Point-of-care testing of $\text{HbA}_1c$ 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

Type 2 diabetes mellitus and its sequelae are a major cause of premature mortality in Aboriginal Australians and Torres Strait Islanders today. Whereas this disease did not seem to exist in Australia before European settlement, 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.

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 ($\text{HbA}_1c$) 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 $\text{HbA}_1c$ testing in remote and rural clinical settings, through the Australian Government’s Quality Assurance for Aboriginal Medical Services (QAAMS) Program, 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 $\text{HbA}_1c$ and glucose measurements for monitoring diabetes in difficult environmental working conditions, with extreme heat and humidity.

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...
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) 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 $\geq 5.0$ 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 $5.5$–$7.0$ 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 $\geq 7.0$ mmol/L, OR
- $2$-h plasma glucose level $\geq 11.1$ 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 capillary 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$_1c$ immunochromically, 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 $27^\circ$C and $31^\circ$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 $\geq 800$ g. Supernatants were stored at $0^\circ$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$_1c$ was measured by immunochemical method using anti-human glycosylated haemoglobin antibody on a Bayer DCA 2000+ analyser. This measures glycosylated haemoglobin using glucose dehydrogenase and produces a result within $4$ minutes.

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adults</th>
<th>Non-diabetic</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n=36$</td>
<td>$n=76$</td>
<td>$n=40$</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of females (%)</td>
<td>27 (75%)</td>
<td>42 (53%)</td>
<td>23 (57%)</td>
</tr>
<tr>
<td>Age in years (Mean (SD))</td>
<td>50.5 (14.1)</td>
<td>37.5 (15.4)</td>
<td>13.7 (1.7)</td>
</tr>
<tr>
<td><strong>Diabetes or POC glucose ≥5.0 mmol/L</strong></td>
<td>$n=36$</td>
<td>$n=38$</td>
<td>$n=14$</td>
</tr>
<tr>
<td>POC glucose (mmol/L) Median (range)</td>
<td>11.16 (4.58)</td>
<td>5.87 (1.04)</td>
<td>5.87 (1.30)</td>
</tr>
<tr>
<td>Laboratory glucose (mmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>11.0 (3.4–22.1)</td>
<td>5.5 (4.5–10.1)</td>
<td>5.3 (5.1–10.1)</td>
</tr>
<tr>
<td><strong>Laboratory HbA$_1c$ (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>9.16 (2.40)</td>
<td>5.74 (0.38)</td>
<td>5.33 (0.34)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>9.5 (5.6–13.4)</td>
<td>5.7 (4.9–6.6)</td>
<td>5.6 (4.7–6.1)</td>
</tr>
</tbody>
</table>

* 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 $\geq 5.0$ mmol/L. HbA$_1c$ = glycosylated haemoglobin.

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

<table>
<thead>
<tr>
<th></th>
<th>Glucose (mmol/L)</th>
<th>HbA$_1c$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>POC</td>
<td>Laboratory</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>3.4–22.2</td>
<td>3.0–28.3</td>
</tr>
<tr>
<td>Mean difference (95% CI)</td>
<td>$+0.36$ (0.13–0.62) ($P=0.007$)*</td>
<td>$0.002$ ($0.07$ to $0.07$) ($P=0.95$)*</td>
</tr>
</tbody>
</table>

* 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 HbA1c.

Statistical methods
Data were analysed using JMP software11 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 plots12 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 HbA1c 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 HbA1c 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.

Comparison of glucose results
POC capillary glucose level is compared with laboratory plasma glucose level for the same patients in Box 2. Mean values for HbA1c concentration by the two methods were identical (0.6%), 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 HbA1c range 6%–10%. The very small bias observed was constant across the range of HbA1c 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 HbA1c 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 HbA1c tests compared with laboratory tests of venous samples transported to the nearest laboratory.

For HbA1c, the values obtained by POC and laboratory testing were statistically, analytically and clinically identical. Thus, POC testing for HbA1c, using the Bayer DCA 200+ 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 HbA1c measurement approaches 3% or less, to ensure that clinically significant changes in serial HbA1c concentrations can be detected.13 In the QAAMS Program (currently being conducted in 60 Aboriginal medical services across Australia), precision of HbA1c measurement using the Bayer DCA 200+ is monitored continuously. For the past 3 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
should still rely on confirmatory tests of plasma
settings. However, the diagnosis of diabetes
glucose meters is known in specific clinical
for people with known diabetes, and it is
ing for diabetes risk, as well as self-monitoring
is uncertain whether the patient has fasted.

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+
on-site training. POC testing provides the
opportunity for immediate feedback and
counselling, making it an ideal tool for inex-
ensive on-site motivational management of
diabetes. Patients expressed their appreciation
of the simultaneous education and opportu-
nity to “see what happens with their blood”.
They generally preferred fingerprick collection
to venepuncture. Other studies in both Indige-
nous and non-Indigenous settings have also
shown that POC HbA1c testing can improve
diabetes control when linked with aggressive
clinical management regimens and specialist
support.15-17

This study shows that HbA1c can be con-
cently and accurately measured by POC testing
with the Bayer DCA 2000+ analyser in rural
and remote clinical settings. This form of test-
ing is suitable for regular HbA1c monitoring
across all concentrations. The study also opens
the way to investigate the contribution of POC
HbA1c testing to diagnosis of diabetes when it
is uncertain whether the patient has fasted.
POC glucose testing has a useful role in screen-
ning 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

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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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