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Analytical performance of publicly dispensed glucometers in primary health care in a southern Brazilian city

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ABSTRACT

Aims: This study aimed to assess the use of glucometers by patients and the analytical performance of glucometers provided by the primary care services.
Methods: The analytical performance of 48 glucometers Accu-Chek® Active, was assessed through quintuplicate analyses of one Roche and one PNCQ (National Quality Control Program) control sample at different concentrations; 31 were also evaluated by a single proficiency testing sample. The evaluation metrics included imprecision, bias, and total error and were measured according to quality specifications based on biological variation (QSBV). Glucometer users answered a questionnaire regarding their experience.
Results: Among the 48 glucometers evaluated with internal control samples, 17 met precision criteria at both control levels according to QSBV, while 24 met the criteria at only one control level. Of the 31 glucometers further evaluated through proficiency test, 11 met accuracy criteria according to QSBV, and only one device showed an unacceptable result. Out of these 31, only 15 demonstrated a total error within the acceptable maximum limits based on QSBV.
Conclusions: Overall, our findings showed that patients had a good understanding of glucometer usage and suggested that some glucometers should be replaced, as they sometimes failed to meet even the manufacturer's acceptable variation limits, and/or did not meet QSBV.

1. Introduction

Measuring capillary blood glucose is crucial for monitoring diabetes and necessitates that the results be reliable, regardless they were obtained by point-of-care testing or in the laboratory [1]. Self-monitoring of capillary blood glucose (SMBG) allows one to quickly identify hypoglycemia and hyperglycemia, thereby enhancing the safety of prescribers in patient management and, consequently, patient safety. It also motivates patients to make the necessary adjustments to their diet, physical activity, and insulin dosages [2].

Several factors can influence the outcomes yielded by SMBG glucometers. These include the blood sample volume, sample handling, the ageing and storage conditions of the strips, environmental factors such as air humidity and temperature, hand hygiene, altered hematocrit levels, and exogenous interfering substances [3–5]. SMBG can preclude or mitigate risks to patients and reduce the direct burden on the public health infrastructure, provided the quality of the glucometers is continuously monitored and they demonstrate adequate performance. In this context, evaluating a control sample by a qualified health care professional mitigates variations inherent to both the sample and the patient and ensures the proper utilization of the glucometer, reagent strip, and test technique, thereby facilitating an analysis of analytical performance.

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According to the list of medicines and supplies provided by Brazil's Unified Health System (SUS) for users with diabetes mellitus (DM), the government is responsible for supplying reagent strips for measuring capillary blood glucose, contingent upon the availability of glucometers and lancets for digital puncture [6].

Glucometers used for SMBG are classified as self-tests and are not subject to quality monitoring regulations. Consequently, they may produce errors that directly affect both the results and subsequent medical decisions based on these results [3,7]. The accuracy of the glucometers must be rigorously evaluated to ensure optimal performance, and monitors that falsely provide low or high readings can increase the risks of hyperglycemia or hypoglycemia, respectively [8]. American Diabetes Association along with international regulatory authorities established analytical performance limits for glucose concentration measurements and discussed glucose monitoring in non-laboratory settings [9–11].

In 2018, the Brazilian Health Regulatory Agency (ANVISA) proceeded to revoke the registration and halt the sales of 17 glucometers within the country [8] due to not complying with ISO 15197:2013. Given this backdrop, it is essential for glucometers and all laboratory tests utilized for DM monitoring to meet established quality specifications to ensure the reliability of the results, which, in turn, guide the treatment of the disease.

The guidelines regarding internal and external quality control, intended for health care facilities [4,12], should be adapted for glucometers used in SMBG and implemented by primary health care professionals to ensure reliable glucose readings, which are critical for diabetic patient management and safety. However, the required materials (control samples) must either be listed in the SUS materials catalog or specified in contracts with suppliers. This would facilitate identifying poorly performing glucometers, thereby reducing health care costs related to complications from inadequate glycemic control.

In this context, control samples are instrumental in assessing equipment quality, and these samples may either accompany the glucometers or be purchased separately. For effective evaluation, the control sample should be run through the device under several conditions: immediately upon opening a new batch and shipment of test strips, if the strip vial has been open for an extended period or exposed to extreme temperatures, if the glucometer has been dropped, or when the test result is inconsistent with the patient's symptoms. Recording and statistically analyzing the results of these control samples allows for assessing the glucometer's imprecision, bias, and total error [4,7,10].

Clinically speaking, the imprecision of glucometers, as indicated here by the coefficient of variation, can impact the interpretation of sequential capillary blood glucose results, thus affecting diabetes monitoring. A glucometer with a high coefficient of variation may yield results that show abrupt fluctuations in a patient's capillary blood glucose levels. These fluctuations could merely reflect the analytical variation of the equipment and not signify a lack of adherence to treatment or treatment ineffectiveness. Consequently, no clinical action may be needed based on these previous results. Such poor performance could lead the patient to distrust the glucometer's readings. Conversely, the inaccuracy of glucometers that exhibit high bias can also affect the interpretation of patients' capillary blood glucose levels, producing results that deviate from the actual value.

Finally, employing a precise and inaccurate glucometer can still facilitate monitoring a patient's blood glucose levels when correlated with clinical data, as any fluctuation between the results is genuine, even if the output diverges from the actual value. Conversely, using an imprecise yet accurate glucometer hampers the sequential monitoring of capillary blood glucose levels. Although the average result may approximate the actual value, this situation is concerning for decision-making related to disease management.

Given the above, this study sought to assess the use of the device by patients and the analytical performance of glucometers provided by the primary care network in a municipality in Santa Catarina State (southern Brazil).

2. Material and methods

2.1. Subjects

This study was approved by the Institution's Human Research Ethics Committee (CAAE no. 46881021.6.0000.0121). The research was carried out between May 2021 and July 2022 in the municipality of Tijucas (Santa Catarina State, southern Brazil), which has an estimated population of 39,155 people and is served by 12 Basic Health Units (BHU) [13]. The municipality has 377 registered glucometer users (Accu-Chek® Active, Roche Diagnostics, USA), provided free of charge by the Municipal Health Department to residents with insulin-dependent DM (Tijucas, 2021, unpublished data). Glucometers/patients were selected based on the researchers' geographical location for convenience. The study included individuals over 18 years of age, who independently operate glucometers, after telephone contact and participation agreement.

2.2. Questionnaire

In addition to providing sociodemographic data, participants answered questions about the use of the devices, how long have they been using glucometers, how long have they been using their current glucometer, whether they have already changed the device (how many times), where they usually dispose of the needles, how many tests they perform per day, and what they usually proceed in cases of blood glucose results above or below reference limits.

2.3. Materials

Participants permitted the analytical performance evaluation of their glucometers. For evaluating the glucometers' analytical precision, control samples known as internal quality control (IQC) were donated by the National Quality Control Program – PNCQ (Rio

de Janeiro, Brazil) in three concentration levels, and by Roche Diagnostics (São Paulo, Brazil) at two levels. Specifications of the IQC samples are listed in Table 1.

A control sample to assess the accuracy (external quality control) was also donated by PNCQ – External Proficiency (PRO-EX). Both the PNCQ and Roche control samples are ready for use; however, the former has a human protein matrix, while the latter is aqueous.

2.4. Statistical analysis

In addition to analyzing the IQC results using the manufacturers' acceptable limits, for each IQC sample, outlier results were also investigated among the glucometers using the Shapiro Wilk test.

Glucometer precision was determined by analyzing two control samples, five times on the same day, in each device. For each glucometer, one internal control sample from PNCQ and one from ROCHE, with different levels, were randomly selected. Precision was defined based on the standard deviation (SD) and mean (M) of these measurements, calculated as coefficient of variation (CV). $CV = (SD/M) \times 100$.

For convenience of location proximity and due to limitation of control sample volume, some glucometers/patients located closest to each other were further selected for accuracy analysis. Glucometer accuracy was assessed at a different moment by comparing the individual results from each glucometer to the average of all devices, excluding outliers. The percentage difference was considered as the glucometer's bias (inaccuracy).

$$\text{Bias} = (\text{result} - \text{average})\text{x}100/\text{Average}$$

Where "result" means the individual glucometer result and "average" means de mean of glucometers assessed through external quality control.

After the proficiency testing, glucometers were rated based on the results from the control samples. A "good" rating indicated results within the mean ± 1 SD, an "acceptable" rating denoted results within the mean ± 2 SD, and an "unacceptable" rating was given for results falling outside these limits [14].

The total analytical error (TAE) was computed using the formula

$$TAE = K \times CV + |\text{bias}|$$

Where K is 1.65 for 90 % confidence [15,16].

The analytical performance of the glucometers was evaluated based on whether the precision, bias, and total error met the quality specifications grounded in biological variation. These specifications consider both intra- and inter-individual biological variations in venous glycemia, as no studies indicate variations in capillary glycemia [17]. The limits of these specifications are described by the European Federation of Laboratory Medicine (EFLM, 2023) and are classified into optimal, desirable or minimum results (Table 2).

Glucometers failing to meet the minimum specifications were considered unacceptable analytical quality [15,18].

Statistics analysis were performed using GraphPad Prism Software, version 8.0.0 for Windows, San Diego, California USA).

The qualitative data from the participants' answers and from the results of the glucometer analysis were presented in percentages and descriptively. Quantitative results with normal distribution were presented as median and maximum and minimum values.

3. Results

The study was conducted using glucometers from patients associated with two of the city's 12 BHUs, representing 146 glucometer users or 39 % of the total user population. Out of these, five (3 %) were excluded due to patient age, 25 (17 %) due to geographical distance from their residence, 12 (8 %) due to a change in address and/or lack of contact information at the BHU, nine (6 %) due to unlocatable addresses, 20 (14 %) due to patient was not at home at the time of the visit, and 27 (18 %) due to unsuccessful telephone contact. Ultimately, 48 users (33 %) consented to participate, resulting in a research margin of error of 10 %.

Thirty users (30/48) were female and 18 (18/48) were male. The age of users ranged from 18 to 94, with a median age of 57.5 years. Reported daily testing frequency ranged from 1 to 6 times, with a median frequency of 3 tests per day.

The median duration of overall glucometer use among participants was 71.5 months, roughly equivalent to 6 years, and ranged from 1 to 240 months. In contrast, the duration of use for the specific glucometers evaluated in this study ranged from 1 to 120 months, with a median of 24 months or 2 years. The number of times glucometers were replaced due to malfunction or breakage varied from 0 to 4 times, with a median of one replacement.

When queried about their course of action if a blood glucose reading fell below 2.3 mmol/L, the majority (42/48) stated they would

Table 1
Information on the control samples used in the study.

Manufacturer	Level	Batch	Average (mmol/L)	Acceptable Limit (mmol/L)
PNCQ	1	TLR02802021	3.3	2.6–4.0
	2	TLR02822021	17.3	8.3–20.7
	3	TLR02812021	9.1	9.0–10.9
	1	12000236	3.1	7.6–10.9
ROCHE	2	22000237	8.9	23–3.9

Table 2
Analytical Performance Specification based on Biological Variation.

Specification of Quality	Precision (CV %)	Accuracy (Bias %)	Total Analytical Error (%)
Minimum	3.8	3.6	9.8
Desirable	2.5	2.4	6.5
Optimal	1.3	1.2	3.3

Source: EFLM, 2023.

consume sugary foods such as candy or chocolate. Four (4/48) indicated they would do nothing, and two (2/48) said they would retest their blood glucose levels for confirmation. Conversely, when faced with a blood glucose reading exceeding 7.3 mmol/L, 42 participants (42/48) stated they would administer insulin, four (4/48) would take no action, and two (2/48) would seek medical assistance.

Most users (29/48) reported disposing of used lancets in a plastic container and taking them to the BHU for proper disposal. The remaining 19 (19/48) indicated that they discard lancets in their household trash.

Out of the 48 glucometers, 16 were analyzed with PNCQ level 1 and Roche level 2, 16 with PNCQ level 2, 16 with PNCQ level 3, 32 with Roche level 1, and only 31 with PRO-EX (Fig. 1).

Each glucometer underwent 11 evaluations: five with a high-level IQC sample from one manufacturer, five with a low-level IQC sample from another manufacturer, and one with an external quality control sample.

Among the 16 glucometers analyzed (80 results) with PNCQ level 1, three units (G7, G8, and G16) produced seven outlier results. However, only two (G8 and G16) showed results outside the manufacturer's acceptable limits (Table 3). The intra-assay analytical coefficient of variation ranged from 1.5 % (G3) to 30.4 % (G16). Based on biological variation, three glucometers demonstrated desirable performance (G3, G11, and G12), five showed minimum performance (G1, G2, G4, G7, and G9), and eight were found to have unacceptable performance in terms of result repeatability (G5, G6, G8, G10, and G13–G16) (Table 3).

Glucometers analyzed with PNCQ levels 2 and 3 did not display outlier results. On the other hand, two glucometer (G18 and G26) showed results outside the manufacturer's acceptable limits for PNCQ level 2 (Table 3). The intra-assay analytical coefficient of variation for the 16 glucometers tested with PNCQ level 2 ranged from 0.7 % (G27) to 4.5 % (G17). Based on biological variation, eleven glucometers exhibited optimal performance (G22–G32), one showed desirable performance (G20), three displayed minimum performance (G18, G19, and G21), and one had unacceptable performance (G17) (Table 3).

For the 16 glucometers analyzed with PNCQ level 3, the intra-assay analytical coefficient of variation ranged from 1.0 % (G39) to 4.8 % (G36 and G37). Based on biological variation two glucometers showed excellent performance (G39 and G40), seven displayed desirable performance (G41–G45, G47, and G48), five had minimum performance (G33–G35, G38, and G46), and two exhibited unacceptable performance (G36 and G37) (Table 3).

Two outlier results were identified among the 32 glucometers tested (160 results) with Roche level 1, each one from different devices (G17, G31) (Table 3). The intra-assay analytical coefficient of variation spanned from 2.5 % (G38) to 16.1 % (G17). One glucometer displayed desirable performance (G38), nine had minimum performance (G20, G21, G23–G26, G28, G31, and G46), and 22 showed unacceptable performance (G17–G19, G22, G27, G29, G30, G32–G37, G39–G45, G47, and G48) (Table 3).

Of the 16 glucometers tested with Roche level 2, three outlier results were found, all from the same device (G16) (Table 3). The intra-assay analytical coefficient of variation ranged from 0.9 % (G9) to 5.8 % (G13). Based on biological variation specifications, one glucometer showed optimal performance (G9), two displayed desirable performance (G3 and G7), seven had minimum performance (G2, G4, G5, G10–G12, and G14), and six exhibited unacceptable performance (G1, G6, G8, G13, G15, and G16) (Table 3).

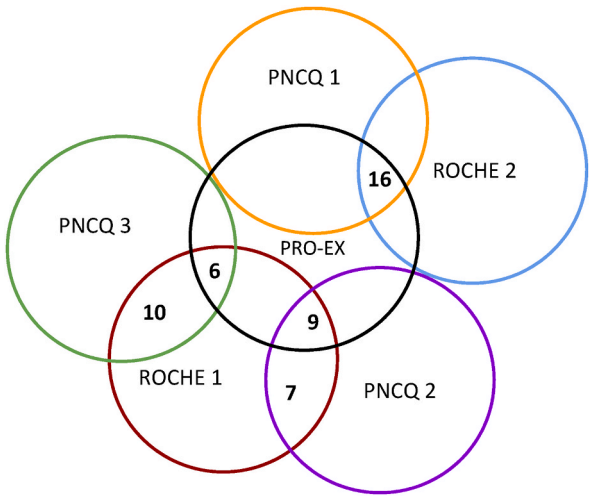

Fig. 1. Number of control samples, by levels, analyzed in the 48 glucometers.

Table 3
Glucose results from different control samples on 48 glucometers provided by Brazilian primary health care.

Glucometer	Glucometer's Mean Result (mmol/L)	Outlier Result[a]	CV	CV classification based on Biological Variation[b]	Glucometer's Mean Result (mmol/L)	Outlier Result[a]	CV	CV classification based on Biological Variation[b]
	Manufacturer Limit for PNCQ 1 (2.6–4.0 mmol/L)				Manufacturer Limit for ROCHE 2 (7.6–10.9 mmol/L)			
1	3.5		3.2	Minimum	9.2		4.5	Unacceptable
2	3.2		4.0	Minimum	8.6		2.8	Minimum
3	3.3		1.5	Desirable	8.9		1.8	Desirable
4	3.1		3.5	Minimum	8.8		3.7	Minimum
5	2.9		5.0	Unacceptable	8.7		3.4	Minimum
6	3.2		5.2	Unacceptable	8.3		4.1	Unacceptable
7	3.7	3.8, 3.9	3.6	Minimum	9.2		2.2	Desirable
8	2.8	2.5	7.8	Unacceptable	8.1		5.1	Unacceptable
9	3.2		3.1	Minimum	8.8		0.9	Optimal
10	3.2		7.1	Unacceptable	8.9		3.0	Minimum
11	3.4		2.5	Desirable	9.1		3.8	Minimum
12	3.2		2.0	Desirable	8.7		3.8	Minimum
13	3.0		5.6	Unacceptable	8.4		5.8	Unacceptable
14	3.0		5.2	Unacceptable	8.9		3.5	Minimum
15	3.0		5.7	Unacceptable	8.8		4.2	Unacceptable
16	1.9	1.5, 1.6, 1.8	30.4	Unacceptable	7.3	6.9, 7.3, 7.3	5.7	Unacceptable
	Manufacturer Limit for PNCQ 2 (8.3–20.7 mmol/L)				Manufacturer Limit for ROCHE 1 (2.3–3.9 mmol/L)			
17	15.5		4.5	Unacceptable	2.1	1.8	16.1	Unacceptable
18	13.5		3.3	Minimum	2.6		12.8	Unacceptable
19	15.9		3.2	Minimum	2.8		6.1	Unacceptable
20	15.2		2.5	Desirable	2.8		3.8	Minimum
21	14.8		2.9	Minimum	2.8		3.2	Minimum
22	14.9		1.1	Optimal	2.8		4.7	Unacceptable
23	16.4		0.8	Optimal	3.5		2.8	Minimum
24	14.2		1.2	Optimal	2.2		2.9	Minimum
25	14.8		0.7	Optimal	2.3		3.2	Minimum
26	13.8		0.9	Optimal	3.4		3.8	Minimum
27	14.7		0.7	Optimal	2.8		5.4	Unacceptable
28	16.3		1.0	Optimal	3.4		3.6	Minimum
29	16.0		1.3	Optimal	2.9		6.0	Unacceptable
30	16.0		1.3	Optimal	2.1		8.6	Unacceptable
31	14.1		1.0	Optimal	3.9	4.0	3.8	Minimum
32	15.3		0.8	Optimal	2.9		5.9	Unacceptable
	Manufacturer Limit for PNCQ 3 (9.0–10.9 mmol/L)							
33	9.0		3.8	Minimum	2.9		4.7	Unacceptable
34	9.1		2.8	Minimum	3.0		7.0	Unacceptable
35	9.1		3.8	Minimum	2.9		5.7	Unacceptable
36	8.9		4.8	Unacceptable	3.0		7.8	Unacceptable
37	8.7		4.8	Unacceptable	3.0		6.1	Unacceptable
38	9.0		3.3	Minimum	3.2		2.5	Desirable
39	7.9		1.0	Optimal	2.8		5.9	Unacceptable
40	8.6		1.2	Optimal	2.8		7.5	Unacceptable
41	9.6		2.3	Desirable	3.6		5.0	Unacceptable
42	9.3		1.7	Desirable	3.0		5.2	Unacceptable
43	10.4		2.3	Desirable	2.7		6.0	Unacceptable
44	10.3		2.0	Desirable	3.2		6.4	Unacceptable
45	10.3		2.1	Desirable	2.8		7.3	Unacceptable
46	10.4		2.9	Minimum	3.6		3.2	Minimum
47	8.2		2.3	Desirable	3.4		4.5	Unacceptable
48	9.2		2.1	Desirable	2.8		4.8	Unacceptable

Note: PNCQ: National Quality Control Program. Glucometer's mean results are as average of 5 analyses (replicates) of each control sample.
[a] Shapiro Wilk test carried out with all the results of the control sample in the different glucometers.
[b] Classification Based on Biological Variation: Unacceptable >3.8 %, Minimum ≤3.8 %, Desirable <2.5 %, Optimal <1.3 %.

The median intra-assay coefficient of variation for the PNCQ control samples was 4.5, 1.1, and 2.3 % for levels 1–3, respectively. For Roche control samples, the median intra-assay coefficient of variation was 3.7 and 5.3 % for levels 1 and 2, respectively.

Of the 31 glucometers analyzed using the PNCQ PRO-EX control, one outlier result was identified (G18). Among the 31 glucometers

evaluated with PNCQ PRO-EX, the Bias of 21 devices received a "Good" rating, seven received an "Acceptable" rating, and three received an "Unacceptable" rating according to PRO-EX (Table 4).

As depicted in Table 4, the total analytical error for the 31 glucometers analyzed with PNCQ's PRO-EX was classified based on biological variation as having desirable performance for two devices (G11 and G23), minimum performance for 13 devices (G1–G4, G9, G12, G14, G19–G21, G24, G25, and G36), and unacceptable performance for 16 devices (G5 to G8, G10, G13, G15 to G18, G22, G33 to G35, G37, and G38).

4. Discussion

In the United States, by the end of 1992, over 3200 glucometer-related incidents were reported to the Food and Drug Administration, culminating in sixteen fatalities [4]. Hence, in addition to distributing glucometers to the populace, it is equally vital to assess the analytical quality of these instruments. In the municipality where the study was conducted, glucometers are procured through a leasing system, following a competitive bidding process, and distributed to users. The glucometers are only replaced if the patient identifies a malfunction. According to the manufacturer, battery issues are the most frequently reported problem, corroborated by the users in the municipality where this study was conducted. Here, individuals are responsible for purchasing and replacing the batteries. If the issue persists, the glucometer is substituted. Consequently, the average duration of glucometer usage in the study (24 months) likely reflects a change in the supplier to the municipality rather than device failure.

As for the demographic data, the higher percentage of female participants (56 %) does not accurately mirror the population of 146 patients. This discrepancy may be attributed to a greater willingness among females to participate in research studies; notably, a study conducted in another region of Brazil reported a similar proportion (67 %) of female diabetic patients [19].

The recommended frequency for SMBG is, on average, three to four times a day [6]. These tests should include one before meals (preprandial), one 2 h after meals (postprandial), and one at bedtime. Nighttime testing is crucial for averting nocturnal hypoglycemia. For those utilizing insulin, oral hypoglycemic agents, and engaging in physical activity, SMBG before, during, and particularly hours after exercise can assist in gauging the body's response to physical exertion [6]. Such data can inform adjustments in dosage or carbohydrate intake to prevent significant glycemic fluctuations, especially hypoglycemia [6]. Most patients in this study adhere to

Table 4
Bias and total analytical error performance of 31 glucometers provided by Brazilian primary health care.

Glucometer	Bias (%)	Bias Classification According to PRO-EX[a]	Bias Classification According to Biological Variation[b]	Total Error (%)	Total error Classification According to Biological Variation[c]
1	2.5	Good	Minimum	7.8	Minimum
2	−0.6	Good	Optimal	7.2	Minimum
3	−6.6	Good	Unacceptable	9.1	Minimum
4	1.5	Good	Desirable	7.3	Minimum
5	5.5	Good	Unacceptable	13.9	Unacceptable
6	6.6	Good	Unacceptable	15.1	Unacceptable
7	−5.6	Good	Unacceptable	12.1	Unacceptable
8	0.5	Good	Optimal	13.3	Unacceptable
9	−1.6	Good	Desirable	6.7	Minimum
10	−3.7	Good	Unacceptable	15.4	Unacceptable
11	−1.58	Good	Desirable	5.7	Desirable
12	4.5	Good	Unacceptable	7.8	Minimum
13	13.7	Acceptable	Unacceptable	22.9	Unacceptable
14	0.5	Good	Optimal	9.1	Minimum
15	6.6	Good	Unacceptable	16.0	Unacceptable
16	13.7	Acceptable	Unacceptable	63.7	Unacceptable
17	19.8	Unacceptable	Unacceptable	27.2	Unacceptable
18	26.9[d]	Unacceptable	Unacceptable	32.3	Unacceptable
19	−3.6	Good	Unacceptable	8.8	Minimum
20	−2.6	Good	Minimum	7.0	Minimum
21	2.5	Good	Minimum	7.3	Minimum
22	10.6	Acceptable	Unacceptable	12.4	Unacceptable
23	3.5	Good	Unacceptable	4.8	Desirable
24	−4.6	Good	Unacceptable	6.6	Minimum
25	7.6	Acceptable	Unacceptable	8.8	Minimum
33	−12.8	Acceptable	Unacceptable	19.0	Unacceptable
34	−8.7	Acceptable	Unacceptable	13.4	Unacceptable
35	−15.8	Unacceptable	Unacceptable	22.0	Unacceptable
36	−1.6	Good	Desirable	9.5	Minimum
37	−2.6	Good	Minimum	10.5	Unacceptable
38	−7.7	Acceptable	Unacceptable	13.1	Unacceptable

[a] PRO-EX Classification: Unacceptable >14 %, Acceptable ≤14 %, Good ≤7 %.
[b] Bias Classification Based on Biological Variation: Unacceptable >3.6 %, Minimum ≤3.6 %, Desirable ≤2.4 %, Optimal ≤1.2 %.
[c] Total Error Classification Based on Biological Variation: Unacceptable >9.8 %, Minimum ≤9.8 %, Desirable ≤6.5 %, Optimal ≤3.3 %.
[d] Outlier result.

these guidelines, and a few reported conducting only one or two daily tests but asserted that their condition is well-managed.

Most patients seem to know about the disease and can recognize results indicative of hypoglycemia or hyperglycemia, or at least suspect such results and opt to retake the test. However, a subset of patients (4/48) seem to lack adequate understanding and management of their condition, stating that they would not take any action in the presence of results suggesting hypoglycemia or hyperglycemia. This is a concerning situation, especially in the case of hypoglycemia, which can lead to accidents, injuries, coma, and even death [20], highlighting the need for health education. Notably, these specific users have only recently started using the glucometer, suggesting a limited understanding of the disease.

Another aspect underscoring the need for patient education on the use of glucometers concerns the disposal of lancets. According to ANVISA [21], lancets are categorized as Group E-waste — sharp materials — and must be discarded in identified, puncture-resistant containers and equipped with a lid. According to the manufacturer's guidelines, these containers should be replaced as needed or when filled to three-quarters of their capacity; manually emptying and reusing these containers are prohibited [21]. Given that these specialized disposal containers are generally only available in health care settings, patients must receive proper guidance on safe waste disposal methods during insulin therapy and glucose monitoring from primary health care professionals [22]. Evidence has shown that only half of the patients received such guidance, typically from nurses, and that age, sex, and duration of diagnosis did not influence waste disposal practices [19]. Similar findings were observed in this study, where roughly 40 % of users are not disposing of lancets correctly. PET bottles should not be used for this purpose due to their fragility [19]; as an alternative, empty and more durable bottles of cleaning products can be used, thereby reducing risks for both those who transport and those who handle the material in health care settings.

Manufacturers of *in vitro* diagnostic equipment often suggest using control samples of their own brand. Some experts, nevertheless, advocate for using third-party control samples [23], implying a potential conflict of interest or bias in evaluating equipment performance. ISO 15189:2015 notes that " [the use of] third-party control materials should be considered, instead of, or in addition to, any control materials provided by the reagent or instrument manufacturer" [24]. These third-party controls are not optimized for specific reagents or test systems, thus offering an unbiased performance evaluation for any instrument/method. Interestingly, in this study, third-party controls (i.e., PNCQ) showed less variation than those from the manufacturer (i.e., Roche), despite having a more complex protein matrix.

Concerning the concentration levels of control samples, it is generally recommended to have two to three levels to monitor analytical performance across the full possible range of results. These should include the most critical concentrations for the clinical interpretation of a test [25], corroborating the experimental design of this study.

Furthermore, there are various methods for evaluating the variability of an analytical technique, including repeatability (intra-assay variation) or reproducibility (inter-assay variation) [16]. In this study, results were acquired by the same operator through repeated measurements on the same day, constituting a repeatability assessment.

In one study, researchers evaluated a different manufacturer of glucometers (InfopiaElement®) and observed a higher coefficient of variation in IQC (5.1 %) when analyzing samples with low glucose concentration (2.4 mmol/L) compared to those with high concentration (14.4 mmol/L), which had a variation of 2.6 % [26]. The glucometers used in this study followed the same logic concerning PNQC levels, although an inversion was observed with Roche levels.

Compared to our findings, one study analyzing a glucometer of the same manufacturer but a different model reported greater imprecision with a CV of 4.6 and 4.9 % for samples with low and high glucose concentrations, respectively. Conversely, a glucometer from another manufacturer (Nova StatStrip) exhibited a CV of 2.3 and 2.0 %, respectively [27]. Additionally, another study evaluating a glucometer of the same manufacturer and model as in this study found a CV of 15–17 % [28]. The higher coefficients of variation observed elsewhere may be attributable to the evaluation of reproducibility, whereas this study assessed repeatability.

In a historical analysis of nine rounds of PRO-EX proficiency testing (PNCQ, 2021, unpublished data), the Accu-Chek Active® glucometer was the most frequently represented among participants. PRO-EX proficiency test reports highlight significant variances in results across different models of the same manufacturer and between manufacturers. More specifically, one round in 2021, which evaluated nine models of glucometers from five different manufacturers, reported that the Accu-Chek® Active device was the most frequently assessed instrument, displaying the lowest CV among participants at 6.2 % for an average of 5.9 mmol/L (PNCQ, 2021, unpublished data). This CV is similar to what was observed with the results of the PRO-EX sample in the current study (7.1 %) for a sample with an average concentration of 5.4 mmol/L. Conversely, in the same round, a glucometer of the same manufacturer but a different model (Accu-Chek® Guide) showed an average result of 13.6 mmol/L and a CV of 8.5 % for the same control sample (PNCQ, 2021, unpublished data). These outcomes suggest that it is not feasible to compare results obtained by different glucometers, and thus, patients should consistently be monitored using the same device model.

Of the 48 glucometers evaluated with IQC samples, 17 displayed precision at both control levels (low and high) in line with quality specifications based on biological variation. However, 23 glucometers demonstrated precision at only one of the levels, and the remaining eight exhibited imprecision at both control levels.

Of the 31 glucometers assessed with PRO-EX, just 11 devices met the accuracy standards according to quality specifications based on biological variation, although only three showed an unacceptable result in the proficiency test. Of the 31 glucometers evaluated with PRO-EX, only 15 devices demonstrated a maximum total error that complies with the stringent quality specifications based on biological variation.

In summary, the findings suggest that some glucometers should be replaced. For example, G16 ICQ results failed to meet even the manufacturer's acceptable variation limits, presented outliers results and unacceptable performance according to biological variation for the two control sample levels assessed. Others, even with a small CV (desirable performance) sometimes fail to meet even the manufacturer's acceptable variation (limits) in results (for example, G47 for PNCQ 3 sample). Furthermore, although accuracy was

assessed in only one round of EQC, some glucometers did not meet the manufacturer's specifications and those based on biological variation (G17, G18, and G35).

Additionally, the analysis of these control samples should be integrated into the care provided to diabetic patients using a glucometer in primary health care settings. This would facilitate the assessment of the quality of patients' glucometers. Considering that patients are scheduled to return to monitor their diabetes, we suggest that at this time the patient should be retrained and the precision and accuracy of the glucometers should be monitored by health professional that deliver the reagent strips, lancets and insulin.

Our study has some limitations such as the control sample's commutability, the smaller number of glucometers evaluated by proficiency test, the compliance with other quality specifications could have been analyzed, the number of glucometers/patients evaluated and the fact that we did not deeply question the patients regarding the training received to use the glucometer. However, our findings can be useful for selecting and acquiring glucometers, in addition to demonstrating the importance of monitoring the quality of these devices, and the study should be extended to other municipalities.

5. Conclusion

Overall, the surveyed glucometer users exhibited a good understanding of how to use these devices, albeit a handful of opportunities for health education were identified. Fewer than half of the glucometers evaluated demonstrated reproducibility and accuracy within the quality specifications based on biological variation. Lastly, our findings could be instrumental in selecting and procuring glucometers and underscore the necessity for new public policies to be introduced to ensure the quality of devices supplied in primary health care settings, along with ongoing monitoring of their analytical performance.

Conflict of interest and funding statement

The authors had no personal or academic conflicts of interest separately. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. No funding was secured for this study.

CRediT authorship contribution statement

Isabelle L. Silva: Writing – original draft, Investigation, Formal analysis, Data curation. **Flávia Martinello:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

None.

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Data availability

Data will be made available on request.

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