically by only 15-20 patients with diabetes. Patients had to travel considerable distances (100 km) to obtain selected specialist services (such as diabetes education) and had to wait several days for pathology results. On average each patient had one haemoglobin A1c (HbA1c) measurement performed annually to assess his or her diabetes control.

Partnerships

The Diabetes Management Along the Mallee Track project was established and directed by the Special Community Health Projects Team from MTH&CS, in partnership with local GPs and MTH&CS Allied Health and community health nurses. A diabetes educator visited the Mallee Track Medical Centre monthly through a partnership with the Mallee

Division of General Practice. A podiatrist was also engaged locally. The Community Point-of-Care Services unit from the Flinders University Rural Clinical School supported the project with POC technology, training and competency certification for local POCT operators, quality management procedures, data management and assistance in designing community surveys. A local Advisory Committee was formed to provide direction and guidance to the program; the committee included local community representation from the Ouyen Diabetes Support Group.

Community-based risk assessment programs

Members of the Mallee Track community were invited to participate in community risk assessment sessions held in seven towns across the region: Ouyen, Murrayville, Walpeup, Underbool, Patchewollock, Speed and Manangatang. Participation in risk assessments was voluntary and opportunistic. Risk assessments were conducted in a local community 'settings' approach; for example, using the local Community Fire Authority (CFA), local schools and colleges, and community field days as venues for risk assessment sessions, as well as targeting specific community groups such as the local walking group and the local men's tennis club. Diabetes risk factor assessment was based on current Australian best practice guidelines[7-11], and included random capillary blood glucose and total cholesterol (measured by fingerprick POCT), blood pressure, age, personal and family history of diabetes, smoking status, and self-assessed weight and level of exercise.

Management of people with established diabetes

Community members with established diabetes were invited to participate in a new multidisciplinary service, which involved a single appointment with their local GP. This appointment also included meeting the diabetes educator and podiatrist and on-site POC testing for HbA1c, urine albumin : creatinine ratio (ACR), blood lipids and glucose performed by the Special Community Health Projects team nurse. Having POCT results available within the single consultation enabled the GP to enact patient management and/or change treatment during the consultation, without the need for the patient to return for a follow-up visit. This integrated approach was designed to provide a more accessible and convenient service for people with diabetes, and to improve patient motivation to self-manage their diabetes. It also overcame the need for patients to travel long distances to access specialist services. A local register of all participants in this service was established, including POCT results conducted at the commencement of the program (0 months) and at every subsequent visit to their local GP. This enabled future tracking of diabetes control and an assessment of clinical outcomes post introduction of the new service.

POCT instruments

The Bayer DCA 2000 (Bayer Australia, Melbourne, Vic, Australia) and the Cholestech LDX Lipid Analyser (Point of Care Diagnostics, Sydney, NSW, Australia) were used for POCT. The Bayer DCA 2000 measured HbA1c on a fingerprick (1 µL) of whole blood in 6 min. HbA1c is a well-established biochemical marker that provides a measure of a person's diabetes control over the preceding 3 months[1,2,7]. The DCA 2000 is currently used for POC HbA1c monitoring for people with diabetes in 60 urban, rural and remote Australian Aboriginal medical services, through the 'QAAMS' program (Quality Assurance for Aboriginal Medical Services)[12-14]. The DCA 2000 has proven safe, analytically reliable and robust, and clinically and culturally effective in this setting[12-15].

The DCA 2000 was also used to measure albumin:creatinine ratio (ACR) on 40 µL of urine in 7 min. Urine ACR is a key biochemical marker for the early detection of microalbuminuria and for monitoring the progression of diabetic nephropathy[16]. The instrument is used in the national "QAAMS" program for point-of-care ACR testing, its analytical performance has been validated against equivalent laboratory-based methods, and it is a useful test for the detection and management of chronic disease in a rural community setting[14,17-19].

Figure 1: Location of Ouyen, the central town in the Mallee Track region of Victoria.

The Cholestech LDX machine measured total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol (calculated) and glucose on a fingerprick (35 µL) of whole blood in 5 min. The analytical performance of the Cholestech machine has been validated in the laboratory and in the rural community setting[20-21].

Quality management of the POCT equipment

The Flinders' Community Point-of-Care Services unit implemented an internal quality management program to monitor the analytical performance of the POC instruments in the field. Local operators of the POC equipment were required to test a commercially available quality control (QC) material for each POC test and on each POC instrument every time a new reagent kit was opened (containing 10 testing cartridges).

Questionnaires to assess project outcomes

With assistance from the Flinders University Centre for Epidemiology and Biostatistics, a questionnaire was developed to assess participants' views on the introduction of POC services and to assist policy development for the future planning and delivery of diabetes services along the Mallee Track region. The questionnaire design was based on the 5-point Likert scale[22], with respondents recording their levels of agreement or disagreement with statements posed. Participants were given equal opportunity to agree or disagree with each statement. The questionnaire for people with established diabetes assessed their level of satisfaction with the POC testing services provided through the project, and was administered at the completion of the project (that is, after 12 months). The President of the Ouyen Diabetes Support Group assisted with the development of this questionnaire. The Manager of the MTH&CS Special Projects team explained the aims and objectives of the questionnaire to people with diabetes at a monthly meeting of the Ouyen Diabetes Support Group. Following this meeting each person filled out a questionnaire in his/her own time and at his/her convenience. Completed questionnaires were returned in a sealed envelope to the Manager of the MTH&CS Special Projects team within 2 weeks. Two further surveys were implemented. Three local GPs were surveyed to assess their satisfaction with the new POC testing services for diabetes management, and the three health professionals responsible

for conducting POC testing also completed a questionnaire to gain information about their acceptance of the POC technology used during the project.

Statistical methods

The demographics and POC results of the participants who underwent community-based risk assessment were examined. Continuous, normally distributed variables were expressed as means and standard deviations (SD), and variables with skewed distributions were reported as medians and inter-quartile ranges (IQR). Categorical variables were reported as frequency and percentage. Comparisons were made between the POC measurements by gender, using Mann-Whitney *U*-tests. The prevalence of risk factors in community participants was reported, and their relationship with age was examined using χ^2 test for trend. For participants with established diabetes, group mean (SD) POC measurements were calculated at the program commencement and at their most recent visit to their local GP.

The results of the satisfaction questionnaires were reported as the number (and percentage) of respondents who agreed, were neutral, or disagreed with the statements presented in the questionnaires. Comparisons were made between the satisfaction with diabetes services provided prior to, and following the program implementation, using a χ^2 test.

Results

Risk assessment

Three hundred and twenty people underwent risk assessment for diabetes during community sessions along the Mallee Track, over the study period. The mean age of those assessed was 50.3 years (SD 14.7, range 16-86 years). POC measurements collected at community risk assessment are described (Table 1). Male participants had higher random blood glucose and higher systolic and diastolic blood pressures, when compared with female participants (Mann-Whitney *U*-test, $p<0.05$).

Risk factors for diabetes among those assessed in the Mallee Track community were common, with over two-thirds ($n = 210$) having an equivocal capillary blood glucose (5.1-11.0 mmol/L) (Figure 2). 38% ($n = 116$) of those tested had abnormal lipids (total cholesterol $\geq$ 5.5 mmol/L), while 44% ($n = 137$) had hypertension (systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg). Smoking rates were low (13%, $n = 37$). These prevalence rates for people in the Mallee Track region are lower than the national average[2] for lipids (38% vs 51% respectively) and smoking (13% vs 16%) but higher for hypertension (44% vs 29%). The latter finding is attributed to a very high rate of hypertension in males in the region (54% vs 31% nationally). A positive trend was identified between hypertension and increasing age ($\chi^2 = 24.5$, $p<0.001$), and between abnormal lipids and increasing age ($\chi^2 = 12.8$, $p = 0.03$). The prevalence of diabetes (random blood glucose $\geq$ 11.1 mmo/L) in those assessed was not associated with age ($\chi^2 = 11.2$, $p = 0.35$), however the number of persons assessed in the lower age groups were small. Three new cases of diabetes were identified as a result of the risk assessments conducted.

Management of established diabetes

Forty-nine persons with established diabetes commenced POC pathology testing at their local general practice across the first 12 months of the program, with another five people with diabetes joining this group over the following 6 months. A local diabetes register was established and all POCT results were entered into this register following each GP visit. The MTH&CS and the Flinders' Community Point-of-Care Services unit jointly maintain the register, which is electronically updated and available to local general practitioners.

Table 1: Baseline characteristics of POC measurements conducted during the community risk assessment program

POC Test	All		Males		Females		*p* Value*
	Median	IQR	Median	IQR	Median	IQR	
Random blood glucose	5.40	1.45	5.50	1.40	5.30	1.40	0.028
Total cholesterol	5.28	1.02	5.31	1.14	5.20	0.92	0.060
Systolic BP	133	27	140	23	130	20	<0.0001
Diastolic BP	80	16	83	16	78	14	0.0002

POC, Point of care; IQR, interquartile range; BP, blood pressure.
*Comparisons were made between males and females, using a Mann-Whitney *U* test.
Random blood glucose mmol/L (n = 319; 160 males), total cholesterol mmol/L (n = 305; 156 males), systolic blood pressure mmHg (n = 310, 156 males) and diastolic blood pressure mmHg (n = 309, 156 males).

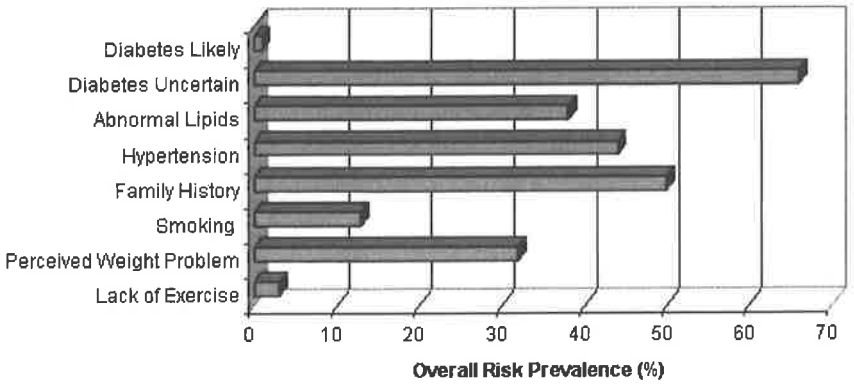

Figure 2: Prevalence of risk factors* for diabetes in the Mallee Track region. *Categorisation of key risk factors: diabetes unlikely, capillary blood glucose ≤ 5.0 mmol/L; diabetes uncertain, capillary blood glucose 5.1-11.0 mmol/L; diabetes likely, capillary blood glucose ≥ 11.0 mmol/L; abnormal lipids, total cholesterol ≥ 5.5 mmol/L; hypertension, sBP ≥ 140 mmHg or dBP ≥ 90 mmHg.

These diabetes patients (n = 54) have now been monitored by POCT for a mean of 10 months (range 3-18 months). A total of 162 POCT HbA1c tests, 91 ACR tests, and 132 lipids tests have been performed since POCT commenced. The percentage of diabetes patients achieving optimal glycaemic control (HbA1c <7%) increased from 33% (start of the program) to 63% (POCT measurement at their most recent visit to the GP). The percentage achieving controlled glycaemia (HbA1c < 8%) increased from 59% to 91%, while the number exhibiting poor control fell from 13% to 6% (Figure 3). Since the commencement of POCT, the mean HbA1c, cholesterol, and systolic blood pressure of the diabetes group has fallen significantly (paired t-test) by 0.5%, 0.36 mmol/L and 9 mmHg as measured by POCT at their most recent visit to the GP (Table 2). Diastolic blood pressure had fallen by 5 mmHg.

Table 2: Mean (SD) of POCT measurements in the Diabetes Management group at the commencement of the program (0 months) and at their most recent visit to the GP (most recent)

Test		Mean (SD)			*p* Value*
	Units	0 Months	Most Recent	*n*	Paired *t*-test
HbA1c	%	7.6 (1.6)	7.1 (1.4)	54	0.03
Cholesterol	mmol/L	4.64 (1.0)	4.28 (0.9)	52	0.01
Systolic blood pressure	mmHg	143 (21)	134 (14)	52	0.004
Diastolic blood pressure	mmHg	81(21)	76 (10)	52	0.09

HbA1c, haemoglobin A1c
$p<0.05$ represents significant change

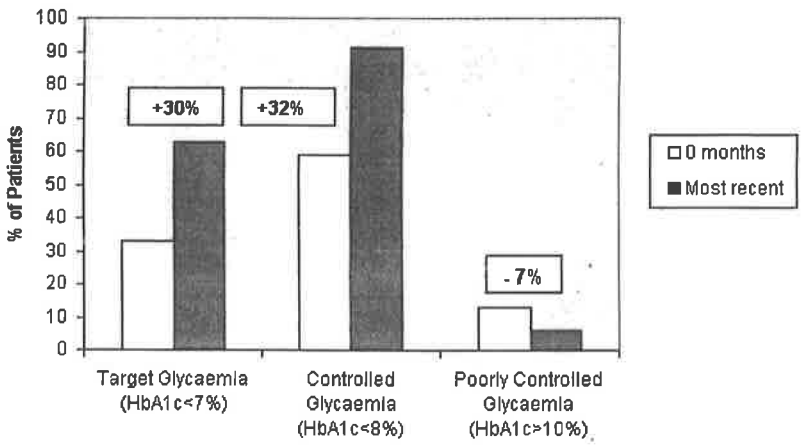

Figure 3: Improvement in glycaemic control among diabetes patients, showing an increase in percentage of diabetes patients attaining glycaemic targets and a decrease in the percentage of patients exhibiting poor control, as measured by POCT at the commencement of the program (0 months) and at their most recent visit to the GP.

Quality management of POC instruments

Twenty-two Bayer HbA1c QC tests, 17 Bayer Urine ACR QC tests and 44 Cholestech lipid QC tests were conducted during the project period (Table 3). The precision of internal quality control testing for HbA1c, urine ACR, urine albumin and urine creatinine met the desirable analytical performance specifications recommended by the Australian Government's 'Interim Standards for Point of Care Testing in General Practice'[23]. For total cholesterol, the precision achieved for quality control testing was very close to the recommended analytical goal.

Table 3: Precision achieved for internal quality control testing on POC instruments

Test	Concentration/ level	Precision (%)	Goal (%)
HbA1c (%)	5.5	2.7	4
	11.0	4.0	
Urine ACR (mg/mmol)	3.6	6.1	12
	6.1	4.1	
Urine Albumin (mg/L)	33.0	8.0	10
	211.0	5.2	
Urine Creatinine (mmol/L)	8.8	3.8	6
	35.4	2.2	
Cholesterol (mmol/L)	4.6	6.6	5
	6.8	6.0	

ACR, Albumin: creatinine ratio; HbA1c, haemoglobin A1c.

Table 4: Results of questionnaire on POC testing for people with established diabetes

Item	Disagree		Neutral		Agree	
	n	*%*	*n*	*%*	*n*	*%*
Convenience						
Satisfied with POC result immediately available	0	-	1	3	35	97
Advantage not having to return to clinic for result	0	-	1	3	35	97
Personal issues						
Fingerprick less stressful than venepuncture	0	-	1	3	35	97
Getting immediate result less stressful	0	-	1	3	35	97
Confident in accuracy of POC result	0	-	1	3	34	97
POC acceptable alternative to laboratory testing	0	-	0	-	35	100
Motivated to look after diabetes because of POC	0	-	2	6	31	94
Happy to return for regular POC testing	0	-	1	3	32	97
Doctor–patient Issues						
Visit more worthwhile with POC results available	1	3	1	3	33	94
Being able to speak about result at visit positive	0	-	2	6	31	94
POC has helped relationship with doctor	0	-	1	3	31	97
Doctor able to manage diabetes better	0	-	1	3	32	97
Specific questions						
Resources and questionnaires easy to use	1	3	1	3	33	94
Should POC program continue	0	-	0	-	35	100
Should POC testing be available to all diabetics in Mallee	0	-	0	-	36	100
Is one-stop diabetes service an improvement	0	-	3	9	31	91

POC, Point of care.

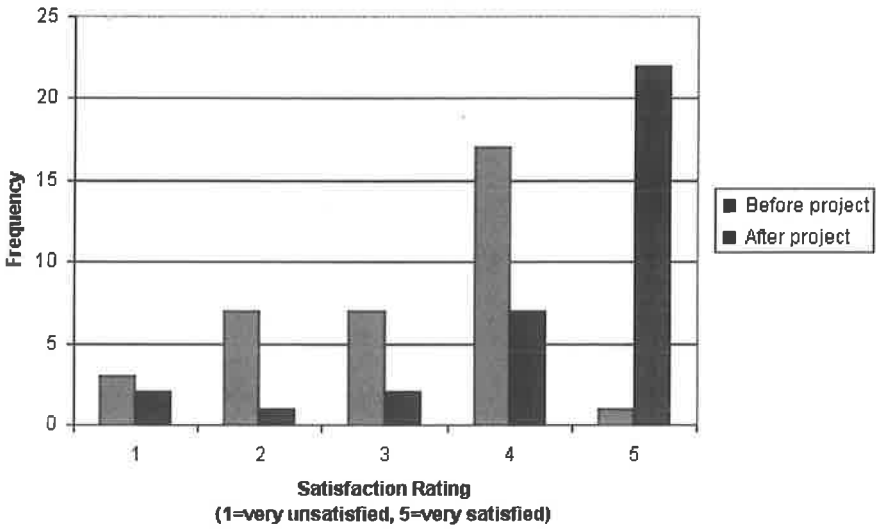

Figure 4: Comparison of the overall level of satisfaction with diabetes services before and after the Diabetes Management Along the Mallee Track project.

Satisfaction with New Management Services for Diabetes

Satisfaction questionnaires were received from 36 people with established diabetes, two-thirds ($n = 28$) of whom were aged 55 years or older. This number of respondents represented 73% (36/49) of all persons in the Mallee Track region known to have diabetes at the time the questionnaires were implemented. The majority of respondents (> 90%) reported a high level of satisfaction with the convenience of the program, personal issues, doctor-patient issues and the program overall (Table 4). There was unanimous agreement among respondents that they would like to see POC testing continue for their own diabetes management, and that they wished POC testing to be available to all people with diabetes across the Mallee Track region.

The proportion of respondents who were satisfied/very satisfied with the available diabetes services was significantly greater following the introduction of the project (before: $n = 18$ [64%], after: $n = 29$ [91%], $\chi^2 = 6.10$, $p = 0.01$) (Figure 4).

Three local GPs completed a satisfaction questionnaire. All agreed that the availability of POCT during consultations was convenient and the opportunity to discuss POC results immediately was advantageous. They had confidence in the accuracy and reliability of the POC result and believed it was an acceptable alternative to laboratory testing. They also agreed that immediate availability of the POC result contributed positively to overall patient care and patient compliance, as well as improving their rapport and relationship with the client. All three strongly agreed that the POCT component of the program made a positive contribution to the management of diabetes within their service.

Three community health nurses responsible for conducting POCT completed a satisfaction questionnaire. All agreed that

the education, training and resources provided by the Flinders' Community Point-of-Care Services unit were useful and appropriate. They had confidence in the accuracy and reliability of the POC results and understood the need to perform quality control testing. Among the three respondents, there was general agreement that patients in the community were happy with POCT services, the program had provided a focus for raising community awareness about diabetes and enhanced the sense of community ownership of the project.

Discussion

The emergence of POC pathology testing throughout the world has paralleled significant advances in medical technology, changes in healthcare delivery, with a more patient-orientated approach to care and an increasing demand for improved turnaround of pathology results[24]. The Australian Federal Government recently commissioned a major review of the role and value of POCT in the general practice environment[25]. This review concluded that only very limited information is currently available on the efficacy of POCT in general practice in Australia[26] but that rural and remote practices could potentially be the greatest beneficiaries of POCT.

In the rural-based Diabetes Management Along the Mallee Track Project, POCT was introduced for both risk assessment and the management of diabetes. The use of the DCA 2000 and Cholestech LDX POC technology for this purpose has proven safe, robust and analytically reliable in rural community hands. As part of the risk assessment sessions, POCT contributed to a greater community understanding of diabetes and its associated risk factors and provided an effective and rapid means for on-going surveillance of community risk. The coordinated, multidisciplinary 'one-stop' approach to diabetes management, combining access to GP and specialist support services with on-site POCT and immediate result availability, has been well supported by the region's diabetes patients. There are now more than two-and-a-half times more patients accessing this new service and receiving closer monitoring of their diabetes control compared to the number utilising the previous diabetes service. The number of patients achieving glycaemic targets has increased greatly, while improvements in diabetes, lipid and blood pressure control have also occurred. Patients with diabetes have expressed a significantly higher level of satisfaction with the new diabetes service, although there is potential for retrospective bias. They were unanimous that they wanted POCT to continue for their personal diabetes management and that POCT should be available for all people with diabetes in the region. Local doctors and health professionals conducting POCT were confident with this mode of health service delivery.

Two key challenges for the program are: (i) the on-going maintenance of the local diabetes register and the commitment to continue performing key POC pathology tests at the frequency recommended for best practice management; and (ii) attention to the care and follow up of people identified at greatest risk for diabetes via the community risk assessment sessions.

The Diabetes Management Along the Mallee Track project was initially selected as one of 19 innovative rural projects funded through the Australian Government's RCDI program. At the conclusion of this RCDI program, the Government selected the Diabetes Management Along the Mallee Track project as one of three demonstration projects for showcasing to all rural and remote health services in Australia through the production of an education resource called Building Healthy Communities[27]. This resource features a DVD and video on how the Diabetes Management Along the Mallee Track project is conducted on a day-to-day basis and aims to provide a framework to assist rural communities throughout Australia to conduct more effective community projects.

While acknowledging the population sample size in this project was relatively small and a larger study would be needed to broaden the generalisability of our findings, the Mallee Track model, with its associated POCT services, has considerable potential to be tailored locally and applied to many similar rural and remote health services in Australia,

where community will and health professional commitment can work together for the common cause of reducing the prevalence and burden of diabetes.

Acknowledgements

The Diabetes Management along the Mallee Track project was supported by a Rural Chronic Disease Initiative program grant from the Australian Government's Department of Health and Ageing, Canberra (2003). Servier Laboratories (Australia) generously sponsor the Community Point-of-Care Services unit at Flinders University. Dean Whiting from Bayer Australia (Melbourne), Rupert Haines from Point of Care Diagnostics Australia Pty Ltd (Sydney) and Pfizer Australia kindly provided equipment, reagents and consumables for the project. Mr John Senior (CEO of the Mallee Track Health & Community Service) is thanked for his encouragement and support during the program.

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APPENDIX I

Questionnaire administered to 36 patients with diabetes to assess their level of satisfaction with their diabetes service after the introduction of the program.

DIABETES MANAGEMENT ACROSS THE MALLEE TRACK
Federally funded by the Department of Health and Ageing
Research and Evaluation conducted by the
Community Point-of-Care Services unit, Flinders University Rural Clinical School

Questionnaire on Point-of-Care Testing For People with Diabetes

The 'Diabetes Management Along the Mallee Track' Special Projects Team in association with the Community Point-of-Care Services unit is very interested to learn about your level of satisfaction with the point-of-care testing service and the point-of-care equipment (Cholestech and DCA 2000) used in this program for your diabetes management.

As a person using our services, your experiences are very important to us and your feedback is greatly valued. The information gathered from this survey will assist in planning for future point-of-care testing services across the Mallee Track region. Your responses will be regarded as strictly confidential.

Thank you for your time in filling out this questionnaire.

Section 1. General Questions

Could you circle your response to the following statements in terms of **how strongly you agree or disagree with the statement**:
1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree:

Regarding Convenience

1. I am satisfied with having the point-of-care result immediately available to me.
   Strongly Disagree 1 2 3 4 5 Strongly Agree
2. An advantage of point-of-care testing for me is that I do not have to come back to the clinic at a later date to get my laboratory result.
   Strongly Disagree 1 2 3 4 5 Strongly Agree

Personal Issues

3. Having my blood test done by finger prick is less stressful than having blood taken from my arm.
   Strongly Disagree 1 2 3 4 5 Strongly Agree
4. Getting my point-of-care result while I wait is less stressful than having to come back later on another day to find out my result.
   Strongly Disagree 1 2 3 4 5 Strongly Agree
5. I have confidence in the accuracy of my point-of-care test result (as compared with the laboratory result).
   Strongly Disagree 1 2 3 4 5 Strongly Agree
6. Point-of-care testing is acceptable to me as an alternative to conventional laboratory testing.
   Strongly Disagree 1 2 3 4 5 Strongly Agree
7. I am more motivated about looking after my diabetes because of regular point-of-care testing.
   Strongly Disagree 1 2 3 4 5 Strongly Agree

8. I am happy to come back regularly for further point-of-care testing as part of the management of my diabetes.

Strongly Disagree 1 2 3 4 5 Strongly Agree

Doctor-Patient Issues

9. My visit to the doctor is more worthwhile because I have my point-of-care results with me when I see the doctor.

Strongly Disagree 1 2 3 4 5 Strongly Agree

10. Being able to speak to the doctor about my result in the same visit makes me more likely to manage my diabetes well (by medication/tablets or diet/exercise).

Strongly Disagree 1 2 3 4 5 Strongly Agree

11. Point-of-care testing has helped my relationship with my doctor.

Strongly Disagree 1 2 3 4 5 Strongly Agree

12. My doctor is better able to help me manage my diabetes with the point-of-care results and the help of the Diabetes Risk Assessment Team?

Strongly Disagree 1 2 3 4 5 Strongly Agree

Section 2. Specific Questions

Please make comments on whether point-of-care testing has helped you look after your diabetes.

Please ***tick*** your response to the following questions:

1. Would you like Point-of-Care Testing program to continue to be used for the management of your diabetes?

Yes No Don't know

2. Would you like to see Point-of-care Testing available to all people with diabetes across the Mallee Track region?

Yes No Don't know

3. Is the 'one-stop' diabetes service, incorporating point-of-care testing and visits to the GP, Diabetes Educator and Podiatrist, now better than the diabetes service that were offered prior to this project.

Yes No Don't know

4. PRIOR to the introduction of this project, what was your level of satisfaction with the diabetes services provided for you?

Very unsatisfied Unsatisfied Unsure Satisfied Very satisfied

5. AFTER to the introduction of this project, what is your level of satisfaction with the diabetes services provided for you?

Very unsatisfied Unsatisfied Unsure Satisfied Very satisfied

Section 3. Demographics

Please complete the following information by ticking the relevant box.

Gender: Male Female

Age Group: 15-24 25-34 35-44 45-54 55-64 65+

My **Home Town** in Mallee Track region is:

Ouyen Murrayville Underbool Patchewollock Other (please specify)

Please give your completed questionnaire to either Pauline Harrison, Diabetes Support Group, or Glennis Barnes, MTH&CS.

If you have any queries or questions concerning the questionnaire, please contact Glennis or Bernard Denner on 50921111.

This questionnaire has been prepared by Community Point-of-Care Services unit, Flinders University Rural Clinical School and the Diabetes Management Across the Mallee Track Special Project Team.

POINT-OF-CARE TESTING TRIAL IN GENERAL PRACTICE.

Mark D.S. Shephard

Community Point-of-Care Services, Flinders University Rural Clinical School, Flinders University, Adelaide, South Australia

Point of Care 2006; 5: 192.

Point-Of-Care Testing Trial In General Practice In Australia.

This final short paper, written at the request of the journal's editor, provided a very general description of the Australian Government's POCT Trial in General Practice, in which the author was the Trial's POCT Device Manager, responsible for the education, training, competency assessment and conduct of quality control testing by nursing staff from the participating general practices across urban, rural and remote Australia.

The training resources and quality framework developed for use in the POCT in General Practice Trial were adapted exactly from the successful strategies utilised in my Indigenous POCT models. The direct transference of education and research tools from an Indigenous to a mainstream health program is a rare occurrence in the Australian health care system but reflects the robustness and adaptability of the POCT models conceived and implemented in this research program.

Point-of-Care Testing Trial in General Practice in Australia

Mark D. S. Shephard, MSc, MAACB

Abstract: A randomized controlled trial of point-of-care testing (POCT) is currently being conducted in approximately 60 general practices in urban, rural, and remote Australia. The trial will investigate clinical and cost–effectiveness, safety, benefits to patients and general practitioners, and clinical outcomes of point-of-care testing. Point-of-care tests measured as part of the trial include hemoglobin A1c, urine albumin-to-creatinine ratio, lipids, and international normalized ratio.

Key Words: point-of-care testing, general practice, hemoglobin A1c, urine albumin-to-creatinine ratio, lipids, international normalized ratio

(*Point of Care* 2006;5:192)

In 2002, the Australian Government commissioned a report on the role and value of point-of-care testing (POCT) in general practice in Australia.[1] This report highlighted that rural and remote general practices could potentially be the main beneficiaries of POCT but that further work was needed to determine the clinical and economic benefits of POCT in general practice. As a result, the government recommended that a trial of POCT in general practice be conducted. The objectives of the trial were to investigate the clinical effectiveness, cost effectiveness and safety of POCT in general practice; to investigate the benefits to the patient and the general practitioner (GP); and to determine whether POCT led to improved health outcomes—all within a structured quality management framework. A design for the trial and an evaluation framework was developed before the commencement of the trial, as were a detailed set of standards for POCT in general practice, which incorporated trial guidelines.[2,3]

The 18-month randomized controlled Point-of-Care Testing Trial in General Practice commenced in 2005 and will finish in 2007. The trial is being conducted in urban, rural, and remote geographic areas, with approximately 20 general practices being recruited from each of the Adelaide, South Australia (urban), Bendigo, Victoria (rural) and Dubbo, New South Wales (remote), regions, respectively (approximately 60 practices overall). Half the general practices will conduct POCT (ie, be in the intervention group), whereas the remainder will be control sites, conducting routine laboratory testing. Approximately 5000 patients have been recruited for the trial. Patients must have a preexisting diagnosis of diabetes or hyperlipidemia or be on anticoagulation therapy. Tests to be measured as part of the trial are hemoglobin A1c and urine albumin-to-creatinine ratio (for diabetes management), lipids (for monitoring patients with hyperlipidemia who are being prescribed lipid lowering drugs), and international normalized ratio (for measuring clotting time for patients receiving anticoagulation [warfarin] therapy). The POCT devices selected for use in the trial were the DCA 2000 (Bayer Australia Ltd, Melbourne, Victoria, Australia) for HbA1c and urine albumin-to-creatinine ratio testing, the Cholestech LDX (Point of Care Diagnostics Australia Pty Ltd, Sydney, New South Wales, Australia) for lipids, and the CoaguChek S (Roche Diagnostics Australia Pty Ltd, Sydney, New South Wales, Australia) for international normalized ratio.

The trial is being delivered by 3 lead organizations, working collaboratively from an Adelaide base. They are the University of Adelaide, Flinders University, and the RCPA (Royal College of Pathologists of Australasia) Quality Assurance Programs Pty Ltd. A trial management group is responsible for day-to-day administration of the trial and for issues relating to accreditation and safety, recruitment of general practices, and evaluation of trial outcomes. A POCT Device Working Group is responsible for the development of a training manual, the delivery of initial and refresher training workshops, competency assessment for POCT operators, the implementation and maintenance of an internal quality control program for the POC tests, and the supply of devices, reagents, quality control materials, and consumables. The External Proficiency Testing Program Group is responsible for the implementation and maintenance of an external quality assurance (proficiency testing) program for the POC tests. All 3 groups report directly to the Australian Government Department of Health and Ageing, through a government-elected POCT Steering Committee.

From the Community Point-of-Care Services, Flinders University Rural Clinical School, Flinders University, Adelaide, South Australia, Australia.
Reprints: Mark D. S. Shephard, MSc, MAACB, Community Point-of-Care Services, Flinders University Rural Clinical School, Flinders University, Bedford Park, Adelaide, South Australia, Australia (e-mail: mark.shephard@flinders.edu.au).

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SECTION 3: CONCLUSION

CHAPTER 8: DISCUSSION

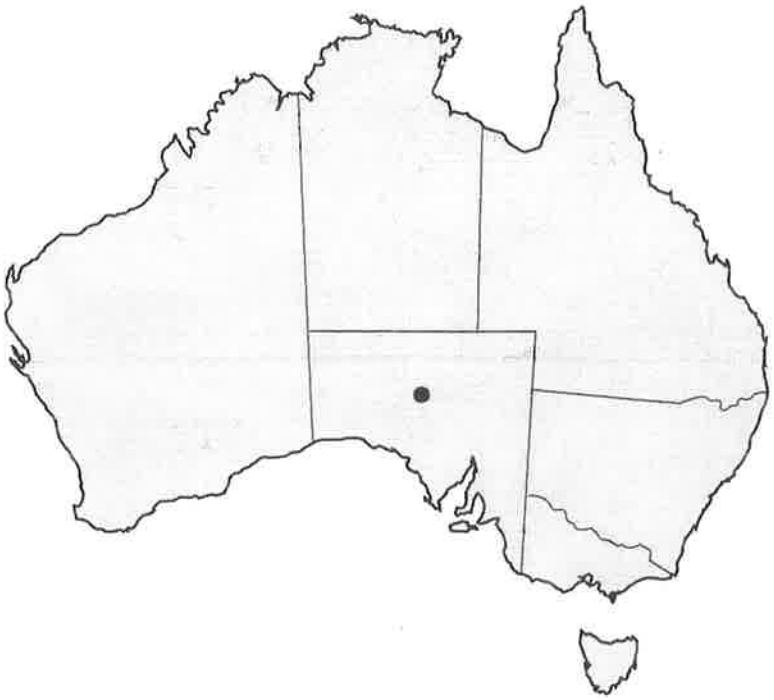
Main Features of this Thesis and Principal Significance of the Research Findings

The peer-reviewed published papers presented in this thesis represent the first and most comprehensive research assessment of the effectiveness of POCT ever conducted in Australia. Significantly, they address and fill the major gaps in the knowledge base of POCT identified in the literature review (Chapter 2 Table 2.25) and answer calls by leading academic researchers for better designed studies to assess the effectiveness of POCT, particularly in the primary care setting (176, 178, 179).

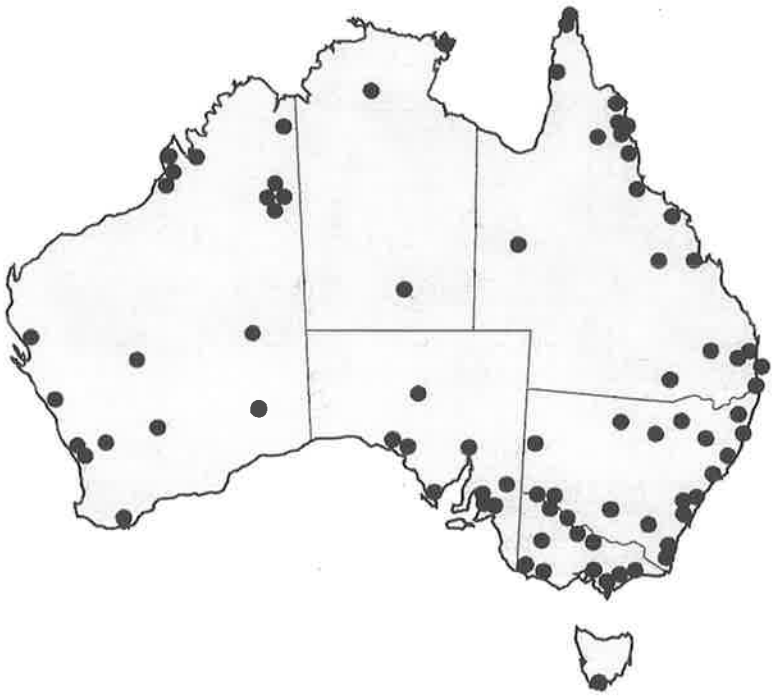
This research program commenced at a time when POCT as a medico-scientific discipline was very much in its formative years in this country and there was only limited interest shown in this field by medical scientists and academic researchers. Critically, this research was conducted in arguably the most difficult and challenging of all non-laboratory primary care environments - the Indigenous medical service. Here the geographic isolation of the largely rural and remote participating services; the diverse mix of services in terms of their size, resources and patient base; and the requisite need to conduct research within a framework of mutual trust and respect and strict observance of cultural sensitivity have truly tested the rigour, adaptability and sustainability of POCT (13). Prior to this research work, implementation of POCT models for chronic disease prevention and management had never before been attempted in the Australian Indigenous medical service setting. In 1997 this research program was initiated at a single site, the Umoona Tjutagku Health Service in Coober Pedy in remote South Australia. During the course of the ensuing decade, as shown in Figure 8.1, the number of Indigenous services engaged in POCT programs developed and managed by the author has expanded to 80 (as at March 2007).

Figure 8.1 Location of Aboriginal medical services engaged in the author's POCT programs (i) in 1997 and (ii) in 2007.

(i) 1997



(ii) 2007



The systematic approach used in this research program has been based on the following common set of overarching methodological principles, which have proven pivotal to the successful application of POCT in the Indigenous health setting:

- the scientific validation of the analytical performance of suitable point-of-care (POC) devices for use in Indigenous medical services,
- the development of a culturally appropriate education and training program for Aboriginal Health Workers (and nurses) as POCT operators,
- the development of a quality management framework for maintaining surveillance of the analytical quality of POCT results, and
- the assessment of qualitative and quantitative research outcome measures to determine the clinical and cultural effectiveness of POCT.

The originality of this research program is evidenced by a number of 'firsts' which have resulted from this work; they include:

- The first peer-reviewed published scientific evaluations of the Bayer DCA 2000 for POC urine ACR measurement and the Cholestech LDX device for POC lipid testing in Australia (9, 25),
- The first demonstration that Aboriginal Health Workers can be successfully trained to be competent POCT operators in a non-laboratory primary care setting (10, 16, 18, 21),
- The first confirmation that Aboriginal Health Workers can conduct POCT to an analytical quality which is equivalent to the laboratory and meets internationally-recognised laboratory-based analytical goals (18, 21),
- The first national framework for quality assurance testing for POC devices used in Indigenous medical services anywhere in the world (18, 21),
- The first published analytical goals specifically for POCT in the non-laboratory setting (35),

- The first reports demonstrating POCT is a culturally effective mode of health service delivery, having gained widespread acceptance by Indigenous POCT operators, Indigenous patients with chronic disease and their treating medical practitioners (22, 26),
- The first reports of the clinical effectiveness of POCT in the Indigenous setting, where POCT has assisted the identification of chronic disease risk in the general community and contributed to improved management of patients with diabetes and renal disease (22, 26),
- The first reports of the successful translation of an Indigenous POCT model to a non-Indigenous setting (32, 36). This is a unique occurrence in the Australian health care system, as so often mainstream health programs are enforced into Indigenous health but rarely does the reverse apply (374).

Collectively, these findings have built a substantial new knowledge base on POCT in the Indigenous medical service setting and, in the process, answered key research questions on the effectiveness of POCT and confirmed its validity and reliability in this setting.

In addition, the HbA1c and urine ACR Medicare rebates now available through the QAAMS Program represent a further significant outcome of this research program. They are the only rebates for POC pathology tests which can be claimed under the Australian Government's Medicare system (other than a small group of qualitative tests such as urine dipstick and pregnancy tests)(34). The approval of these rebates by two Australian Government Federal Health Ministers (the Hon Dr Michael Wooldridge in 2000 and the Hon Tony Abbott in 2006) indicates the Government's acceptance of (i) the research findings of the QAAMS Program and (ii) POCT as a legitimate and credible means of pathology service delivery in Australia.

Problems Encountered with the Current Research Program and Future Research Directions

Several problems and challenges were encountered during the development and implementation of the POCT models presented in this thesis, in particular the QAAMS Program. These are highlighted in the ensuing text and, where appropriate, are discussed in the context of future research directions (Table 2.26).

Maintaining POCT Operator Competency and Analytical Standards through Continuing Education and Training

As the number of Indigenous medical services participating in the QAAMS Program continued to grow across the years, it became increasingly difficult to provide timely access to education and training programs for both (i) new services joining the program and (ii) services that had recently lost their current POCT operator(s). In relation to the latter, high rates of POCT operator turnover not only represented the most significant challenge to the continued sustainability of the QAAMS program but also meant that this pool of research subjects was constantly changing. At the end of 2004, an audit was undertaken regarding the number of changes in POCT operators within the QAAMS program at each site during the first five years of operation. 21% of services experienced four or more POCT operator changes (with one site experiencing seven operator changes) (375). These latter sites were spread broadly across urban, rural and remote geographic locations and not restricted to one particular geographical zone. In many instances, when POCT operators left their service, they took the QAAMS education and training resources with them and provided little or no handover to their replacement.

On-site, face-to-face training for individual services (especially those with immediate training needs) has proven increasingly impractical and inefficient in a management sense and it has been necessary to continually explore and engage an ever-evolving array of culturally appropriate training options.

The annual QAAMS Workshop, which has been a particularly successful training forum, now specifically prioritises the funded attendance of those services with the most pressing training needs. On-site training is generally only conducted for groups of services within a common geographic region at a location convenient to the participating services. Training by videoconference also commenced in 2006 and has been particularly useful as a 'by distance' training option for remote medical services with immediate training needs.

In terms of future directions, web-based POCT training has recently been developed in the United Kingdom (376) and, with further advances in web-streaming technology, this mode of training delivery will undoubtedly become more widely used for large POCT programs, especially those that have a national or international focus with large numbers of participating services. Advantages of web-based training include around-the-clock availability, with the opportunity to progress through training at one's own pace and to complete at least the theoretical component of competency assessment online (376). I am currently developing a website for the QAAMS Program, in which enrolled participants will be able to access the program's full training program in a 'live' web-streamed format. While broadband access required to view the web-based training still remains limited in some remote parts of Australia, the concept of web-based training for POCT will provide a significant further advance for services to gain immediate access to training. For those services unable to access the web, the training presentation could be burned to a DVD and sent to these sites as a further 'by distance' training option.

The introduction of web-based training methods begs the interesting and important research questions for my future work:

- Can web-based training for POCT be as culturally effective as face-to-face training, and
- Will web-based training be accepted as a training strategy by Indigenous POCT operators?

Assessment of Clinical Outcomes in the Indigenous Health Setting

The ability to investigate the clinical effectiveness of POCT has been limited by several factors. As noted in the literature review, in terms of study design, randomised controlled studies provide the highest quality of evidence for assessing outcome measures (170). However, in working in the Indigenous health setting, it has certainly been the author's experience that Aboriginal Health Research Ethics Committees are reluctant to permit the conduct of randomised controlled studies as they hold the view that they do not want to preclude any community members from receiving potential benefits of a successful intervention strategy. Secondly, at the request of the participating Indigenous medical services, the outcome studies investigating the effect of the introduction of POCT on diabetes control were conducted as 'real time' prospective studies following commencement of patient POCT. The author was not able to gain access to patient data on HbA1c measurements conducted by the laboratory prior to POCT; therefore changes in glycaemic control before POCT was introduced were not able to be compared with changes post POCT. At one of the services in the POCT in Aboriginal Hands program and also in the non-Indigenous Diabetes Management Along the Mallee Track Program, POCT was integrated into a new multi-faceted diabetes care strategy and therefore the observed improvements in glycaemic control cannot solely be attributed to the introduction of POCT. The difficulty of 'teasing out' the direct contribution of POCT to improved patient care is certainly not restricted to the present research program and, as indicated in the literature review, is a major issue in many POCT outcome studies (203, 204).

Future research on the clinical effectiveness of POCT should continue to monitor changes in glycaemic control (and other related parameters) in patients with diabetes across time, but be based on an improved research design which includes the following elements: (i) the ability to source laboratory HbA1c prior to the introduction of POCT to enable a true 'before and after' study, (ii) the monitoring of diabetes patients who have received no change in clinical care pre and post POCT to determine the direct assessment of the impact of POCT only and (iii) the tracking of diabetes

patients over the long-term (3-5 years) to validate the sustainability of improved clinical outcomes. The ability to conduct research in this manner will however be contingent on the approval of both the relevant ethics committees and the participating Indigenous medical service(s).

Cost Effectiveness of POCT

It has not been possible to undertake a detailed analysis of the cost effectiveness of POCT during the current research program, due to lack of resources and personal expertise in this field. As evidenced by the literature review, cost effectiveness remains the most poorly researched area in the field of POCT, with the longer-term cost benefits of POCT in particular being extremely difficult to quantitate (79, 118, 174).

Cost effectiveness will be assessed as an outcome measure of the Australian Government's POCT in General Practice Trial by the Evaluation Committee within the Trial Management Group and the findings of this economic assessment will be eagerly awaited by all POCT researchers. Future research in this field would require the engagement of health economists and should focus on directly comparing the total cost of diabetes care in patients having POCT with the total cost of patients having the *same* clinical care in patients without POCT.

PoCT Devices and Continuous Quality Improvement

The Bayer DCA 2000 POC device has proven robust and analytically sound during the course of this research program. The Cholestech LDX lipid analyser, used at different times during this research, has also demonstrated acceptable analytical performance. However these devices have now been in the global POCT market place for more than 10 years and represent 'first generation' POCT devices.

Although simple to use, they lack some of the modern connectivity features now demanded by current international industry standards (104, 377). The DCA 2000 has limited capacity to connect to an external printer, while the Cholestech LDX system does include an optional basic printer with

hard copy readout. The DCA 2000 can store 16 patient results in its display memory but the Cholestech LDX device only holds the most recently performed test result. It is currently not possible to download patient or quality control results to a central laboratory or clinical information system with either device. While relatively compact in design, neither device could be considered to be on the miniaturised size-scale of most modern POCT devices. Battery operation is also not possible with either device.

The research and development division of Bayer Diagnostics in the USA will be releasing a 'second generation' DCA 2000 device in late 2007/2008. In 2005, the author was consulted by Bayer USA and my direct input was requested into the design and specifications of this new model. While featuring a more streamlined and modern appearance, the overall size of the new DCA 2000 will remain unchanged, as will the analytical method principle (immunoassay) which has rigorously stood the test of time. However, the new DCA 2000 will incorporate the full suite of connectivity features, including the ability to electronically download and transfer patient and quality control results, track individual patient test results, plot serial quality control results and calculate imprecision statistics.

More than half of the DCA 2000 devices currently used in the QAAMS program are over 7 years of age, having originally been purchased by the Department of Health and Ageing in a bulk order from Bayer Australia at the commencement of the QAAMS Program. While the devices have proven robust, the author has recently held discussions with the Department of Health and Ageing regarding the development and implementation of a replacement policy for ageing devices and well as seeking funding support for an annual DCA 2000 service contract for each participating QAAMS service. The latter will guarantee a loan device will be sent to each service within 48 hours of receipt of their original device and minimum downtime of POCT service provision. These initiatives will be integral to the continuing sustainability of this national POCT program.

A specific area of future research interest is the measurement of blood creatinine by POCT. As discussed in the literature review, the clinical use of an estimated GFR measurement (eGFR) based on blood creatinine measurement has sparked renewed interest in this test (289). In my discussions with clinicians working with chronic disease patients in the Indigenous medical services around Australia, the one POC test that I am consistently asked about is creatinine. In 2000 I conducted the first evaluation in Australia of the portable i-STAT POCT device (Abbott Diagnostics, Australia), which included an assessment of a new creatinine module (378) and the device was trialled in an Indigenous medical service in remote Western Australia. However, the creatinine POC test exhibited poor analytical performance, with a high cartridge error rate and unacceptable imprecision; as a result this device was not included in my current research models. Since that time, I have attempted to identify a suitable alternate POCT device for creatinine measurement without success. The challenge exists for POCT manufacturers to improve current technology for this test as there will be considerable market interest in such a device with eGFR now an integral component of renal disease assessment. A key research question for the future will be: Will new and improved POCT devices for blood creatinine be able to demonstrate acceptable analytical accuracy and imprecision and prove clinically useful in the Indigenous health care setting?

In a more general sense, the literature review highlighted the recent development of, and technological advances with, *in vivo*, *ex vivo* and minimally invasive POCT devices which can, for example, provide continuous glucose measurements that could potentially result in improved glycaemic control (64, 82, 85, 95). However there remain many unanswered research questions in this area, particularly how analytically reliable will these devices be in practice compared to existing technology and will a change to this new technology result in clinical and cost benefits for the patient and health services.

Developing an Accreditation Framework for Indigenous POCT

As mentioned in the literature review, there are currently no specific government regulations or accreditation requirements for POC devices and POCT testing in Australia including Indigenous medical services (167), other than the provisional accreditation framework being trialled in the Australian Government's POCT in General Practice Trial (which was developed by the Trial Management Committee's Accreditation Working Group, of which I was a member) (34, 36, 113, 168).

With the continued growth of the QAAMS Program, a future direction of this work will involve the development of a national accreditation framework for this Indigenous POCT model. The challenge will be to construct an accreditation checklist that is comprehensive but remains culturally appropriate, relevant and practical. In many ways this task has been made simpler and more straightforward by the current research program, as my research findings have (i) set the agenda and determined what many of the standards for accreditation should be (particularly in relation to education, training, competency assessment, quality control, quality assurance, analytical goals and clinical governance) and (ii) provided the evidence that they can be achieved in the Indigenous heath care setting.

Uncertainty Regarding International Standardisation of HbA1c and UACR Methods

During the current research program, the conduct of POCT for HbA1c in Indigenous medical services has continued across a period of professional uncertainty regarding the development and introduction of procedures for the international standardisation of HbA1c methods. As mentioned in the literature review, the International Federation of Clinical Chemistry (IFCC), through its Working Party on HbA1c Standardisation, has established a reference system for global standardisation (239, 254-260). This reference system has been developed to a stage which now includes a specific chemical and analytical definition of the measurand, the development of a primary reference

material, two reference methods (mass spectroscopy and capillary electrophoresis), an international Network of Reference Laboratories and secondary reference material that is available for all manufacturers of HbA1c methods. A plan for the worldwide implementation of the reference system is also underway (260).

In relation to the latter, the topic of most contentious debate is the HbA1c reporting units to be adopted globally. Two main options are being considered: (i) the use of an IFCC HbA1c SI unit which will necessitate the introduction of a new reference interval of 3-5% HbA1c, with an optimal treatment target of 5% and a change of therapy proposed at HbA1c values greater than 6% and (ii) the reporting of HbA1c as 'glucose equivalents', which requires further prospective clinical studies to re-confirm and establish with certainty the relationship between HbA1c and mean blood glucose levels (255, 260).

While the push for global HbA1c method standardisation has had negligible impact on the day to day management of current POCT models developed in this research program, in the longer term, implementation of the planned change of reporting units will unquestionably require a significant re-education program for clinicians, POCT operators and patients with diabetes in the interpretation and clinical use of HbA1c results. Key research questions that will need to be answered to assess the effectiveness of global standardisation include:

- Will global standardisation be adopted uniformly by all countries of the world (in particular the USA where resistance to global standardisation has been most pronounced)?
- Can the recommended changes to HbA1c reporting units be translated seamlessly into routine clinical practice across the world?
- What will the rate of errors in clinical management of diabetes patients be as a result of initial clinician and patient uncertainty about changes to HbA1c reporting units?

As mentioned in the literature review, the accuracy of urine albumin (and hence urine ACR) methods are also the subject of professional scrutiny following the recent published description of non-immunoreactive form of albumin in the urine of diabetes patients (283-286). At the time of writing this thesis, an IFCC Working Party has been established to address this issue but minimal work has been conducted. In the future, however, the global adoption of a new system for reporting urine albumin and the classification of albuminuria status will require a new education program for all stakeholders, including POCT operators, diabetes patients and their clinicians and present similar future research questions to those posed for HbA1c.

Formal Teaching of POCT at University and Other Teaching Institutions

In the current research program, 301 Aboriginal Health Workers, nurses and doctors have undertaken specific training programs in the use of POCT for the management of diabetes and renal disease. However, to the author's knowledge, there is minimal, if not a total lack, of formal teaching of POCT in universities and other teaching institutions such as TAFE colleges. An important future direction for POCT will be to develop and introduce structured teaching programs/modules about POCT to Australian and overseas undergraduate and post graduate medical students and related health professionals groups (for example nurses, Aboriginal Health Workers, diabetes educators, and pharmacists). A key future research question will be: Can POCT teaching modules be integrated effectively into coursework for a range of different health professional groups?

Translation of POCT Models on a Larger Scale both Overseas and in Australian General Practice

The research findings presented in this thesis represent the first substantial body of evidence base to support the effectiveness of POCT in the Australian Indigenous medical service setting. Together with preliminary evidence from the quality assurance testing conducted in the island of Tonga, these findings also form the basis for the compelling argument that the foundation elements of the POCT models developed in this research program should be adaptable to Indigenous communities and/or rural and remote communities globally and have immeasurable potential to address the global

burden of diabetes and renal disease now present among world's Indigenous peoples. This is a significant potential long-term future outcome of this work and one which will be the subject of future planned research beyond this thesis.

I have held several rounds of discussions with senior managers within both Bayer Australia and the parent company in the USA and have prepared a written proposal for the development and implementation of an international program based on the QAAMS model, which is currently being considered by these managers. The proposed name for the international model is the ACE Program for Diabetes Management, ACE being an acronym for Analytical and Clinical Excellence and reflecting my desire for this program to not only maintain standards of high analytical quality but also have a strong clinical focus with outcome assessments a high priority.

The QAAMS POCT model has already attracted world-wide interest and led to national and international collaborations with clinical and research colleagues and industry in the Western Pacific region, Canada, North America, New Zealand, India and South Africa, making the vision of the international ACE model feasible and attainable in the future, albeit on a significantly larger scale than the QAAMS model and necessitating the answering of a further suite of research questions including:

- Will the QAAMS model be robust enough to be successfully introduced overseas?
- Can web-based training be used on an international scale as a practical and effective mode of training?
- How will competency standards for POCT operators be assessed practically at the 'ground level' and how can issues of anticipated even higher rates of staff turnover be addressed on a larger scale?

- Will standards of analytical quality observed with the QAAMS program be achievable or be compromised by the likely more diverse and more remote nature of international participants?
- Can POCT continue to be clinically and culturally effective when conducted across different participating countries?

As described in Chapter 7, I have also played a major role in the establishment and delivery of the Australian Government's Point of Care Testing in General Practice Trial. The results of the Trial will not be completed and published until 2008. Should the Government decide to support the national rollout of POCT into general practice in Australia, similar research questions to those posed for the ACE program will need to be addressed as POCT is expanded on a significantly larger scale to general practices across the country.

Table 8.1. Future research directions for this POCT work.

Area of Future POCT Research	Key Future POCT Research Questions
Education and training	Can web-based training for POCT be as culturally effective as face-to-face training and will it be accepted as a training strategy by Indigenous POCT operators?
Assessment of clinical outcomes	Using a before and after study design, what is the long-term clinical effectiveness of POCT for monitoring diabetes patients compared to patients undergoing the *same* clinical care without POCT?
Cost effectiveness	What is the total cost of diabetes care in patients having POCT compared to the total cost of patients having the *same* clinical care without POCT?
Research and evaluation of new POCT devices and test applications	Will new and improved *in vivo, ex vivo* and minimally invasive POCT devices be able to demonstrate acceptable analytical accuracy and imprecision and prove clinically useful and cost effective?
Accreditation for Indigenous POCT	Can an accreditation framework be developed for the conduct of POCT in the Indigenous health setting that is culturally appropriate, relevant and practical?
International standardisation of HbA1c and urine albumin methods	Can global standardisation of HbA1c and urine albumin assays (including those conducted by POCT) occur seamlessly across the world with minimal clinical management errors occurring as a result of the introduction of new reporting units?
Formal teaching of POCT	Can POCT teaching modules be integrated effectively into coursework for a range of different health professional groups?
Translation of POCT models on a larger scale	Is the QAAMS model robust enough to be successfully introduced overseas? Can web-based training be used on an international scale as a practical and effective mode of training? How will competency standards for POCT operators be assessed practically at the 'ground level' and how can issues of anticipated even high rates of staff turnover be addressed on a larger scale? Will standards of analytical quality observed with the QAAMS program be achievable or be compromised by the likely more diverse and more remote nature of international participants? Can POCT continue to be clinically and culturally effective when conducted across different participating countries?

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