



Original Article

Should capillary blood glucose measurements be used in population surveys?

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ABSTRACT

Objective: To determine the accuracy and appropriateness of capillary blood glucose testing in population surveys.**Materials and methods:** Capillary blood glucose using the Roche ACCU-CHEK instrument and Advantage 11 Test Strips was compared to a laboratory instrument. Three independent cross-sectional risk factor surveys ($n = 1432$) and baseline individuals from the Greater Green Triangle Diabetes Prevention Project ($n = 341$) provided both fasting plasma and capillary blood glucose measurements. Accuracy of capillary glucoses was assessed using the ISO 15197 standard. The median age of the participants was 71 years, ranging from 25 to 84 years. There were 799 males and 974 females.**Results:** Capillary glucose method had poorer precision at lower concentrations (CV: 9.50%, mean = 3.09 mmol/L, CV: 4.90%, mean = 16.78 mmol/L, $n = 233$ replicates). Individual discrepancies were seen across the measuring range (2.8–19.9 mmol/L, $n = 1773$). In total, 94.5% of results fell within the minimum acceptable accuracy standards. This was slightly short of the 95% of results required to meet the ISO 15197 standard. The prevalence of diabetes in the study population using glucose ≥ 7.0 mmol/L was 2.4% (95%CI 1.8–3.3%) according to fasting plasma glucose and 2.8% (2.1–3.8%) according to fasting capillary glucose. The lower WHO-defined cut-off of 6.1 mmol/L for capillary blood glucose testing gave a prevalence of 10.7% (9.0–12.5%).**Conclusions:** This study of matched capillary and plasma glucose results concludes that while it is appropriate to use fasting capillary glucose levels to determine the prevalence of diabetes in populations, it should not be used to reliably diagnose diabetes in individuals.

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1. Introduction

Currently, 240 million people around the world are living with diabetes with predictions showing that it will increase by 58% to 380 million by 2025. Globally, diabetes is the fourth biggest cause of death affecting countries of all income levels and a wide variety of epidemiological profiles [1]. The American Diabetes Association has reported that medical expenditure for patients with diagnosed diabetes is, on average, up to three times higher than in patients without diabetes [2].

National data indicates that Australia has many cases of diabetes that have not been diagnosed, with one undiagnosed case for

every diagnosed case. Direct health care expenditure on diabetes for Australia in 2004–2005 was \$907 million, representing 2% of the allocated recurrent health expenditure [3].

As the impact of diabetes on the total burden of disease in Australia, along with the rest of the world is increasing, it is important that we monitor the prevalence of the disease, to guide the implementation of health promotion interventions.

Cardiovascular risk factor surveys with anthropometric measurements and venous plasma sampling are an expensive, but necessary exercise to determine the prevalence of cardiovascular disease within populations. In particular, venous plasma sampling for biochemical tests is costly, and in rural areas, the transport of blood to laboratories for analysis is problematic. Analytes such as glucose have to be collected and processed in a timely fashion to ensure accurate results.

Capillary blood glucose testing, using portable point of care devices, may be an alternative to venous plasma samples, because they are easier, less expensive overall, and less invasive to obtain. If capillary blood glucose testing is to be used in public health

Abbreviations: *r*, Bland Altman Pearson correlation coefficient; GGT, Greater Green Triangle; ISO, International Organisation for Standardisation; BMI, body mass index.

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screening programs, the devices selected need to be accurate and precise.

The technology of glucose meters has improved, and capillary monitoring glucose testing is now also widely used in the home, general practice and hospital settings to assess glycaemic control and to confirm hypoglycaemia. A glucose meter which converts capillary blood results to plasma levels has been reported as being reliable for individuals with normal glucose tolerance and for type 2 diabetes subjects [4]. Many studies have concluded that glucose meters should not be used for diagnosis, only for self-monitoring [5–7].

In clinical practice, plasma and capillary blood glucose values are often used interchangeably, despite levels of glucose being higher in plasma than in erythrocytes [8].

Standards are in place which relate to monitoring systems for self-testing in managing diabetes, but these should apply to all capillary glucose monitoring performed with glucose meters [9].

There is a clear distinction in objectives between an epidemiological and a clinical diagnosis of diabetes. An epidemiological diagnosis of diabetes is based on a fasting glucose or a glucose tolerance test, whereas a clinical diagnosis requires laboratory confirmation if the patient has no symptoms. Accurate glucose testing is required for epidemiological studies to ensure participants with dysglycaemia can be reliably identified.

As part of a study to determine the level and prevalence of cardiovascular risk factors in rural Australia, we evaluated the accuracy and appropriateness of capillary blood glucose in population surveys.

2. Materials and methods

Three independent cross-sectional surveys ($n = 1432$, 41%) of chronic disease risk factors and related health behaviour were performed in the Greater Green Triangle (GGT) region of south eastern Australia, in 2004–2006 [10]. Additional data was obtained during the GGT Diabetes Prevention Project ($n = 341$) in 2004–2006 [11]. The median age of the participants was 71 years, ranging from 25 to 84 years. There were 799 males and 974 females. There were 16 (0.01%) participants with a body mass index (BMI) of <18, 386 (22%) with a BMI of 18–25, 669 (38%) with a BMI of 25–30, and 702 (40%) with a BMI of >30.

Health checks, including anthropometric measurements and venous plasma sampling (fasting at least 10 h) were carried out at survey sites by specially trained nurses. A fasting capillary blood glucose and plasma glucose test was included in the health check.

The Roche ACCU-CHEK instrument and Advantage 11 Test Strips (Roche Diagnostics, Sydney, Australia) were used to perform the capillary blood capillary glucose tests. The test strip contains the enzyme glucose dehydrogenase, which converts the glucose in whole blood to gluconolactone. This reaction liberates an electron that reacts with a mediator generating a small current that is read by the instrument.

Roche liquid internal quality control material (Levels 1 and 2) was run each morning prior to commencing the health checks.

To check the linearity of the ACCU-CHEK 11 strips, we ran Roche Diagnostics Glucose Monitoring Quality Assurance samples distributed through RCPA Chemical Pathology Quality Assurance Programs.

The venous blood samples were centrifuged and the plasma frozen at the field survey sites before being transferred to the Flinders Medical Centre Clinical Trials Laboratory. An Hitachi 917 clinical chemistry analyser (Roche Diagnostics, Sydney, Australia), hexokinase/glucose-6-phosphate dehydrogenase method was used to measure plasma glucose. Samples from all health surveys were processed by Flinders Medical Centre Clinical Trials Laboratory.

Statistical analysis was performed using MedCalc[®] version 10.0.2 and PASW Statistics version 17.0.3. The results of the paired plasma and capillary blood glucose measurements were used for statistical analysis. Mean (standard error, SE) and 95% confidence intervals, as well as percentages, are presented as necessary. Statistically significant differences in mean values were determined with a two-sided paired *t*-test.

The Pearson correlation coefficient (*r*) was determined by linear regression. A Bland–Altman plot was constructed by plotting the absolute differences between paired samples against the average of these paired samples.

Agreement between methods was also assessed by Passing & Bablok Regression.

Accuracy of capillary gluces was assessed using the International Organisation for Standardisation (ISO) 15197 standard, which states that 95% of the individual results for the glucose meter shall fall within ± 0.83 mmol/L of the results at glucose concentrations ≤ 4.1 and $\pm 20\%$ at glucose concentrations > 4.1 mmol/L.

3. Results

Two levels of quality control were run each day that health checks were performed. The glucose meter produced a CV of 9.50% for the Level 1 control (mean = 3.09 mmol/L, SD = 0.29 mmol/L, $n = 233$) and a CV of 4.90% for the level 2 control (mean = 16.78 mmol/L, SD = 0.82 mmol/L, $n = 233$). This shows that the glucose meter is less precise (i.e. reproducible) at lower levels of glucose concentration than higher concentrations.

Twelve Roche Diagnostics Glucose Monitoring Quality Assurance samples were analysed by us and the result plotted against median result of all participants of the RCPA Quality Assurance program. The ACCU-CHEK method was shown to be linear for glucose concentrations from 2.0 to 25.0 mmol/L (data not shown).

Fasting PoCT (1773 pairs) capillary and plasma laboratory glucose results from the GGT data were compared. No difference was observed between the mean fasting plasma glucose (5.41 mmol/L, 95% CI: 5.37–5.46) and capillary glucose (5.40 mmol/L, 95% CI: 5.35–5.45).

Fig. 1 shows a Bland–Altman plot demonstrating the differences between plasma glucose and capillary glucose for paired samples plotted versus the mean of the plasma and capillary glucose for each pair. The mean plasma glucose was 0.015 mmol/L (95% CI: –0.011 to 0.0414) lower than the mean capillary glucose. Although the mean difference between plasma and capillary glucose is small,

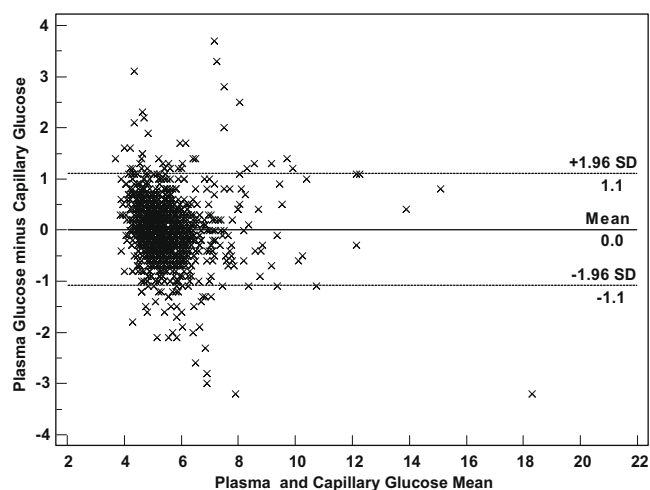


Fig. 1. Bland–Altman plot: difference between venous plasma laboratory glucose and capillary blood glucose. Mean difference 0.015, 95%CI: 0.011–0.0414.

discrepancies between paired samples using the two methods can be seen across the measuring range (2.8–19.9 mmol/L).

The Passing & Bablok Regression Equation for the relationship between plasma glucose and capillary glucose was $y = 1.167x - 0.90$ (Fig. 2). A strong correlation was observed between plasma and capillary glucose, with a Pearson concordance correlation coefficient of 0.84 (95% CI: 0.83–0.85).

Overall, 94.5% of results fell within the minimum acceptable accuracy standards, slightly short of the 95% of results needed to meet standard requirements (Tables 1a and 1b). Forty six percent

of capillary glucose results ≤ 4.1 mmol/L, and 3.8% of results > 4.1 mmol/L, were inaccurate.

Table 2 shows the effect of patient characteristics on the capillary blood glucose results compared to the plasma laboratory result. Statistically significant differences were observed in the mean results for participants > 75 years of age, females and those with a BMI of 18–24.9 and ≥ 30 .

Table 3 shows that in normoglycaemic patients, there is an 84.5% concordance between capillary and plasma glucose. Overall, 185 patients displayed an impaired fasting capillary glucose and would have undergone further testing to be classified as normoglycaemic by venous plasma glucose. Capillary testing would have incorrectly identified 121 patients as normoglycaemic when the fasting plasma glucose identified them as having an impaired fasting glucose or diabetes. Sixteen participants identified as having diabetes by plasma glucose testing would not have been identified with fasting capillary glucose testing.

If WHO-defined values for diagnosis of diabetes are used (plasma ≥ 7.0 mmol/L, capillary blood ≥ 6.1 mmol/L), concordance with plasma glucose results is excellent, but 217 participants would have been diagnosed with diabetes incorrectly and undergone further testing (Table 4).

In separate analyses of Risk Factor Study data only (1432 individuals aged 25–74, weighted to the local population), the prevalence of diabetes using glucose ≥ 7.0 mmol/L was 2.4% (95% CI 1.8–3.3%) according to fasting plasma glucose and 2.8% (2.1–3.8%) according to fasting capillary glucose. The lower WHO-defined cut-off of 6.1 mmol/L for capillary glucose testing gave a prevalence of 10.7% (9.0–12.5%). Prevalence figures within the population are higher when a history of known diabetes is also included.

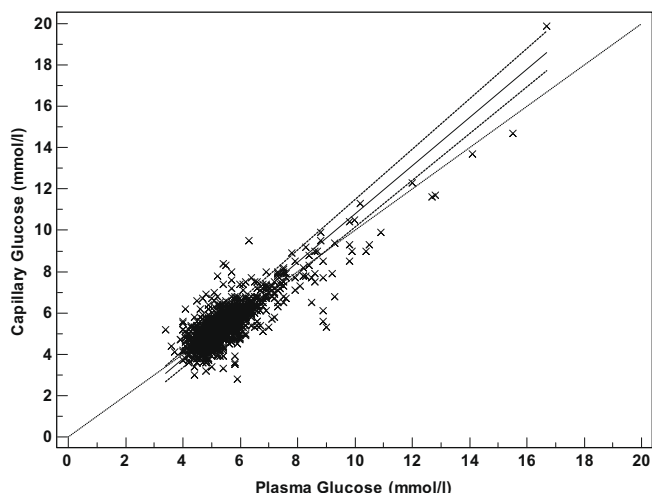


Fig. 2. Passing and Bablok Regression: Capillary blood glucose = $1.167 \times$ Venous plasma laboratory glucose – 0.9 mmol/L.

Table 1a

Accuracy of capillary blood glucose results ≤ 4.1 mmol/L ($n = 70$).

	n	% of results
Accuracy of results for glucose ≤ 4.1 mmol/L		
± 0.3 mmol/L	6	8.6
± 0.6 mmol/L	19	27.1
± 0.8 mmol/L	38	54.3
± 1.1 mmol/L	55	78.6

Table 1b

Accuracy of capillary blood glucose results > 4.1 mmol/L ($n = 1773$).

	n	% of results
Accuracy of results for glucose > 4.1 mmol/L		
Within $\pm 5\%$	865	50.8
Within $\pm 10\%$	1369	80.4
Within $\pm 15\%$	1568	92.1
Within $\pm 20\%$	1638	96.2

Table 2

Comparison of capillary blood glucose and venous plasma laboratory glucose measurements [mean (SE)] by participant characteristic.

Characteristic	Capillary blood glucose		Plasma laboratory glucose	
	n (%)	Mean (SE)	Mean (SE)	
Age	25–44	256 (14)	5.04 (0.05)	5.04 (0.05)
	45–54	459 (26)	5.31 (0.04)	5.29 (0.03)
	55–64	498 (28)	5.46 (0.05)	5.47 (0.04)
	65–74	441 (25)	5.64 (0.06)	5.66 (0.06)
	> 75	117 (7)	5.34 (0.07)	5.52 (0.09)
Gender	Male	799 (45)	5.53 (0.04)	5.52 (0.03)
	Female	974 (55)	5.29 (0.03)	5.33 (0.03)
BMI	< 18	16 (1)	5.19 (0.29)	5.35 (0.34)
	18–24.9	386 (22%)	5.03 (0.06)	5.18 (0.05)
	25–29.9	669 (38)	5.30 (0.03)	5.32 (0.03)
	≥ 30	702 (40)	5.70 (0.04)	5.63 (0.04)
Smoking	Smoker	1622 (92)	5.40 (0.03)	5.42 (0.02)
	Non-smoker	149 (8)	5.38 (0.07)	5.34 (0.06)

* $p < 0.05$.

** $p < 0.01$.

Table 3

Agreement for the classification of patients using the same fasting cut-off values for venous plasma laboratory and capillary blood samples. % of total represented in brackets.

Classification	Capillary blood glucose			Total
	Normoglycaemic	Impaired fasting glucose (5.6–6.9 mmol/L)	Diabetes (≥ 7.0 mmol/L)	
Venous plasma glucose				
Normoglycaemic	1035 (84.5)	185 (15.1)	5 (0.4)	1225 (69.1)
Impaired fasting glucose (5.6–6.9 mmol/L)	119 (25.4)	328 (69.9)	22 (4.7)	469 (26.5)
Diabetes (≥ 7.0 mmol/L)	2 (2.5)	14 (17.7)	63 (79.7)	79 (4.5)
Total	1156 (65.2)	527 (29.7)	90 (5.1)	1773 (100)

Table 4

Utility for screening for diabetes. Criteria for diabetes classification was capillary blood ≥ 6.1 mmol/L, venous plasma ≥ 7.0 mmol/L.

PoCT classification	Capillary (%)	Plasma classification agreement with capillary	% Agreement capillary with plasma
Non-diabetes	1482 (83.6)	1477 (<7.0)	99.7
Diabetes	291 (16.4)	74 (≥ 7.0)	25.4

4. Discussion

Results of this study show that although capillary and plasma glucose measurements correlate well, they fall short of meeting the ISO 15197 guidelines for minimum acceptable accuracy standards. Inaccuracies were predominantly in the low glucose range (≤ 4.1 mmol/L) with almost 50% of results not falling within the recommended ± 0.83 mmol/L of plasma value. This is not surprising, as our study has shown poorer precision of capillary glucose method at lower concentrations.

The differences observed between the mean capillary blood glucose levels and mean plasma laboratory glucose levels for participants aged >75 years might be explained by decreased blood flow from impaired circulation in the finger tip, possibly resulting in a poor capillary blood sample, which affects the accuracy of the reading. A significant difference between the mean values was also observed for participants with a BMI of 18–24.9. There was a marked difference between the mean values for participants with a BMI of <18, however the small sample size for this group meant it was not statistically significant. However, these results are consistent with a paper by Weinstein et al, who noted inaccuracies in a glucose meter for patients with a low BMI [12].

Statistically significant differences were also observed between the mean capillary blood glucose levels and mean plasma laboratory glucose levels for female participants and participants with a BMI > 30. The reasons for these differences are unclear; however, the differences in these means were much smaller than those seen for participants >75 years of age and those with a BMI of 18–24.9.

Current clinical practice generally uses plasma and capillary blood glucoses interchangeably with a risk of clinical misinterpretation. In human blood, glucose, like water, is distributed between erythrocytes and plasma. The amount of glucose per unit of water mass is the same throughout the sample. Because the water concentration in plasma is higher than in capillary blood, the concentration of glucose is also higher in plasma than in erythrocytes.

IFCC Scientific Division Working Group on selective electrodes and point-of-care testing have recommended that a constant factor of 1.11 be used to convert the concentration of capillary blood glucose to plasma glucose to reduce clinical misinterpretations when using point of care devices to measure glucose. The calculated result equals the concentration of glucose in plasma when the haematocrit and water concentrations are normal [8]. In public health screening or in epidemiological surveys, the subject's haematocrit concentration is not known, and it would be more appropriate to use capillary blood specific cut-off points.

From this study, it can be concluded that it is acceptable to use fasting capillary glucose levels to determine the prevalence of diabetes in populations. Although the capillary glucose testing mis-

classified a large number of individual patients, the overall prevalence of diabetes in the population using the capillary glucose cut-off of ≥ 7.0 mmol/L was similar to the prevalence determined by the plasma glucose cut-off of ≥ 7.0 mmol/L. Using the lower WHO-defined cut-off of 6.1 mmol/L for capillary testing resulted, as expected, in a significant rise in the prevalence of diabetes in the population.

Fasting capillary glucose method is not suitable to reliably identify individuals with impaired fasting glucose or diabetes. Nurses performing risk factor surveys using capillary blood glucose results should tell patients with a result <6.1 mmol/L that they probably do not have diabetes (unless displaying clinical symptoms). Patients with results ≥ 6.1 mmol/L should be told that their result was inconclusive and that they should visit their doctor for a repeat fasting and 2 h post-glucose load plasma glucose levels before any diagnosis can be made.

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References

- [1] IDF diabetes atlas, 3rd ed; 2007.
- [2] Zimmet P. Preventing diabetic complications: a primary care perspective. *Diabet Clin Pract* 2009;84:107–16.
- [3] Australian Institute of Health and Welfare. Diabetes: Australian facts 2008. Diabetes series no. 8. Cat. no. CVD 40. Canberra: AIHW; 2008.
- [4] Sandbaek A, Lauritzen T, Borch-Johnsen K, Mai K, Christiansen JS. The comparison of venous plasma glucose and whole blood capillary glucose in diagnoses of type 2 diabetes: a population-based screening study. *Diabet Med* 2005;22:1173–7.
- [5] Kruijshoop M, Feskens EJ, Blaak EE, de Bruin TW. Validation of capillary glucose measurements to detect glucose intolerance or type 2 diabetes mellitus in the general population. *Clin Chim Acta* 2004;341:33–40.
- [6] Higgins T. Use of glucose meters to establish a cutpoint for nonperformance of an oral glucose tolerance test. *Point Care* 2003;2(1):12–3.
- [7] Nichols JH. A critical review of blood glucose testing. *Point Care* 2003;2(1):49–61.
- [8] D'Orazio P, Burnett RW, Fogh-Andersen N, Jacobs E, Kuwa K, Kulpmann WR, et al. Approved IFCC recommendation on reporting results for blood glucose (abbreviated). *Clin Chem* 2005;51:1573–6.
- [9] International Organization for Standardization. In vitro diagnostic test systems – requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus. International standard report number ISO 15197:2003(E). Geneva: International Organization for Standardization; 2003.
- [10] Laatikainen T, Janus E, Kilkkinen A, Heistaro S, Tideman P, Baird A, et al. Chronic disease risk factors in rural Australia: results from the Greater Green Triangle risk factor surveys. *Asia Pac J Publ Health* 2009;21(51):51–62.
- [11] Laatikainen T, Dunbar J, Chapman A, Kilkkinen A, Vartiainen E, Heistaro S, et al. Prevention of type 2 diabetes by lifestyle intervention in an Australian primary health care setting: Greater Green Triangle (GGT) Diabetes Prevention Project. *BMC Publ Health* 2007;7:249.
- [12] Weinstein R, Schwartz S, Brazg R, Bugler JR, Peyser TA, McGarraugh GV. Accuracy of the 5-day freestyle navigator continuous glucose monitoring system: comparison with frequent laboratory reference measurements. *Diabet Care* 2007;30:1125–30.