

## A comparison of five glucometers in South Africa

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### Abstract

**Objective:** To assess the accuracy and precision of five currently available blood glucose meters in South Africa

**Background:** Since the introduction of glucometers, there has been an ongoing, competition-driven development in both meter and strip technology, which has allowed for greater accuracy and reliability of results. Despite the advances in technology, there is significant variation amongst these glucometers necessitating a proper evaluation before use.

**Methods:** Glucose levels in capillary blood samples from 115 patients attending the diabetic clinic at Tygerberg Hospital were measured with each meter, and compared with the laboratory reference method.

**Results:** The coefficients of variation (CVs) (imprecision) of most meters were acceptable at less than 5%, with a bias ranging from 1.7 to 6.8%. None of the glucometers satisfied the American Diabetes Association (ADA) recommendation of less than 5% bias.

**Conclusions:** The study highlights the need for an objective and independent comparison of all glucometers in South Africa, as the variability observed can impact on patient care.

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### Introduction

Diabetes mellitus is a disease reaching epidemic proportions globally. It is predicted that the impact on the developing world will soon outweigh that on the developed world. In the year 2000, the developing world accounted for 72.5% of the world total of diabetes sufferers. This number is projected to double in sub-Saharan Africa by the year 2030.<sup>1</sup> Very few epidemiological studies regarding the prevalence of diabetes have been conducted and reported in South Africa since 1994. One of the landmark studies in 1998 estimated the prevalence of self-reported diabetes in the age group older than 15 years to be 2.4% and 3.7% among males and females respectively. This study also revealed racial and geographic variations in the prevalence of diabetes. In another study, Levitt and co-workers demonstrated an age-standardised prevalence of 10.8% of type 2 diabetes in the age group 30 to 65 years in a coloured community in Mamre, Cape Town.<sup>2</sup> With the rising rates of obesity and metabolic syndrome in the young and with the urbanisation of African communities, it is clear that the number of people with diabetes will increase.

The burden and economical strain of this disease due to associated complications, such as cardiovascular and renal disease, is estimated to increase dramatically and could consume as much as 40% of some countries' health budgets.<sup>3</sup> This increase will probably lead to an increased usage of glucometers in the home care, clinic and emergency care setting. It is also estimated that more models

of glucometers will be introduced into the market in response to this demand.

Self-monitoring of blood glucose (SMBG) allows diabetic patients to achieve and maintain specific glycaemic goals. Since both type 1 and type 2 diabetes show a direct relationship between the degree of glucose control and the risk of systemic complications, many clinical organisations such as the American Diabetes Association (ADA) promote self-monitoring.<sup>4</sup> According to the current position statement of the ADA, SMBG is considered an important component of diabetes in controlling the risk of late renal, retinal and neurological complications. It is therefore recommended that all insulin-treated patients perform SMBG to (a) achieve and maintain glycaemic control, (b) prevent and detect hypoglycaemia, (c) avoid severe hypoglycaemia, and (d) adjust changes in lifestyle. It is also used in establishing the need for insulin therapy in gestational diabetes mellitus.<sup>5</sup>

With the introduction of glucometers, there has been an ongoing, competition-driven development in both meter and strip technology, which has allowed for greater accuracy and reliability of results.<sup>4</sup> However, despite the advances in technology, there is significant variation among these monitoring devices, which has necessitated the development of performance guidelines by organisations such as the ADA and the International Standardization Organization (ISO).<sup>3</sup> The ISO guidelines recommend that the total analytical error of the

glucometers be within  $\pm 0.83$  mmol/l of the laboratory blood glucose concentrations when values are  $< 4.2$  mmol/l. For laboratory values above 4.2 mmol/L, the allowable analytical error for glucometers should be within  $\pm 20\%$ . When comparing the ISO to the ADA guidelines, the ADA recommends an analytical error of  $\leq 5\%$  across all levels. Translating these recommendations using a laboratory value of 5 mmol/L, an acceptable meter reading according to the ISO criteria would be between 4 and 6 mmol/L; however 4.75 to 5.25 mmol/L is deemed acceptable according to ADA.<sup>6</sup>

It is therefore important that a direct and independent comparison be made of glucometers currently available in South Africa. The aim of the study was to provide an independent assessment of the accuracy and reliability of five models of glucose meters available in South Africa, and to establish whether they fall within the recommended performance standards of the ISO and ADA.

## Materials and methods

The following glucometers were evaluated in this study: GlucoPlus™ (Dibcare), OneTouch® Ultra™ (LifeScan Inc, Johnson & Johnson), OneTouch® Horizon™ (Johnson & Johnson), Accu-Chek® Active (Roche) and Accu-Chek® Advantage (Roche). The study was conducted in two phases, the first of which took place in the laboratory and the second at the diabetic clinic of a tertiary hospital in Cape Town, South Africa. Phase one included the determination of precision of the glucometers using the various levels of control solutions. The second phase included a comparison of capillary whole blood glucometer readings to a laboratory reference method in 115 individuals attending the clinic. The testing process was carried out by experienced diabetic clinic nursing staff and a pathology registrar familiar with blood glucose meter requirements. In order to limit operator variability, all glucometer readings were conducted by the same individual. The study was conducted over a six-week period.

Successive drops of blood were applied to each meter, using a single fingerprick site. The meters were rotated in systematic fashion so that no glucometer occupied a fixed position during the application process. A venous plasma sample was collected in a sodium fluoride tube within five minutes of the fingerprick tests. The laboratory measured the plasma glucose on the Siemens™ Advia 1650 analyser, using the glucose oxidase method. The analysis was performed within  $\pm$  one and a half hour of sample collection.

In comparing the performance of each meter to the reference method, a number of analyses were performed. The traditional Clarke error grid analysis<sup>4</sup> was performed to determine the clinical significance of the differences between the meter and reference value. This error grid analysis was developed to classify measurement errors according to their perceived clinical significance. The errors are grouped into different levels or 'zones' in order of assessed importance. The Bland-Altman plots and the regression equations for each meter were included in the statistical analysis. The Bland-Altman plot is a useful tool in method-comparison studies, where the observed deviations (i.e. meter) results can be graphically appreciated in relation to a clinical decision limit. The ISO-allowable analytical error was also depicted in these plots.

It is well known that whole blood glucose concentrations are 10 to 15% lower than that of plasma/serum, but meters can be calibrated to plasma glucose values even when the sample is whole blood.<sup>7</sup>

All glucose meters in our study were plasma-calibrated, except for the Roche glucometers, which were whole blood-calibrated. A factor of 1.1 was used as a conversion factor for the Roche glucometers (Accu-Chek® Active and Advantage) to overcome this difference.

A statistical software package, Analyse-it®, was used for the statistical analysis.

## Results

The coefficients of variation (CV) of the meters were calculated using the manufacturers' control solutions and are shown in Table I. The within-run imprecision ranged from 3.7 to 5.5% for the low control, and 2.2 to 4.4 % for the high control.

**Table I: Coefficient of variation (CV) of glucose meters for the low and high control solutions**

Glucometer	CV % (low control)	CV % (high control)
GlucoPlus™	5.1	2.2
OneTouch® Ultra™	3.7	–
OneTouch® Horizon™	3.9	–
Accu-Chek® Active	5.5	4.4
Accu-Chek® Advantage	5.1	3.2

The accuracy of the meters was determined using the regression equations, error grid analysis and the Bland-Altman Plots. The bias and regression equation of all meters is shown in Table II. Most glucometer readings revealed a negative bias, with mean differences being  $-0.31$  mmol/l for GlucoPlus™,  $-0.65$  mmol/l for OneTouch® Horizon™,  $-0.48$  mmol/l for OneTouch® Ultra™, and  $-0.62$  mmol/l for Accu-Chek® Active. The Accu-Chek® Advantage was the only glucometer having a positive bias with a mean difference of 0.68 mmol/l. The Clarke error grid analysis indicated adequate clinical accuracy of the glucometers with most measurements lying in zones A and B, as seen in Figure 1.

**Table II: Regression equations calculated from paired values obtained from reference method and each glucose meter**

Reference/Glucometer	Glucose concentration (mmol/l). Mean (SD)	% bias	Regression equation
Bayer Advia (Reference)	11.6 (4.9)	–	
GlucoPlus™	11.3 (4.7)	-2.6	$y = 0.91x + 0.69$
OneTouch® Ultra™	11.2 (4.6)	-3.4	$y = 0.88x + 0.94$
OneTouch® Horizon™	10.9 (4.6)	-6.0	$y = 0.88x + 0.69$
Accu-Chek® Active	11.0 (4.4)	-5.2	$y = 0.88x + 0.82$
Accu-Chek® Advantage	12.3 (4.9)	+6.0	$y = 0.96x + 1.1$

The extent to which the glucometers deviated from the reference method is represented in Bland-Altman plots, as shown in Figure 2. In view of the hierarchy, i.e. laboratory glucose higher than the meter glucose, the Bland-Altman plot was constructed using the laboratory glucose as the x axis and the difference between the methods as the y axis. The mean bias of the glucometers ranged from  $-6$  to  $6\%$ , as shown in Table II. The magnitude of the differences seen in the Bland-Altman plots reveals a proportional bias for all glucometers. A proportional bias is an increase in the magnitude of

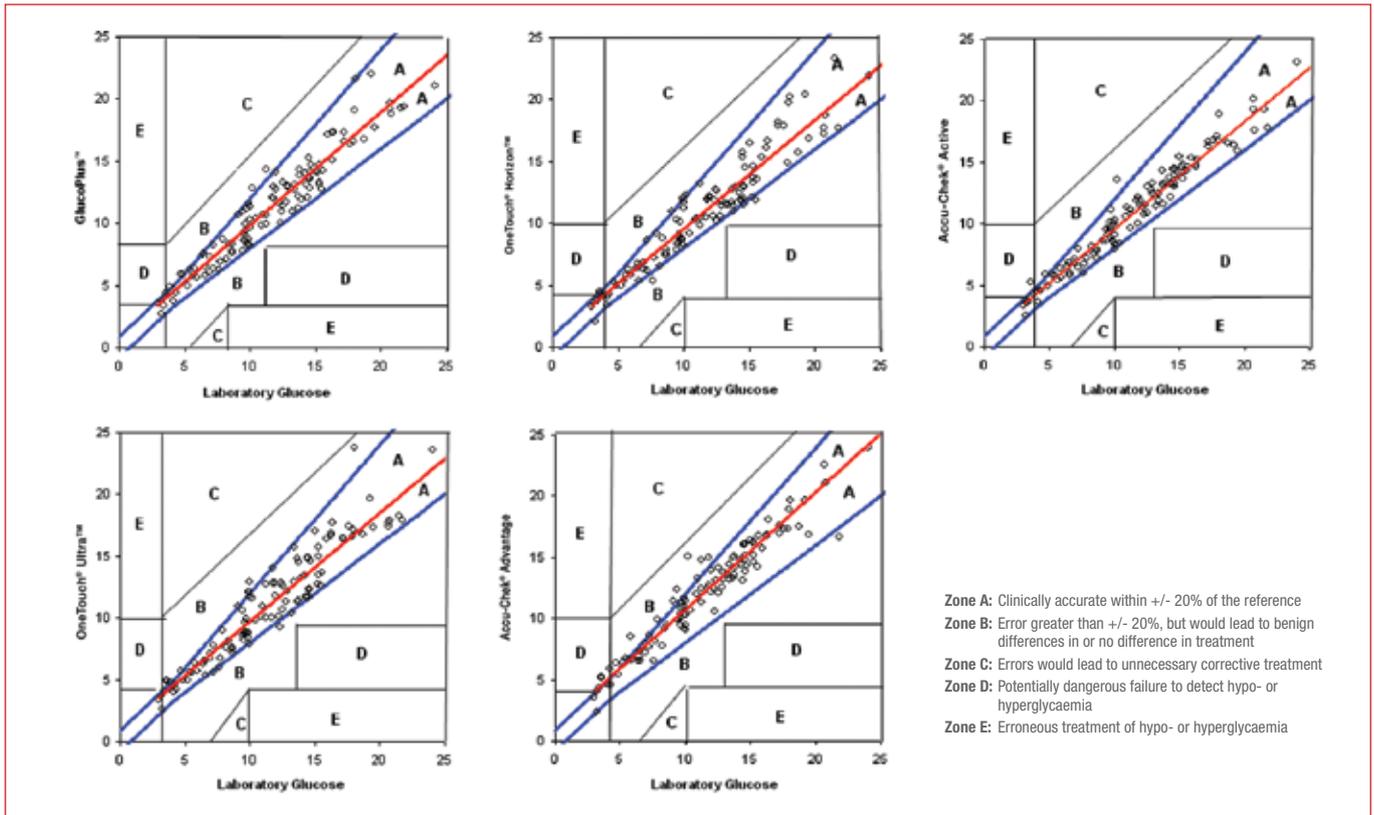


Figure 1: Clarke error grid analysis

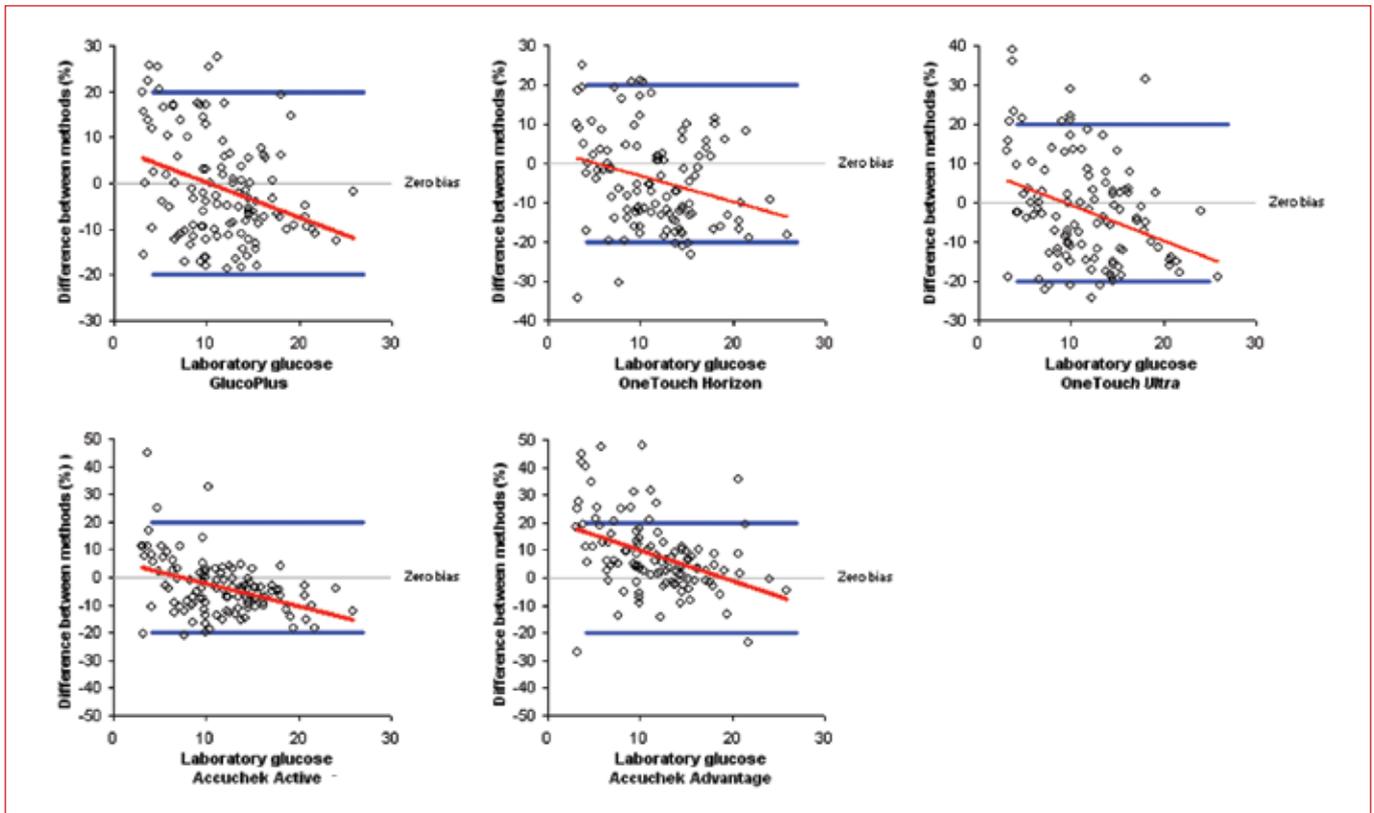


Figure 2: Bland-Altman Plot analysis with glucometer readings compared to plasma glucose assayed on a secondary laboratory instrument. Horizontal lines in blue represent the allowable error according to ISO.

**Table III: Analytical performance of glucometers according to the error tolerance limit as suggested by the American Diabetes Association (ADA) and the International Standardization Organisation (ISO)/NCCLS**

Allowable percentage of measures deviating from the guidelines	(%)	GlucoPlus™ (%)	OneTouch® Ultra™ (%)	OneTouch® Horizon™ (%)	Accu-Chek® Active (%)	Accu-Chek® Advantage (%)
ISO/NCCLS	< 5	4.3	8.7	4.3	2.6	15.7
ADA	0	72.2	73.0	68.7	87.8	64.3

the error as the test result increases. The analytical performance of the meters compared to the guidelines recommended by ISO/NCCLS (National Committee for Clinical Laboratory Standards) and ADA is shown in Table III. It can clearly be seen that only three out of the five glucometers conformed to the ISO guidelines (Gluco-Plus™, OneTouch® Horizon™ and Accu-Check® Active), while none of the glucometers satisfied the guidelines recommended by the ADA.

## Discussion

SMBG with portable instruments became available to persons with diabetes mellitus in the mid-1970s and has been used on a regular basis in developed countries since 1980. These glucometers have traditionally been subjected to less rigorous analytical requirements. Even though the precision and accuracy of most meters have improved over the years, there are still concerns regarding the standardisation of these glucometers and their failure in satisfying the recommendation of less than 5% deviation when compared to a reference method.

In our study a group of glucometers that utilise different analytical techniques (reflectometry or amperometry) were investigated. These meters are also calibrated according to whole blood or plasma. Although all the devices have shown satisfactory precision, with a CV of less than 5.5%, there was substantial discordance when their results were compared to a laboratory reference. Only three out of the five glucometers fulfilled the criteria suggested by the ISO. All meters demonstrated significant deviation from the ADA guidelines, as more than 60% of the measurements exceeded the recommended percentage of deviation.

The variability observed with glucometers can impact on patient care in different settings, some of which include the diabetic patient on insulin in a home care or clinic setting, and emergency care units in tertiary hospitals. Frequent glucose determinations and insulin adjustments are made according to glucometer readings. Inaccuracies can lead to misclassification of hypo- or hyperglycaemic episodes. Although most emergency units and tertiary hospitals have access to laboratory glucose measurements, SMBG plays an important role in clinical intervention and in the monitoring process of diabetic patients. It is therefore imperative that glucometer values are accurate and precise at important medical-decision thresholds. A failure in this regard may lead to critical medical errors.

The Clarke error grid analysis revealed that all glucometers demonstrated adequate clinical accuracy, with most measurements falling in zones A and B. Accu-Chek® Active and Accu-Chek® Advantage recorded one and two measurements in Zone D respectively. It is not known whether this finding is significant, as these two meters are calibrated to whole blood rather than plasma. Although the conversion factor of 1.1 was used, the factor used by the manufacturer remains unknown. Even though all glucometers

demonstrated adequate clinical accuracy using the error grid analysis, it has been suggested that this can be misleading, and that the Bland-Altman plots are favoured in appreciating the deviations at key clinical-decision limits. This was evident in the study, as all glucometers were shown to have a proportional bias.

Although we were unable to include measurements in the hypoglycaemic range, this study highlights the need for an objective and independent comparison of all glucometers available in South Africa. It also allows medical personnel and patients to choose glucometers more objectively, thereby improving the quality of care.

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## Statement of competing interests

The manufacturers of Gluco-Plus™ provided funds for the glucose analysis on the secondary reference method, while other manufacturers supplied the device, strips and control solutions for the study. This study was conducted independently and none of the commercial organisations were involved in the data analysis and interpretation, or in the decision to publish this article.

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