Does cheap equal bad? System accuracy of blood glucose monitoring systems for personal use and the aspect of pricing: discounter versus brand

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Introduction

Directive ISO 15197 is an internationally accepted standard that harmonizes the performance evaluation procedures of, and defines minimum acceptance requirements for Blood Glucose Monitoring Systems (BGMS). Regarding the system's accuracy (i.e. *system accuracy*), in its current revision ISO 15197:2015 [1] stipulates that at least 95% of measurements must not have deviations to the results of a reference greater than 15 mg/dL at glucose concentrations < 100 mg/dL, and 15 % at glucose concentrations ≥ 100 mg/dL, respectively. The directive thus leaves a certain degree of leeway in which *quality* can be defined, assessed and further categorized along a spectrum. Along these lines, we assessed the system accuracy of medium to low price "discounter" BGMS for personal use following amended test procedures specified in ISO 15197:2015, and by using two established comparison measurement methods.

Material, Methods and Procedure

The study was conducted between September and October 2021 at the Institut für Diabetes Karlsburg in compliance with the German Medical Devices Act. The study was reviewed and approved by the responsible human subjects ethical review board under the approval number BB106-21, and registered under the clinicaltrials.gov-ID NCT05031000. Initially, five BGMSs purchased from local pharmacies and/or health centers were evaluated using a single test strip lot each (Table 1). Data and results on three devices, however, were excluded from this article on request of the respective manufacturer. All meters displayed plasma-equivalent blood glucose values in mg/dL.

Table 1 *Blood Glucose Monitoring Systems, Test Strip Enzyme and Lots, and control solutions evaluated.*

BGM		Manufacturer/ Distributor	enzyme	Calibration	LOT	LOT exp	CS	CS exp
1	adia	OSANG Healthcare Co., Ltd., Korea	GDH-FDA	plasma	Z21A215F1	01/23	CLXWA07 CNXWB01 CHXWB15	01/23 01/23 02/23
2	OneTouch select® Plus	LifeScan Europe GmbH, Switzerland	GOx	plasma	4730966	11/22	0AA2M27	07/22

A total of 122 subjects with clinical indication for blood glucose measurements were included to obtain 100 evaluable data sets for each system. All tests with the devices were performed on the same capillary blood samples from these subjects after a study physician reviewed the subject's anamnesis and checked the inclusion and exclusion criteria for study participation. For unaltered samples, measurements were performed directly from the fingertip. For blood glucose concentrations < 80 mg/dL and > 300 mg/dL, the glucose concentration of the sample was adjusted by either glucose supplementation or glycolysis. The hematocrit value was checked for each subject with on an alignment chart with an accuracy of ±1 % to comply with the respective BGM's specifications. Reference method measurements were performed with a glucose oxidase system (YSI 2300 STAT Plus glucose analyzer; YSI Inc.) and a hexokinase (Cobas c111 analyzer; Roche) method in duplicate, prior to and after BGM testing. Compliance with ISO 15197:2015 accuracy criteria was determined by calculating the percentage of results within ±15 mg/dL or ±15 % of the comparison method measurements for glucose concentrations at and above, or below 100 mg/dL, respectively, and by calculating the percentage of results within zones A and B of a consensus error grid. Data were excluded from the analysis in case of a handling error, a technical error, incomplete data set (missing reference value, missing or incompatible hematocrit), oversampling of a glucose range, environmental conditions outside prescribed parameters, and/or a drift of reference measurements greater 4 mg/dL or 4 %, respectively.

Results

The system accuracy of two BGM systems was assessed with samples ranging between 37.4 mg/dL and 528 mg/dL. For both systems 200 measurements were obtained from 100 subjects using one lot each. The results are summarized in Table 2 and Figure 1. The minimum acceptance criteria of ISO 15197:2015 were fulfilled by all systems with the tested lots, and in with both reference measurement methods, showing an average compliance of 95.5–99% of BGM measurement results to reside within ±15 mg/dL or ±15%, respectively.

Table 2 *System accuracy results are calculated within ± 5, ± 10, and ±15 mg/dL and % of the respective reference measurement method at blood glucose concentrations of < 100 mg/dL and ≥ 100 mg/dL, respectively.*

BGMS	Reference method	within limits (±15 mg/dL / ±15%)		blood glucose < 100 mg/dL			blood glucose ≥ 100 mg/dL			Bias
				±5 mg/dL	±10 mg/dL	±15 mg/dL	±5 %	±10 %	±15 %	
		n	%	%	%	%	%	%	%	%
adia	HK	191/200	95.5	65.2	100	100	46.7	70.1	94.2	-2.4
	GOD	198/200	99.0	50	91.7	100	52.6	82.9	98.7	1.4
OneTouch select® Plus	HK	198/200	99.0	60.9	91.3	95.6	59.1	94.8	100	-0.7
	GOD	196/200	98.0	56.2	85.4	95.8	63.2	93.4	98.7	3.2

In glucose concentrations <100 mg/dL, between 95.8% (system 2) and 100% (system 1) of measurements reside within ±15 mg/dL for the GOD reference measurement method, and between 95.6% (system 2) and 100% (system 1) of measurements within ±15 mg/dL for the hexokinase method. In glucose concentrations ≥100 mg/dL, 98.7% of measurements reside within ± 15% for the GOD reference measurement method in both systems. Using the alternative method, system 1 narrowly misses to reach the acceptance criteria at 94.2%, while system 2 excels at 100% of measurements residing within ± 15 % of hexokinase method measurements (Fig.1). The relative bias of the tested BGMS was consistently positive when evaluated against the GOD comparison method (system 1: +1.4%, system 2: +3.2%). Against the hexokinase method, relative bias was consistently negative (system 1: -2.4%, system 2: –0.7%). The difference is mirrored in an average deviation between both reference methods of 3.8 % (±2.1, n= 100, ranging from -1.4% to 8.6%).

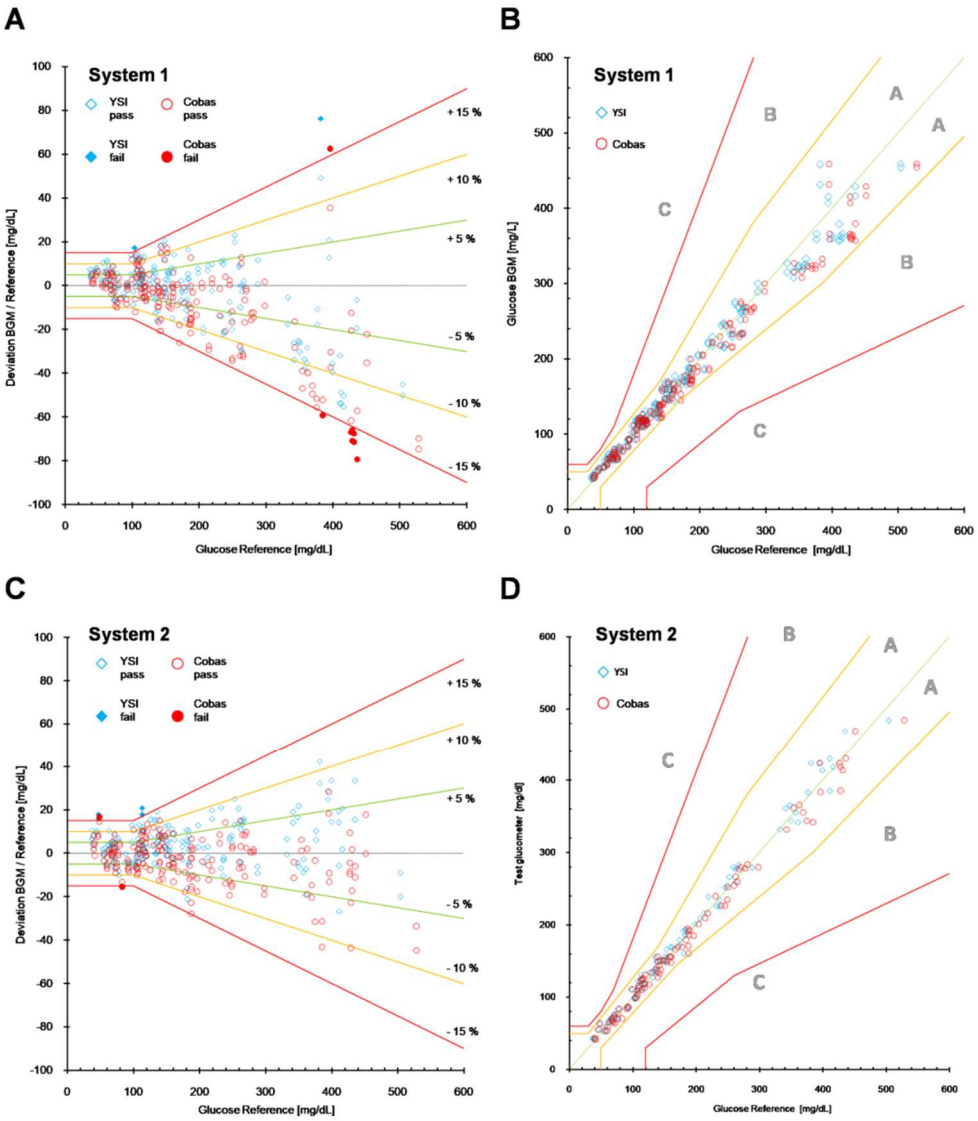

Figure 1 *System accuracy of 2 BGMS. (A) and (C) Bland Altman plots of system 1 and 2 showing the relative deviation of BGM measurements to both reference method GOD (YSI, cyan) and Hexokinase (Cobas, red). Open symbols indicate measurements met minimum acceptance criteria, solid symbols indicate failed measurements. Accuracy levels of ± 5%, ± 10%, and ± 15% indicated by green, yellow, and red line, respectively. (B) and (D) consensus error grids of system 1 and 2 with minimum acceptability zones A and B indicated by yellow and red line, respectively.*

Discussion

The "accuracy" of blood glucose measurements of BGM is estimated by comparison with two validated reference methods. In dependence of the actual deviation of BGM and reference values, system accuracy achieves a relevance with regard to therapeutic decision making, medication and therapy that should not be underestimated. In this study the acceptability requirements were satisfactorily met

with 95.6 % to 100 % of measurements within the specified acceptance limits of ± 15 mg/dL / ± 15 %, based on the respective reference method. However as demonstrated with system 1, the choice of reference method in the performance evaluation is equally important.

Although in the light of the retracted data we refrain from a cost-benefit assessment, it has to be noted that system 1 is one of the most cost-effective systems tested as compared to system 2 being in the more moderate price range. Based on the results it is obvious that it is in no way inferior to system 2, procured for about twice the price as system 1. Although as the saying goes quality has its price, this is not readily transferred to blood glucose monitoring systems without further ado, when in terms of BGM performance quality is translated to accuracy.

References

[1] International Organization for Standardization. *In vitro diagnostic test systems—requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus*. ISO 15197:2015-12.