Evaluation of Accuracy and User Performance of the TRUE METRIX® Self-Monitoring Blood Glucose System

TRIVIDIA HEALTH™

Summary

Objectives:

To demonstrate that the TRUE METRIX® Self-Monitoring Blood Glucose System*, from Trividia Health, Inc., meets the International Organization for Standardization (ISO) 15197:2013 standard for accuracy requirements and can be accurately used by patients after minimal instructions for use and review of training materials.

Methods:

This trial was designed in accordance with the ISO 15197:2013 standard. Clinical accuracy was determined by comparing fingerstick blood sample results obtained by healthcare professionals using the TRUE METRIX® System and the Yellow Springs Instruments (YSI) laboratory reference instrument for the measurement of glucose in whole blood samples. The accuracy of the TRUE METRIX® System during patient use was also evaluated, and healthcare professionals assessed each patient's testing technique. In addition, patients rated aspects of the TRUE METRIX® System and user instructions.

Results:

Study participation included trained healthcare professionals and a total of 109 adult patients with type 1 or type 2 diabetes. The TRUE METRIX® System exceeded the minimum ISO standard for accuracy, with 99% of healthcare professionals' results falling within limits defined by the ISO 15197:2013 standard. Additionally, all results were within Zone A of a Parkes Error Grid analysis. Patients were also able to obtain clinically accurate results with the TRUE METRIX® System, and healthcare professionals rated patients' compliance with the testing procedure as favorable. Patients reported good ease-of-use for the TRUE METRIX® System and clarity of the user instructions.

Conclusion:

The TRUE METRIX® Self-Monitoring Blood Glucose System meets current ISO 15197:2013 standard for accuracy and is considered easy to use by patients.

INTRODUCTION

The International Organization for Standardization (ISO) is a global federation of national standards bodies that develops and publishes international standards.[1] The ISO 15197 *In Vitro Diagnostic Test Systems–Requirements for Blood-Glucose Monitoring Systems for Self-Testing in Managing Diabetes Mellitus* was first published in 2003 (ISO 15197:2003),[2] with the updated standard published in 2013 (ISO 15197:2013).[1] The ISO 15197 standards specify requirements for the acceptable performance of Self-Monitoring Blood Glucose Systems intended to be used by untrained patients, and include guidance on accuracy limits, procedures for performance and design verification, and validation of performance by the intended users.[1,2]

The TRUE METRIX® Self-Monitoring Blood Glucose System is comprised of glucose reagent test strips using glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) chemistry, a portable hand-held electronic meter, and glucose control solution. The system is intended for in vitro self-testing of glucose in fresh capillary whole blood samples by diabetic patients at home as an aid to monitor the effectiveness of diabetes control. The TRUE METRIX® System, featuring TRIPLE SENSE TECHNOLOGY®, provides patients with testing confidence and convenience when using the device (**Figure 1**). TRUE METRIX® also features automatic detection of control solution (no marking required) and test strip guiding and ejection for ease-of-use. Advanced event markers and download capability empower patients to make the connection between personal lifestyle and results. Providing this information helps patients make informed choices to actively manage diabetes. A summary of TRUE METRIX® performance criteria is provided in **Table 1**.

Table 1. Summary of TRUE METRIX® Performance Criteria

Features	Performance
Coding	No coding
Blood volume	0.5 µL
Testing time	As little as 4 seconds
Sample type	Fingerstick capillary blood
Alternate site testing	Forearm
Enzyme	GDH-FAD*
Control detection	Automatic detection
Fill detection	Audible indication
Blood glucose range	20-600 mg/dL
Maltose interference	No
Hematocrit range	20%-70%
Altitude range	Up to 10,200 ft
Operating temperature range	41°F-104°F
Test memory	500 tests
Test averaging	7, 14, and 30 days
Time/date tracking	Both time and date
Event tagging	6 event tags
Testing reminders	4 audible alarms
Data management	TRUEmanager® Diabetes Management Software

*GDH-FAD, glucose dehydrogenase flavin-adenine dinucleotide.

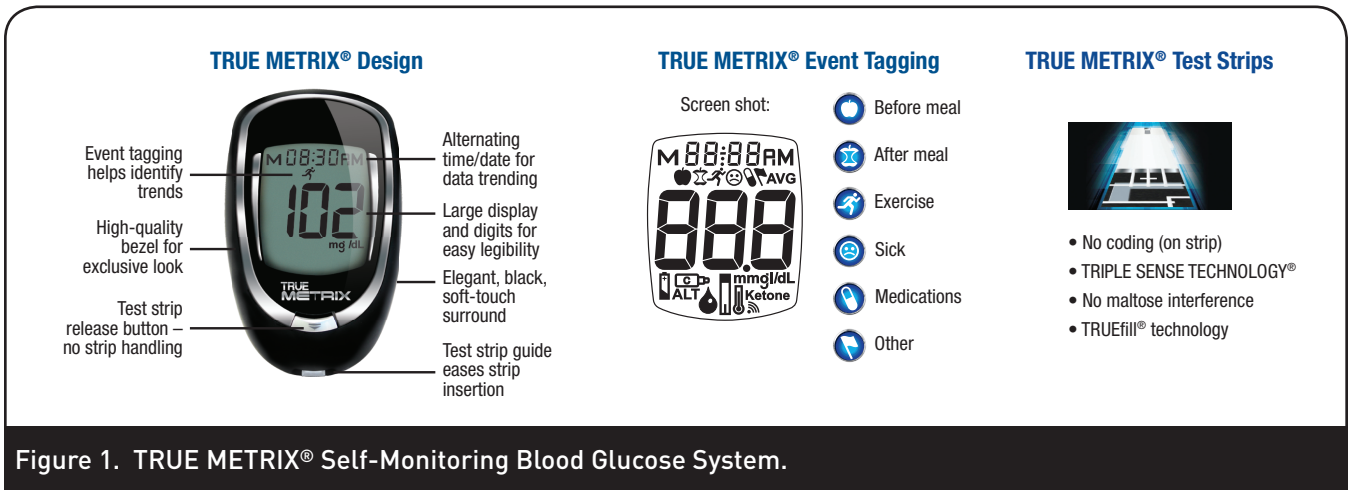


Figure 1. TRUE METRIX® Self-Monitoring Blood Glucose System.

OBJECTIVES

The objectives of this study were to demonstrate that the TRUE METRIX® Self-Monitoring Blood Glucose System, from Trividia Health, Inc., meets the accuracy requirements set forth by the ISO 15197:2013 standard, and that patients are able to obtain accurate results using the TRUE METRIX® System after minimal instructions for use and review of training materials.

METHODOLOGY

Research Design

The clinical study protocol was designed to evaluate the TRUE METRIX® System in accordance with the ISO 15197:2013 clinical accuracy and user performance evaluation requirements.[1] The ISO 15197:2013 standard requires clinical evaluation of both healthcare professionals using the system and of lay users (patients) using the system, with results compared against a reference method. The patient performance evaluation demonstrates whether or not intended users are able to obtain accurate glucose measurements when using the system, based only on the instructions for use and other training materials that are typically provided with the system.[1] ISO 15197:2013 standard also requires that healthcare professionals observe and assess the ability of patients to perform a glucose test using only the instructions for use as a guide, and that patients provide feedback on the clarity and usefulness of the system's instructions for use.[1]

Testing was performed at Medical Research South (Charleston, SC). Accuracy of capillary (fingerstick) blood glucose results was determined by comparing TRUE METRIX® System results with standard laboratory reference (Yellow Springs Instruments [YSI] Blood Glucose Analyzer) results.

Healthcare professionals, as well as adult patients diagnosed with type 1 or type 2 diabetes, participated in the study. Healthcare professionals were trained on how to use the device prior to testing. Patients who had participated in a prior study or other activity involving TRUE METRIX® were excluded. Patients must have been fasting for ≥2 hours prior to participating in the study. Prior to blood glucose testing, the patients' hematocrit values were determined to ensure the hematocrit was within the acceptable range of 20% to 70%. Reference blood glucose results were obtained for each patient by a healthcare professional using the YSI reference instrument both before and after testing with TRUE METRIX®; data for patients whose ending YSI reference value was not within 4 mg/dL (for glucose values <100 mg/dL) or 4% (for glucose values ≥100 mg/dL) of their beginning YSI value were not included in the analysis to ensure that included patients had not experienced significant changes in their blood glucose levels during testing. Additionally, only data from patients whose whole blood glucose level met the ISO 15197:2013 glucose distribution for accuracy evaluation (**Table 2**) were included in the analysis; once all needed samples for a glucose concentration range had been tested, no additional samples were added for that concentration range. If necessary, samples for the lowest and highest glucose ranges could be obtained with patient blood manipulated in the laboratory.

Table 2. ISO 15197:2013 Glucose Distribution for Blood Glucose System Accuracy[1]

ISO category	Glucose concentration	Proportion of samples for clinical evaluation
	mg/dL	%
1	≤50	5
2	>50-80	15
3	>80-120	20
4	>120-200	30
5	>200-300	15
6	>300-400	10
7	400	5

Data Collection

All testing and data collection were consistent with the ISO 15197:2013 standard.[1] User performance of TRUE METRIX® was evaluated in a setting that allowed patients to perform blood glucose measurements without outside influence while observed by a healthcare provider trained in the use of the TRUE METRIX® System. Patients were given the TRUE METRIX® instructions for use and then asked to perform a self-test using a fingerstick sample. The observing healthcare professional or other study investigator was not allowed to intervene or answer questions from the patients during testing. Healthcare professionals monitored the patients to evaluate how compliant each user was with following the instructions, and then rated the patient's performance using a scale of 1 to 5 (1 = non-compliance; 5 = full compliance). Patient performance was considered acceptable if the average score for all patients was ≥3.0. Patients were also asked questions about the quality of the TRUE METRIX® instructions for use and about ease-of-use of the TRUE METRIX® System, ranking specified aspects on a scale of 1 to 5 (1 = strongly disagree, 5 = total agreement). The instructions for use were considered acceptable if the

average score for all patients was ≥3.0.

Once patient testing was completed, a healthcare professional obtained fingerstick samples from the patients for accuracy testing (duplicate tests on each of 3 test strip lots) using the same TRUE METRIX® System.

Data Analysis

ISO 15197 has defined acceptable limits for blood glucose system accuracy based on glucose concentration level, with a requirement that 95% of all glucose results be within those limits; the specific accuracy criteria for the ISO 15197:2013 accuracy standard are shown in **Table 3**.[1] System accuracy is also shown graphically using a bias plot, which shows the difference (bias) between individual TRUE METRIX® glucose results and average YSI reference method glucose results across all glucose concentration intervals.

Table 3. ISO 15197:2013 Defined Limits for Blood Glucose System Accuracy[1]

Glucose concentration	ISO limits	Criteria for accuracy
<100 mg/dL	±15 mg/dL	95% of all results must be within ISO limits[a]
≥100 mg/dL	±15%	
99% of measured glucose values shall fall within Zones A and B of the Parkes Error Grid.		

[a]ISO 15197:2013 standard requires that all 3 lots tested should pass these criteria.

In addition to the bias plot, the Parkes Error Grid (a consensus error grid)[3] was used to evaluate the clinical significance of the bias between the TRUE METRIX® glucose results and results generated using the YSI reference method. The Parkes Error Grid represents a generally accepted method of assessing the potential clinical impact of glucose meter results as a function of their deviation from a standard reference method. The 5 Zones (A-E) within the Parkes Error Grid provide risk levels as they relate to potential clinical outcomes. Glucose results falling within Zones A and B represent values that have no or little effect on clinical action, while glucose results that fall within Zones C, D, and E represent altered clinical action with increasing negative effect on the clinical outcome.

RESULTS

Patient Participants

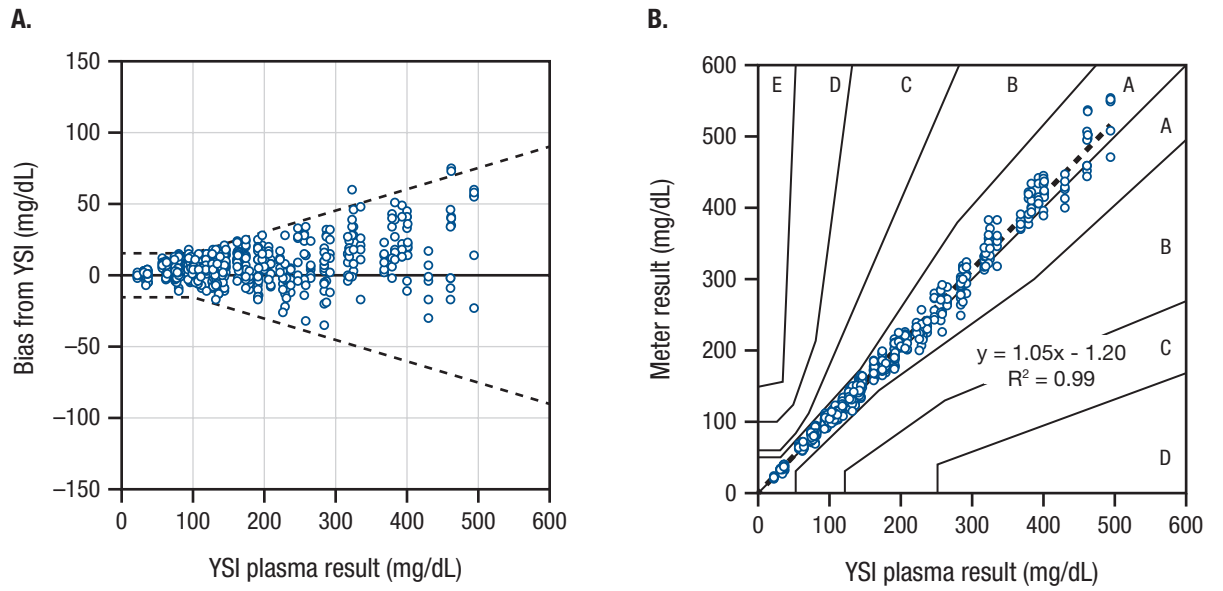
A total of 109 patients being treated for diabetes or with a recent diagnosis of diabetes were enrolled in the study, and 100 of these (34% male; 62% female) were included in the patient evaluation. The mean patient age was 58 years (range, 26-77 years). Sixty-seven percent of patients were African American, 32% were White, and 1% were not identified. Half (50%) of patients completed more than 12 years of education, and another 39% completed 12 years of education; 11% completed less than 12 years of education. Data from 89 patients whose whole blood glucose level met the ISO 15197:2013 glucose distribution for accuracy evaluation were included in the healthcare provider accuracy analysis; an additional 11 samples manipulated in the Trividia Health laboratory were included in the analysis to meet the distribution needs.

Device Accuracy

Healthcare professional results using the TRUE METRIX® System exceeded the minimum ISO 15197:2013 accuracy criteria, with 99% of results within the specified limits (**Table 4** and **Figure 2A**). The Parkes Error Grid analysis for TRUE METRIX® versus the YSI reference method for fingerstick samples tested by healthcare professionals is presented in **Figure 2B**; 100% of the data points fell within Zone A. The slope of the regression line was 1.05 (standard error [SE] ± 0.00), and the intercept was –1.20 (SE ± 0.93) mg/dL. The results demonstrate that the TRUE METRIX® System correlates well with the YSI reference glucose analyzer when tested by trained healthcare professionals using fresh capillary whole blood taken from the fingertip.

Table 4. ISO 15197:2013 Accuracy Results for Healthcare Professionals Using TRUE METRIX® Versus YSI Reference Instrument

	Within ±5 mg/dL	Within ±10 mg/dL	Within ±15 mg/dL
Results <100 mg/dL	99/156 (64%)	135/156 (87%)	155/156 (99%)
	Within ±5%	**Within ±10%**	**Within ±15%**
Results ≥100 mg/dL	207/444 (47%)	364/444 (82%)	441/444 (99%)



A. Bias plot of all TRUE METRIX® results versus YSI reference instrument results analyzed per the ISO 15197:2013 accuracy standard.
B. Parkes Error Grid of TRUE METRIX® results versus YSI reference instrument results.

Figure 2. ISO 15197:2013 Accuracy Results for Healthcare Professionals Using TRUE METRIX® Versus YSI Reference Instrument

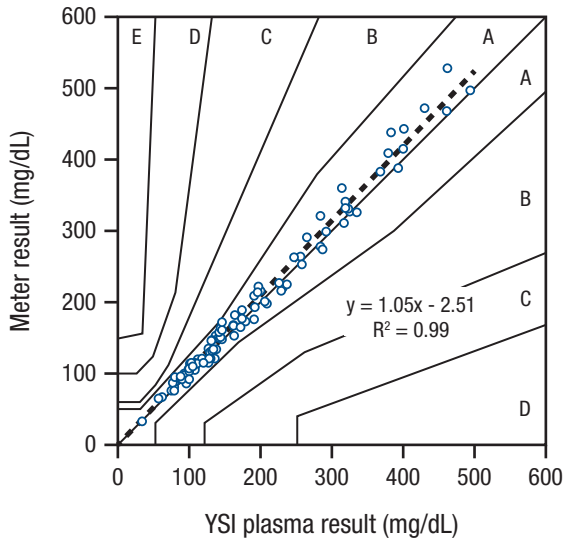
User Evaluation

TRUE METRIX® patient results also exceeded the minimum ISO 15197:2013 accuracy criteria, with 99% of results within the specified limits (**Table 5**). The Parkes Error Grid presented in **Figure 3** shows a comparison of TRUE METRIX® versus the YSI reference method for fingerstick samples tested by patients; 100% of the results fell within Zone A. The slope of the regression line was 1.05 (SE ± 0.01), and the intercept was –2.51 (SE ± 2.71) mg/dL. These analyses demonstrated that results obtained by patients with the TRUE METRIX® System are similar to those obtained with the YSI reference glucose analyzer using fresh fingerstick capillary whole blood.

Table 5. ISO 15197:2013 Accuracy Results for Patients Using TRUE METRIX® Versus YSI Reference Instrument

	Within ±5 mg/dL	Within ±10 mg/dL	Within ±15 mg/dL
Results <100 mg/dL	9/18 (50%)	17/18 (94%)	18/18 (100%)
	Within ±5%	**Within ±10%**	**Within ±15%**
Results ≥100 mg/dL	39/82 (48%)	65/82 (79%)	81/82 (99%)

A total of 109 patients being treated for diabetes or with a recent diagnosis of diabetes were enrolled in the study, and 100 of these were included in the patient evaluation.



Parkes Error Grid for TRUE METRIX® results versus YSI reference instrument results.

Figure 3. ISO 15197:2013 Accuracy Results for Patients Using TRUE METRIX® Versus YSI Reference Instrument

Trained healthcare professionals observed each patient during blood glucose testing and evaluated patient compliance with following the TRUE METRIX® instructions for use. The healthcare professionals' ratings indicate good patient performance, with average response scores >4.90 out of a maximum score of 5 for all questions (**Table 6**).

Table 6. Healthcare Professional Evaluation of Patient Performance Using the TRUE METRIX® System

Questions asked of healthcare professionals	Average response
Was the patient able to insert the strip correctly?	4.90
Was the patient able to apply blood correctly?	4.90
Was the patient able to read the result?	5.00
Did the patient correctly follow the written instructions?	4.90

Responses on a scale of 1 to 5, with 1 = non-compliance and 5 = full compliance.

When asked to rate their experience using the TRUE METRIX® System, patients responded favorably, indicating that the user testing instructions are clear and easily understood and that the system is easy to use (**Table 7**).

Table 7. Patient Evaluation of the TRUE METRIX® System Instructions and Ease-of-Use

Questions asked of patients	Average response
Are the instructions for use generally easy to understand?	5.00
Did the instructions clearly state how to apply blood to the test strip?	5.00
Did the instructions clearly state how to read the result?	4.90
Was the display easy to read?	5.00
Was the system easy to use?	5.00

Responses on a scale of 1 to 5, with 1 = strongly disagree and 5 = total agreement.

CONCLUSIONS

The TRUE METRIX® Self-Monitoring Blood Glucose System, from Trividia Health, Inc., meets the accuracy criteria of the ISO 15197:2013 standard for self-testing Self-Monitoring Blood Glucose Systems. Clinical study results demonstrate that both healthcare professionals and first-time patient users are able to achieve accurate results when testing blood glucose levels using the TRUE METRIX® System. The TRUE METRIX® System's instructions for use are considered to be clear and easy to understand by patient users, and healthcare professionals reported good patient user compliance with the testing procedure. Additionally, patients rated the TRUE METRIX® System as easy to use. Together, these results indicate that the TRUE METRIX® System is accurate and easy to use, and that it can be recommended for self-testing by diabetes patients.

* TRUE METRIX is intended for self-monitoring blood glucose only and not for multiple patient use. Only TRUE METRIX PRO is intended for multiple patient use.

REFERENCES

1. International Organization for Standardization. ISO 15197:2013: *In vitro diagnostic test systems — Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus*. Geneva: International Organization for Standardization; 2013.
2. International Organization for Standardization. ISO 15197:2003: *In vitro diagnostic test systems — Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus*. Geneva: International Organization for Standardization; 2003.
3. Parkes JL, Slatin SL, Pardo S, Ginsberg BH. A new consensus error grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose. *Diabetes Care*. 2000;23(8):1143-1148.

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