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.


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. 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.

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 glycaated haemoglobin (HbA1c) testing in indigenous primary health-care services. 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 HbA1c 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 HbA1c 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. 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, 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.

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. 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 and in the laboratory, 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 HbA1c 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
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). 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...
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

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.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Cycle 1</th>
<th>Cycle 2</th>
<th>Cycle 3</th>
<th>Cycle 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR</td>
<td>91%</td>
<td>88%</td>
<td>99%</td>
<td>98%</td>
</tr>
<tr>
<td>Albumin</td>
<td>80%</td>
<td>77%</td>
<td>89%</td>
<td>90%</td>
</tr>
<tr>
<td>Creatinine</td>
<td>83%</td>
<td>83%</td>
<td>87%</td>
<td>88%</td>
</tr>
</tbody>
</table>

Table 1 Percentage acceptable results for urine ACR, albumin and creatinine during the first four QAAMS testing cycles

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Median precision observed (CV%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2003</td>
</tr>
<tr>
<td>ACR</td>
<td>7.2% 7.7% 3.6% 3.0% 12%</td>
</tr>
<tr>
<td>Albumin</td>
<td>11.8% 13.2% 6.7% 5.9% 10%</td>
</tr>
<tr>
<td>Creatinine</td>
<td>4.3% 5.3% 4.2% 4.5% 6%</td>
</tr>
</tbody>
</table>

Table 2 Median precision achieved for urine ACR, albumin and creatinine across the first four testing cycles in the QAAMS urine ACR programme

*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.
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

<table>
<thead>
<tr>
<th>Test</th>
<th>2003</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Level</td>
<td>Cycle 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine ACR (mg/mmol)</td>
<td>3.7</td>
<td>6.0</td>
</tr>
<tr>
<td></td>
<td>6.0</td>
<td>4.8</td>
</tr>
<tr>
<td>Urine albumin (mg/L)</td>
<td>35.0</td>
<td>8.8</td>
</tr>
<tr>
<td></td>
<td>215.0</td>
<td>4.3</td>
</tr>
<tr>
<td>Urine creatinine (mmol/L)</td>
<td>9.0</td>
<td>6.5</td>
</tr>
<tr>
<td></td>
<td>35.5</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Three different lot numbers (LN) of QC material have been used across four testing cycles.

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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.2,7,30–31,36,20,22

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 HbA1c monitoring of glycemic control performed on the same analyser.

The QAAMS model, which has proven successful for POC HbA1c 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 HbA1c, 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.

Acknowledgements

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