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REVIEW ARTICLE

# Blood Glucose Measurement in the Intensive Care Unit: What Is the Best Method?

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## Abstract

Abnormal glucose measurements are common among intensive care unit (ICU) patients for numerous reasons and hypoglycemia is especially dangerous because these patients are often sedated and unable to relate the associated symptoms. Additionally, wide swings in blood glucose have been closely tied to increased mortality. Therefore, accurate and timely glucose measurement in this population is critical. Clinicians have several choices available to assess blood glucose values in the ICU, including central laboratory devices, blood gas analyzers, and point-of-care meters. In this review, the method of glucose measurement will be reviewed for each device, and the important characteristics, including accuracy, cost, speed of result, and sample volume, will be reviewed, specifically as these are used in the ICU environment. Following evaluation of the individual measurement devices and after considering the many features of each, recommendations are made for optimal ICU glucose determination.

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## The Importance of Glucose Control in the Critically Ill

Both hyperglycemia and hypoglycemia in the intensive care unit (ICU) patient have long been associated with increased morbidity and mortality.[1–3] The worsened outcome from hyperglycemia occurs not only in patients with diabetes, but also in nondiabetics when enhanced glycogenolysis and gluconeogenesis combined with impaired glucose consumption and impaired glycogen production lead to stress-induced hyperglycemia.[4,5] Additionally, patients with hyperglycemia are at a greater risk for wound infections, bacteremia, septicemia, and ischemic events.[6,7] In an attempt to improve patient outcomes, the American Diabetes Association and the American Association of Clinical Endocrinologists recommend maintaining blood glucose levels close to 110 mg/dl and generally <140 mg/dl.[8,9] When euglycemia resulted from tight glucose control, it was first reported that there was a reduction in morbidity[10] and mortality.[11] However, this aggressive treatment of hyperglycemia resulted in an increased incidence of hypoglycemia.[12,13]

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**Abbreviations:** (BGA) blood gas analyzer,(CLD) central laboratory device, (CV) coefficient of variation, (EGA) error grid analysis, (FDA) Food and Drug Administration, (GDH) glucose-1-dehydrogenase, (GOx) glucose oxidase, (ICU) intensive care unit, (IIT) intense insulin therapy, (NAD) nicotinamide adenine dinucleotide, (POC) point of care, (PQQ) pyrroloquinoline quinone, (TAT) turnaround time

**Keywords:** central laboratory device, cost, critical care, glucose, point of care, turnaround time

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Iatrogenic hypoglycemia has since been reported to be an independent risk factor for mortality and multi-organ system morbidity in the ICU population.[14] The NICE-SUGAR trial, a large study of adult ICU patients, showed that intense insulin therapy (IIT) led to more hypoglycemia and increased mortality.[12] This landmark paper made the point that the type of blood sample, method of acquisition, and method of glucose measurement were all important. A subsequent meta-analysis including this trial reinforced to clinicians the dangers of hypoglycemia.[15]

Intensive care unit patients are particularly vulnerable to an unrecognized hypoglycemic event because they are more likely to be intubated and sedated and less likely to report symptoms of hypoglycemia. In addition, they frequently experience interruptions in the delivery of their nutritional intake secondary to events such as airway management issues and diagnostic or therapeutic procedures.[16] These patients are also more likely to be experiencing other pathologies that may mask the classic signs of hypoglycemia or have other acute organ failures that may distract their caregivers from consistently attending to proper glucose control.

There are two options to accomplish frequent ICU blood glucose monitoring: traditional central laboratory devices (CLDs) or point-of-care (POC) meters. Blood gas analyzers (BGAs), which measure glucose as part of a panel of other laboratory values, can be considered as an alternative form of a CLD. Self-monitoring of blood glucose devices, originally designed and manufactured for home use, have been redesigned for inpatient POC use at the hospital bedside. For a review of these meters, including their methodology, accuracy, and interferences, see the work of Pitkin and Rice.[17] These meters have the advantage of being very portable, providing quick results, and requiring very little blood sample volume. However, there is a decrement in accuracy compared with CLDs. The CLDs are very accurate yet require larger blood volumes and may not be in close proximity to the ICU patient. Though not used primarily for glucose management, BGAs have similar accuracy and precision to CLDs. Blood gas analyzers also benefit from being stationed closer to the ICU and thus could be considered as POC devices. However, for the ICU staff that must run the samples to the blood gas laboratory, they are potentially more time consuming than handheld POC meters. Also, as BGAs automatically process other blood chemistry values (e.g., pH, $PaCO_2$, potassium, and sodium levels), the cost of using this method for IIT in the ICU may be substantial. This review evaluates the differences in acquiring blood glucose measurements using CLDs and BGAs versus POC meters in the ICU, while balancing cost, accuracy, time to the result, and other important metrics.

## Overall Performance Requirements

When choosing between the various devices for ICU glucose measurement, the factors to consider include accuracy, speed of results, cost per test, and sample volumes. In the classic ICU glucose studies, some have used CLDs, others have used POC meters, and some studies have used a combination of the two. The classic study of Van den Berghe and coauthors[11] in the surgical ICU, using a BGA, showed a reduction in morbidity and mortality with IIT. Van den Berghe and coauthors'[10] subsequent medical ICU study used similar guidelines but measured glucose with a POC meter and used capillary blood when an arterial catheter was not available. That study showed decreased morbidity but not mortality with IIT. The subsequent NICE-SUGAR trial included 38 academic tertiary care centers and four community hospitals, and the measurement device used varied from hospital to hospital. The accuracy between systems has been well documented,[17] but the tradeoffs of this accuracy versus cost, sample size volume, and speed of results has not been studied and is the focus of this review.

### *Accuracy*

There are a number of different statistical methods used to assess accuracy. Correlation and regression analysis, Bland–Altman, and Clarke error grids all serve as accepted metrics. Although bias affects the validity of using correlation to compare two different methods of measurement,[18] regression analysis will show the deviation from the line of equality in blood glucose values between devices. This has been particularly illustrative at hypoglycemic levels.[19] The Bland–Altman method plots the mean of paired glucose values versus the absolute difference between the paired values.[20] One value comes from the reference instrument and the other comes from the instrument under evaluation. The 95% limits of agreement is calculated from the standard deviation of the difference values × 1.96. These graphs show bias and variation between two different instruments. To assess the clinical impact of differences

between glucose measuring devices, the Clarke error grid analysis (EGA) is the most often accepted tool. The EGA depicts the relative difference in values between devices, with the reference device usually on the *x* axis. An ideal device should have a high degree of accuracy (i.e., zone A and B values). A number of physiologic derangements in the ICU patient may affect accuracy, including poor perfusion states,[21] pH,[22] anemia,[23] renal failure,[24] and high oxygen tension levels.[25]

### *Time to Result: Turnaround Time*

In the critical care setting, timely results are vitally important. D'Ancona and coauthors[14] detailed iatrogenic hypoglycemia secondary to insulin therapy in ICU patients, even when glucose is monitored every hour. Swings in capillary glucose levels over 30 min in ICU patients receiving concomitant insulin therapy and nutritional delivery,[26] and indications that the blood glucose rate of change during descent versus ascent differs, reaffirms the desire for rapid results.[27] Historically, turnaround time (TAT) is divided into three parts.[28] The preanalytic phase begins when the order is given and ends when the laboratory begins testing the specimen. The time required to test the specimen is the analytic phase. After the laboratory obtains and verifies a result, the postanalytic phase starts and ends once the results have been reported. To allow for appropriate clinical interpretation and intervention, the TAT from order processing to result reporting must be short.

### *Cost*

With the rising cost of medical care and declining reimbursement, a successful system for monitoring blood glucose must also be cost efficient. Howanitz and Jones[29] compared glucose testing costs from a database of 445 institutions and found that CLD costs were significantly lower than POC testing costs. In addition, the POC costs were quite variable and highly dependent upon testing volume. This study, however, did not specifically target ICU glucose measurements.

The cost of a laboratory test will be seriously underestimated if one accounts for only the cost of the reagent. There are a number of both direct and indirect costs.[30] These costs may further be divided into labor, supplies, and equipment. As a point of reference, we report internal data collected from our hospital system (Shands at the University of Florida) under the individual categories in the following section.

### *Minimal Sample Volume*

Sample size requirements vary widely among the various devices. Although ambulatory patients may monitor their blood glucose levels infrequently, ICU patients, especially those on an insulin infusion, may merit hourly blood glucose analysis. Test devices may require anywhere from microliters to a milliliter of whole blood for processing. In the ICU, with frequent blood glucose analyses, the total volume of blood needed over the course of a day may become significant. Blood loss from diagnostic laboratory testing may lead to decreased hematocrit to the point of provoking blood transfusion.[31]

## Central Laboratory Devices

In the central laboratory, glucose is determined by an end point optical method using two linked enzyme reactions. Clotted blood serum, heparinized plasma, and even ethylenediaminetetraacetic acid plasma are usually suitable for CLD glucose analysis. An essential point is that serum or plasma must be separated from the clot or red cells within 30 min of collection to prevent significant consumption of glucose by the erythrocytes. If plasma separation is likely to be delayed, the specimen should be collected in a tube containing an inhibitor of glycolysis such as sodium fluoride.

In the usual first analytical step, serum (or plasma) glucose in the presence of adenosine-5′-triphosphate is phosphorylated by the enzyme hexokinase to form glucose-6-phosphate. The glucose-6-phosphate is subsequently oxidized to 6-phosphogluconolactone by glucose-6-phosphate dehydrogenase. This second step is associated with the reduction of nicotinamide adenine dinucleotide $(NAD)P^+$ to NADPH and $H^+$. The reaction is monitored by spectrophotometrically determining absorbance at 340 nm.

Other sugars such as fructose and mannose may also be phosphorylated by hexokinase, if present at high concentrations. However, the second (glucose-6-phosphate dehydrogenase) step is specific for glucose-6-phosphate and thus the combined specificities of the two enzymes limit interference by other sugars.[32]

### *Accuracy*

As CLDs centrifuge the specimen in the process of obtaining the plasma glucose level, the resulting glucose value does not require hematocrit correction. Additionally, the glucose systems used in the central laboratory have a lower limit of detection of 2 mg/dl and a lower limit of quantitation (functional sensitivity) of approximately 5 mg/dl. The limit of detection is the lowest analyte concentration likely to be reliably distinguished from a blank sample. The limit of quantitation is the lowest concentration at which the analyte can not only be reliably detected but at which some predefined goals for bias and coefficient of variation (CV) are met. The upper linear analytical limit is often as high as 750 mg/dl. The analytical precision is high, with a CV of less than 2%. The 2011 recommendations for the desirable performance characteristics of a central laboratory glucose determination include a percentage CV of <2.9%, an analytical bias or inaccuracy of <2.2%, and a total error of <6.0%.[33] The 2012 updated guidelines (**Table 1**) for CLD plasma glucose is CV of <2.3% and an inaccuracy or bias <1.8%. The total error is usually calculated as (absolute bias or inaccuracy) + (1.96 × standard deviation).[34]

In the majority of central laboratories, the measurement of glucose is performed on analyzers that perform multiple assays using single-wavelength absorbance and turbidometric techniques. The stand-alone glucose analyzers of decades past are rarely encountered. Modern analyzers are "random-access," meaning they can selectively perform one assay or multiple combinations of assays.

**Table 1.**
**2012 Updated Guideline for Central Laboratory Glucose Accuracy and Precision[a]**

| | Analyte | Biological variation | | Desirable specification | | |
|---|---|---|---|---|---|---|
| | | CVw | CVg | I(%) | B(%) | TE(%) |
| P- | Glucose | 4.5 | 5.8 | 2.3 | 1.8 | 5.5 |
| S- | Glucose | 6.1 | 6.1 | 2.9 | 2.2 | 6.9 |

[a] CVw, within-subject biologic variation; CVg, between-subject biologic variation; I, desirable specification for imprecision; B, desirable specification for inaccuracy; TE, desirable specification for allowable total error. Adapted from Ricos and coauthors.[34]

### *Cost*

With respect to labor, central laboratory specimens are typically handled by the front-end processing staff (i.e., medical laboratory assistants or preanalytical assistants) and then by licensed medical technologists. Supplies include reagents, calibrators, and controls. The equipment is frequently a major capital expense, because modern-day random-access chemistry analyzers are sophisticated robotic systems that can perform multiple assays at high speed. An approximate cost analysis for a medium-sized hospital laboratory (Shands at the University of Florida) is depicted in **Table 2**. These are cost data for glucose analysis on a small analyzer that performs multiple chemistry studies. For CLDs, the vast majority of the cost is labor.

### *Rapidity/Turnaround Time*

Though CLDs have long served as the gold standard for accuracy and precision for blood glucose analysis, their usefulness in glycemic control in a busy ICU has been hampered by the perception of a lengthy TAT. For a central-laboratory-processed blood glucose level, TAT varies widely from institution to institution. Kilgore and coauthors[28] reported that, at a 746-bed tertiary care teaching hospital (University of Alabama at Birmingham Hospital), 6% of the stat and critical value central laboratory analytic times for glucose level were reported within 18 min and 94% were reported within 60 min.[28] Preanalytic factors such as difficulty with phlebotomy and transport to the CLD may increase mean TAT to 2.5 h.[35] **Table 3** summarizes the estimated TAT at Shands at the University of Florida and will, of course, vary between institutions. Even when an order is deemed "stat," the in-laboratory estimated TAT remains above 10 min. The time from adding the sample tube to the analyzer to production of a result is 12 to 15 min. The actual physical reaction time onboard the analyzer is 10 min. When blood glucose orders are not stat, the process of receiving or acknowledging receipt of specimen is estimated to be closer to 10 min, and the analytic portion of the process is also closer to 20 min.[36] The increased analytical time is due to the time that the specimen spends waiting in the queue.

**Table 2.**
**Central Laboratory Device Cost**

| Labor | | Salary per hour | Minutes needed | Average labor cost per test |
|---|---|---|---|---|
| Medical laboratory assistant front-end processing | | $15.00 | 5.00 | $1.25 |
| Medical technician | | $40.00 | 1.00 | $0.67 |
| | | | | $1.92 |
| Supplies | Cost | Number of test per pack | | Cost of reagent per test |
| Reagent pack | $29.00 | 800.00 | | $0.04 |
| Equipment | Purchasing cost | Expected life (years) | Cost per year | Cost of equipment per test |
| Analyzer | $80,000.00 | 5 | $16,000.00 | |
| Maintenance | | | $8,000.00 | |
| Number of tests per day | | | 1200 | |
| Number of tests per week | | | 8400 | |
| Number of tests per year | | | 436,800 | |
| | | | | $0.05 |
| Total direct cost per test | | | | $2.01 |

### *Minimal Sample Volume*

Central laboratory devices require a minimal sample volume of 0.5 ml serum or plasma (from whole blood, by centrifugation). Therefore, 1 ml or more is preferred during collection.

**Table 3.**
**Summary of Turnaround Time for Central Laboratory Testing for Stat Glucose Testing[a]**

| Steps | Estimated time (minutes) | Phase |
|---|---|---|
| Order test and acknowledge order | 1 | Preanalytic |
| Label tubes , collect and package specimen | 1[b] | Preanalytic |
| Transport specimen | 2 (pneumatic tube system) | Preanalytic |
| Receive or acknowledge receipt | 2 | Preanalytic |
| Process specimen | 5 | Preanalytic |
| Perform test | 10 | Analytic |
| Release result | 1 | Postanalytic |
| Receive result | 1 | Postanalytic |

[a] Data based on personal communication with author Neil S. Harris.
[b] Estimated time for patients with preexisting access (e.g., arterial line or central venous line).

### *Blood Gas Analyzers*

Blood gas analyzers are a type of bench laboratory analyzers that have the additional capability of measuring pH, $pO_2$, and $pCO_2$ often combined with oximetry. They utilize whole blood, and the glucose measurement is typically performed with a glucose electrode that generates hydrogen peroxide via glucose oxidase (GOx). The hydrogen peroxide is detected using an amperometric (current-detecting) electrode where the $H_2O_2$ is reduced to oxygen, releasing an electron. Compared with hand-held POC meters, BGAs are close to laboratory standards of centrifuged plasma glucose levels. They are generally considered to be as accurate as core CLDs.[37] The precision with a BGA is aided by the frequency at which it calibrates itself and its daily servicing by central laboratory staff. Their cycle time from when the syringe is attached to display of results is approximately 2 min (Siemens RAPIDLab). The analyzer at our institution, ABL 800 (Radiometer), has an analytical time of approximately 1 min. With the addition of the preanalytic steps of ordering, obtaining, and transporting specimen, the TAT for these devices is approximately 10 min. This time does not account for the periods in which the analyzer is being calibrated or used by another ICU provider, which may add additional minutes to TAT. The GEM Premier 3000,[37] for example, performs one-point calibrations every 20 min and after every sample analysis and two-point calibrations every 2 h. In terms of sample size, the minimal sample volume of 0.25 to 0.5 ml whole blood is needed for processing (Radiometer stat laboratory BGA). Having said that, it is common for 1 ml samples to be taken during specimen acquisition. **Table 4** shows the labor, supply and equipment cost at our institution (Shands at

**Table 4.**
**Blood Gas Analyzer Costs**

| Labor | Salary per hour | Minutes needed | | Average labor cost per test |
|---|---|---|---|---|
| Medical technician | $40.00 | 0.50 | | $0.33 |
| | | | | $0.33 |
| Supplies | Cost | Number of test per pack | | Cost of reagent per test |
| Cleaning solution | $56.00 | 250 | | $0.22 |
| Calibration solution 1 | $20.69 | 750 | | $0.03 |
| Calibration solution 2 | $55.94 | 750 | | $0.07 |
| Glucose membrane | $194.69 | 7000 | | $0.03 |
| Miscellaneous | $150.00 | 1750 | | $0.09 |
| | | | | $0.44 |
| Equipment | Purchasing cost | Expected life (years) | Cost per year | Cost of equipment per test |
| Analyzer | $40,000.00 | 6 | $6,666.67 | |
| Maintenance | | | $3,000.00 | |
| Number of tests per day | | | 250 | |
| Number of tests per week | | | 1750 | |
| Number of tests per year | | | 91,000 | |
| | | | | $0.11 |
| Total direct cost per test | | | | $0.88 |

the University of Florida) associated with using a BGA in the stat laboratory to obtain blood glucose values. Labor cost may be altered for BGAs located directly in the ICU, particularly when the ICU nursing staff directly runs the sample.

## Point-of-Care Devices

Unlike CLDs, which measure blood glucose levels from plasma, POC meters analyze whole blood. After the blood drops onto the test strip, plasma from the whole blood percolates into the strip layer which, in the majority of POC meters, contains one of two enzymes: GOx or glucose-1-dehydrogenase (GDH). The GOx methodology produces gluconic acid and hydrogen peroxide or ferrocyanide. The amount of hydrogen peroxide produced results in a color change (reflectometric), and the density of the color change is proportional to the blood glucose value. When ferrocyanide is the byproduct, its concentration is measured by current, and the amount of the current (amperometric) is proportional to the blood glucose level. In the GDH method, NAD is converted to NAD H. The concentration of NAD H is proportional to the blood glucose level. Glucose is also oxidized by the enzyme glucose dehydrogenase. In older GDH meters, pyrroloquinoline quinone (PQQ) is reduced to $PQQH_2$. The latter interacts with ferricyanide, which is reduced to ferrocyanide. The ferrocyanide donates its electron to a palladium electrode, converting the ferrocyanide back to ferricyanide.[38] For a complete discussion of various POC technologies, including the given examples, see the work of Pitkin and Rice.[17]

There are a number of POC glucose meters that are targeted for the hospital market.[39] However, the accuracy standard that is currently applied to POC meters for the home market is the only regulatory hurdle needed for hospital use. The International Organization for Standardization guideline (ISO 15197) states that "ninety-five (95%) of the individual glucose results shall fall within ±15 mg/dl of the results of the manufacturer's measurement procedure at glucose concentrations ≤75 mg/dl and within ±20% at glucose concentrations >75 mg/dl."[40] Clearly, allowing up to 5% of results outside of these already loose targets seems to be inadequate for hospital use. Although these meters are marketed by various manufacturers specifically for use in the hospital environment, it is unclear if the technologies or accuracy profiles are actually any different or better than what these companies are marketing to the home glucose market.

The Food and Drug Administration (FDA) is well aware of the problem of home glucose meters migrating into the hospital arenas with no increased accuracy and interference requirements. The FDA's plan is to convert to a "two-track process" and, in May 2010, the FDA organized a meeting to begin the process of developing separate regulatory framework for hospital POC meters.[41] Although not yet completed, *POCT12-A3: Point-of-Care Glucose Testing in Acute and Chronic Care Facilities: Approved Guideline: Third Edition* will attempt to define these new standards and set them apart from the current ISO 15197 self-testing requirements.

As of this time, there are a number of glucose meters marketed for the hospital care markets. The coming regulatory requirements will certainly force answers to the questions of accuracy and accompanying technology differences.

### *Point-of-Care Accuracy*

**Figure 1** compares what different organizations worldwide consider as acceptable agreement between POC meters and CLDs.[42] There are a few factors affecting accuracy that are common in the ICU population and worth mentioning.

Whole blood glucose is lower than plasma glucose concentrations by approximately 10–12%. For this reason, almost all whole blood analyzers (specifically, POC meters) have a built-in offset to correct to expected plasma glucose levels. When the hematocrit is abnormally high or low, the difference between whole blood glucose and plasma glucose can be insufficiently corrected in meters that do not directly measure hematocrit. However, anemia or polycythemia may affect the accuracy of some older POC meters. Newer meters have the technology to concomitantly measure hematocrit with glucose levels and then correct the glucose level based on abnormal red cell levels.[43] This is usually done by measuring conductivity, much like some POC meters measure hematocrit. Please see the work of Wu and coauthors[44] for a more complete discussion of conductivity and impact on hematocrit analysis.

Hypotension and hemodynamic lability can also affect the accuracy of POC meters. This inaccuracy exists in both GOx and GDH methodologies. Intensive care unit patients are often taking many different types of medications, another potential source for error with these meters.[17] Elevated $PaO_2$ levels have also been shown to affect the accuracy of POC meters that use GOx. When the $PO_2$ level of the blood sample exceeds 100 torr, the true value of the blood glucose level can be under-estimated by greater than 15% of the true value.[25]

Because of their historical use in home testing, POC glucose meters are often associated with capillary blood testing. Although ICU patients almost always have intravascular access, capillary blood (usually obtained from a "finger stick") is sometimes used for glucose analysis. Because blood located in the fingertip is actually a pool of blood, there must be a time constant associated with a sample from this location, and depending on the blood glucose concentration rate of change, the result may differ from either arterial or venous blood. Several studies

**Table 1.**
**Meter Performance Criteria for Acceptable Agreement between a Glucose Meter and Results from a Comparative Laboratory Method**

| Organization or society | Glucose range | Performance criteria |
|---|---|---|
| ADA 1987 | All levels | ±15% |
| ADA 1994 | All levels | ±5% |
| CSA | <45 mg/dl (2.5 mmol/liter) | ±25% (CV < 12.5%) |
| | ≥90 mg/dl (5.0 mmol/liter) | ±15% (CV < 7.5%) |
| FDA (95% of data) | <100 mg/dl (5.6 mmol/liter) | ±20 mg/dl (1.1 mmol/liter) |
| | ≥100 mg/dl (5.6 mmol/liter) | ±20% |
| ISO (95% of data) | <100 mg/dl (5.6 mmol/liter) | ±10 mg/dl (1.1 mmol/liter) |
| | ≥100 mg/dl (5.6 mmol/liter) | ±20% |
| IMSS | <60 mg/dl (3.3 mmol/liter) | ±25% |
| | ≥60 mg/dl (3.3 mmol/liter) | ±20% |
| CLSI (C30A) | <100 mg/dl (5.6 mmol/liter) | <15 mg/dl (0.83 mmol/liter) |
| | ≥100 mg/dl (5.6 mmol/liter) | ±20% |
| TNO | <117 mg/dl (6.5 mmol/liter) | ±20 mg/dl (1.11 mmol/liter) |
| | ≥117 mg/dl (6.5 mmol/liter) | ±15 mg/dl (0.83 mmol/liter) (CV < 10%) |

CV, coefficient of variation; CSA, Canadian Standards Association; FDA, U.S. Food and Drug Administration; ISO, International Organization for Standardization; IMSS, Instituto Mexicano del Seguro Social; CLSI, Clinical and Laboratory Standards Institute; TNO, Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek

**Figure 1.** A previously published table showing meter performance criteria for acceptable agreement between a glucose meter and a CLD. Reprinted with permission from *Journal of Diabetes Science and Technology*.[42]

have shown high variability when using capillary samples, and we recommend not using these with critically ill patients.[45,46]

Glucose-1-dehydrogenase–PQQ-based meters are insensitive to ambient oxygen. They are also less affected by other interferences with one dangerous exception. These devices have their accuracy affected by the presence of maltose, maltotriose, or maltotetrose.[24] This occurs in patients who are receiving peritoneal dialysis whose dialysate contains icodextrin, because it is hydrolyzed to maltose, maltotriose, or maltotestrose. Following a number of well-documented deaths, this technology is being abandoned, although a number of these meters still exist in service.

### *Cost*

In terms of cost, POC devices are the most affordable. Although the reagent per test cost is many times more than CLDs, the labor costs are substantially less (**Table 5**).

### *Rapidity/Turnaround Time*

One of the most often quoted benefits of POC meters is the speed that results are obtained and that a reduced TAT improves patient outcome. Blood samples are taken by nurses in the ICU and placed on the test strip, and the results are displayed within 1 min. In our survey, the average time for a nurse to run the POC glucose test was 1 min. This compares favorably to the 0.5 to 1.5 min that Grek and coauthors[47] reported, that POC testing increased patient holding time when a POC glucose test was added to the preoperative testing. In addition to analysis time, liquid controls are run every 8 h. There are two levels of control used: normal and high. Failure to run the controls will "lock" many of these instruments. After quality control testing time is factored in, the TAT of bedside testing has been reported to be, on average, 5–8.5 min.[35,48] By eliminating multiple steps in the preanalytic phase and reducing the time in the analytic phase, POC meters clearly improve TAT.

### *Minimal Sample Volume*

Handheld glucometers generally only require microliters of whole blood for analysis.[49] This is in contrast to CLD and BGA, which may need only 25–50 microliters of serum for analysis, but often 1–2 ml of whole blood is taken from the patient. The minute sample size requirement of POC devices is particularly advantageous in the ICU setting, where patients receive multiple blood draws throughout the day. If the blood specimen comes from an indwelling catheter as opposed to finger stick, the actual volume removed from the patient may be considerably larger.

**Table 5.**
**Handheld Point-of-Care Glucose Meters Costs**

| Labor | Salary per hour | Minutes needed | | Average labor cost per test |
|---|---|---|---|---|
| Patient case assistant | $20.00 | 1.00 | | $0.33 |
| | | | | $0.33 |
| Supplies | Cost | Number of test per pack | | Cost of reagent per test |
| Reagent pack | $18.00 | 50 | | $0.36 |
| | | | | $0.36 |
| Equipment | Purchasing cost | Expected life (years) | Cost per year | Cost of equipment per test |
| Analyzer | $120,000.00[a] | 5 | $24,000.00 | |
| Maintenance | | | $0.00 | |
| Number of tests per day | | | 1200 | |
| Number of tests per week | | | 8400 | |
| Number of tests per year | | | 436,800 | |
| | | | | $0.05 |
| Total direct cost per test | | | | $0.75 |

[a] Based on purchasing 214 handheld POC glucose meters.

## Summary

Although accuracy is arguably the most important metric in selecting the best glycemic management device for critically ill patients, speed, sample size, and cost are also important factors. **Table 6** summarizes how the various metrics compare among the available devices and highlights the various features of each system. When these factors are considered, it is our opinion that BGAs, when located in proximity to the ICU and functioning as a POC device, provide the best balanced option when considering accuracy, cost, and TAT. Although central laboratory testing remains the gold standard for blood glucose measurement, the TAT, sample size requirement, and increased cost compared with BGAs make it an illogical choice for IIT in the ICU when a BGA is available. Furthermore, the accuracy of BGAs is equal to CLDs. In contrast, handheld POC meters require minimal sample size and are relatively affordable, although our data show that the cost per test is not much different from a BGA. However, the inaccuracy of the POC meters has been well documented, and their possible role in iatrogenic hypoglycemia should not be ignored.

**Table 6.**
**Comparison of Point-of-Care Meters, Blood Gas Analyzers, Central Laboratory Devices, and Continuous Glucose Monitors[a]**

| Feature | CLD | BGA | POC meter | Continuous glucose monitoring[b] |
|---|---|---|---|---|
| Available for ICU | Yes | Yes | Yes | No |
| Space requirement | 53 inches | 25 inches | 4 inches | 3 inches |
| Weight and portability | 462 pounds and stationary | 70 pounds and stationary | 4 ounces and portable | 3 ounces and portable |
| Suitable for bedside testing | No | No | Yes | Yes |
| Sample size[c] | 1-2 ml | 1-2 ml | 10 µl | Not applicable |
| Analysis time | 10 min | 1 min | 1 min | 1/6$^{th}$ min |
| Purchase cost per device | $80,000 | $40,000 | $100 | Not applicable |
| Routine maintenance by technician | Necessary | Necessary | Not necessary | Not applicable |
| Standard reference materials | Yes | Yes | Yes | No |
| Daily calibration requirement | Multiple | Multiple | Once | Twice |

[a] Figures are typical. Adapted from Klonoff[50] and Diabetesnet.com.[51]
[b] Although not currently approved in the United States for inpatient use, continuous glucose monitoring systems have been tested for the ICU population. Based on devices for outpatient use.
[c] Based on a whole blood sample typically taken from patient for processing.

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