

Are blood glucose meters for home use acceptable for making appropriate diabetes management decisions?



Joan Lee Parkes*¹



Bern Harrison¹



Scott Pardo¹

Self-monitoring of blood glucose (SMBG) provides significant benefits to both people with diabetes (PWD) and their healthcare providers in a number of ways. SMBG allows for detection of hyperglycemia and hypoglycemia, as well as gathering necessary information to adjust diabetes therapy to improve glycemic control [1].

Whether or not insulin therapy is used, SMBG has been shown to help PWD to better understand their disease, thus improving their self-care [2–7]. Moreover, the act of a PWD engaging in SMBG can be a motivator toward healthier behaviors [1,8,9].

In addition to assisting PWD and/or their healthcare providers to determine appropriate therapeutic changes (e.g., insulin dosing), blood glucose meter (BGM) results are also used to calibrate continuous glucose monitoring (CGM) devices. Much of the accuracy of a CGM device relies on the accuracy of the BGM that is used to calibrate it. Therefore, the accuracy of the BGM is of utmost importance.

Since BGM results have the potential to affect patient outcomes, it is important for devices used for SMBG to have acceptable performance, that is, to be accurate and precise [10].

Furthermore, while the analytical performance of a BGM under ideal conditions (i.e., in the hands of professionals in a laboratory setting) is important, a BGM system can be used most successfully to manage a person's diabetes if it is easy to learn, easy to use, easy to maintain, reliable and affordable, as well as accurate in the hands of lay users (i.e., PWD).

How do we determine accuracy?

Accuracy of a BGM is a measure of the closeness of the blood glucose (BG) value read on the meter compared with the average BG result of an acceptable laboratory BG instrument. It is also important that a BGM is precise, not just accurate. Precision is a measure of the reproducibility of the system. It is possible for a BGM to be precise but not accurate, or accurate but not precise; a BGM should be both accurate and precise [11]. In terms of accuracy and precision, the first question one may ask is what is accurate and precise enough? What are the expectations? How are accuracy and precision measured?

A combination of analytical and clinical analyses can be used to provide a more complete picture of BGM accuracy and precision. Analytical measures include



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¹Bayer HealthCare LLC Diabetes Care, 555 White Plains Road, Tarrytown, NY 10591, USA

*Author for correspondence: Tel.: +1 574 257 3060; Fax: +1 574 257 3029; joan.parkes@bayer.com

ISO 15197 criteria, regression analysis, mean absolute relative difference (MARD; in percent) and mean absolute difference (MAD; in BG units). MARD and MAD represent the average deviation of meter results from reference results. Therefore, lower values for MARD and MAD indicate higher accuracy. Other measures are more clinical in nature (e.g., Parkes Error Grid analysis [12,13]) and take into account the impact of the error in measurement on the potential effect of incorrect actions on diabetes management. Although Parkes Error Grid evaluations are favored by many healthcare providers, they are not accepted by some regulatory agencies.

ISO 15197 criteria are used by regulatory agencies and others to determine whether a BGM system is sufficiently accurate and precise to be marketed and used by PWD. Current ISO criteria state that for BG values <75 mg/dl, at least 95% of the BGM results should fall within 15 mg/dl of the laboratory results, and for glucose values ≥75 mg/dl, 95% of the BGM results should fall within 20% of the laboratory results [101]. More stringent criteria that use a glucose cut-off point of 100 mg/dl instead of 75 mg/dl have been proposed, and these require 95% of BGM results <100 mg/dl to be within 15 mg/dl of the laboratory results and 95% of glucose values ≥100 mg/dl to fall within 15% of the laboratory results.

However, there are several questions left unanswered by solely using ISO 15197 criteria to determine the acceptability of a BGM system:

- Are the ISO 15197 criteria to be met under optimal conditions in the laboratory when a pristine system is used by professionals or in the hands of naive lay users?
- What is the nature of the outliers (i.e., the remaining 5% of BG values)? Are they far from the actual value or only just out of the acceptable range?
- ISO 15197 speaks to an absolute number (i.e., 95% of values shall fall within 20 or 15% for the current and proposed ISO, respectively), but it does not take into account experimental variation, that is, when a system is assayed many times one would not expect identical results each time. ISO 15197 does not require confidence intervals.

Additional measures of performance (e.g., MAD and MARD) can be particularly useful when comparing different meters. If all of the

meters being evaluated meet ISO 15197 criteria, these other analyses can be used to distinguish between the meters. In order to make an unbiased comparison between meters, the same blood sample would need to be tested on each meter using the same protocol under the same conditions. For example, results obtained in a controlled laboratory setting by trained users should not be compared with results obtained in a clinical setting by end users. In addition, it is important to note that it is not appropriate to directly compare the results of one meter to another; rather, all meter results should be compared with a reference standard.

How important is the performance of a BGM?

To determine the importance of accuracy and precision for a BGM, one may ask what types of decisions are being made from these BG values? There may indeed be some instances where an approximation of the true BG value is sufficient; however, there are many circumstances where an accurate BGM reading can be of great importance, such as for drug therapy changes, including insulin dosing as well as changes in noninsulin diabetes therapies, treatment decisions for hyper- or hypoglycemia, effective carbohydrate counting, assessing the effect of exercise on BG, and glucose control in special circumstances such as illness, pregnancy and CGM calibration.

In a study that assessed differences between BG values estimated by people with Type 2 diabetes and those determined by testing on a BGM, 77% of PWD reported that they can predict their BG value based on the way they feel [14]. However, 46% of PWD estimated BG values that were outside of the current ISO criteria, and 58% of PWD estimated BG values that were outside of the proposed ISO criteria. After being told their BG value as measured on a meter, 99% of PWD reported that knowing their BG value by testing on a meter could help them to make different decisions about their diabetes. These findings suggest that having accurate BG measurements from testing on a meter can help PWD to make better-informed decisions in the management of their diabetes.

It is important to know what factors may affect the performance of a BGM system

To understand sources of error in BG measurements, it is helpful to consider that the testing process can be separated into three components:

blood sample; user and environment; and test strip sensor and meter. The performance of a BGM system is a combination of all sources of error.

Blood sample variation includes factors, such as hematocrit, and interfering molecules, such as oxygen or acetaminophen [10,11]. To address these sources of error, modern systems include enzymes and mediators designed to avoid or minimize chemical interference. Additionally, hematocrit may be independently measured by the monitoring system so that its effect on the measured signal can be compensated [15,102].

User and environment variation includes temperature. Variation in temperature affects the rate of the chemical reaction, and this can be addressed by either measuring temperature and compensating for its effect [15] or by measuring the total signal rather than the signal rate (coulometry) [102]. Temperature can also cause long-term shifts in test strip reactivity due to gradual degradation of the chemical components, and stability is a critical requirement of the chemical formulation.

Variation in the sensor or meter can affect the measured end product or any other signals that are used to calculate the glucose concentration. Manufacturing technology has evolved over the years, and modern processes are capable of producing test strips and BGMs within tight tolerances.

The user of the meter can be a large contributor to error in a BGM reading. One potential source of large errors in BGM readings is the failure of the users to properly clean their hands. Any amount of sugar on the finger can result in significantly erroneous BG measurements. Other sources of end user error include miscoding [16], an unclean or broken meter, expired or compromised test strips, a lack of proper training, incorrect use of control solution, or disease states affecting the patient's blood sample [17,18].

Finally, it is important to note that artifactual error can be introduced when assessing the accuracy and precision of BGMs [19]. In addition to errors that arise from improper technique on the part of the end user, some sources of error may be inherent to the design of the protocol used in the study. Some problems associated with assessments of BGM system performance include:

- Accuracy and precision of laboratory glucose instrument – reference value
- Handling of blood samples – proper technique
- Blood sample type – only compare the same blood sample types (i.e., capillary to capillary or venous to venous)

In summary, because SMBG results have the potential to affect patient outcomes, it is important for devices used for SMBG to be accurate and precise, and to minimize sources of error in the hands of the intended users. Accuracy and precision of SMBG systems can be evaluated in many ways, some of which relate to their analytical performance (e.g., ISO 15197) and others to the clinical relevance of errors (e.g., Parkes Error Grid). There are many sources of error, some that the designers and manufacturers of these devices can control, but some that can only be controlled by appropriate education of the end user, the PWD who ultimately depends on these devices to help manage his or her diabetes.

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