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

TRIVIDIA
HEALTH AUSTRALIA

Summary

Objectives:

To demonstrate that the TRUE METRIX Blood Glucose Monitoring System, from Trividia Health, Inc., meets the International Organization for Standardization EN ISO 15197:2015 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 EN ISO 15197:2015 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 EN ISO 15197:2015 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 Blood Glucose Monitoring System meets current EN ISO 15197:2015 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 (EN ISO 15197:2003),[2] with the updated standard published in 2013 (ISO 15197:2013) and in 2015 (EN ISO 15197:2015).[1,4] The ISO 15197 standards specify requirements for the acceptable performance of blood glucose monitoring 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.[1,2,4]

The TRUE METRIX Blood Glucose Monitoring System is comprised of glucose reagent test strips using glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) chemistry, a portable hand-held electronic meter, and control solution. The TRUE METRIX System is intended for the quantitative determination of glucose in human whole blood taken from the fingertip or forearm (capillary) or from the vein (venous) during either at-home use (self-testing) by diabetic patients or use by healthcare professionals in physicians' offices and in acute and convalescent care bedside testing facilities, in order to assist in the management of diabetes. The system may not be used for neonates. The TRUE METRIX System, featuring TRIPLE SENSE TECHNOLOGY, provides patients with testing confidence and convenience when using the device (**Figure 1**). The TRUE METRIX System 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 the TRUE METRIX Blood Glucose Monitoring System 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	Capillary or venous blood
Alternate site testing	Forearm
Enzyme	GDH-FAD*
Control detection	Automatic detection
Fill detection	Audible indication
Blood glucose range	1.1-33.3 mmol/L
Maltose interference	No
Hematocrit range	20%-70%
Altitude range	Up to 3,109 m
Temperature range	5°C-40°C
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

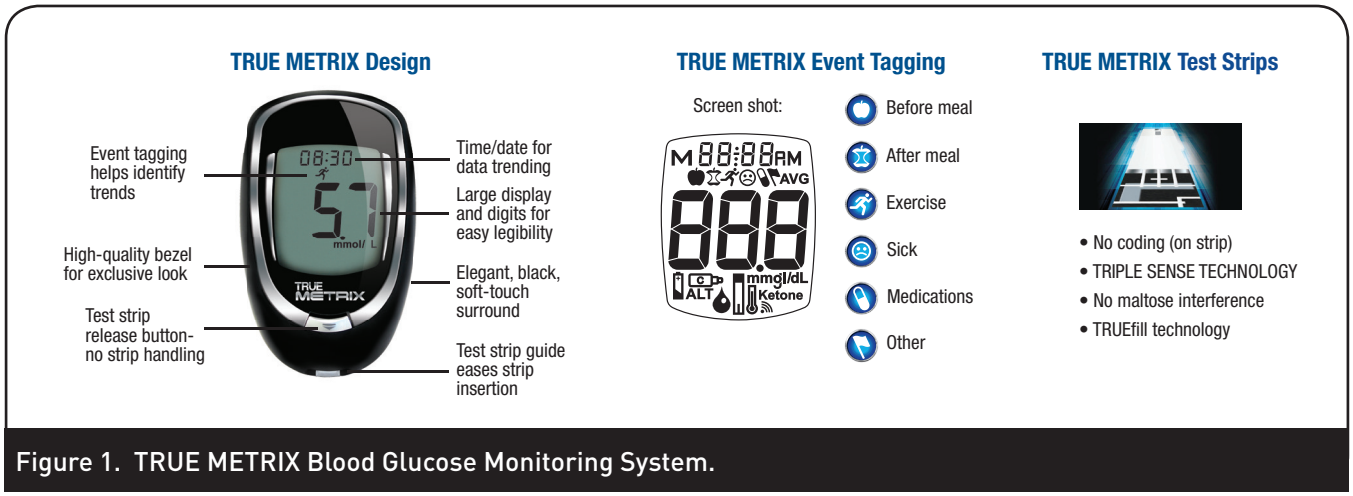


Figure 1. TRUE METRIX Blood Glucose Monitoring System.

OBJECTIVES

The objectives of this study were to demonstrate that the TRUE METRIX Blood Glucose Monitoring System, from Trividia Health, Inc., meets the accuracy requirements set forth by the EN ISO 15197:2015 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 EN ISO 15197:2015 clinical accuracy and user performance evaluation requirements.[4] The EN ISO 15197:2015 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.[4] EN ISO 15197:2015 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.[1,4]

Testing was performed at Medical Research South (Charleston, SC). Clinical 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 0.22 mmol/L (for glucose values <5.55 mmol/L) or 4% (for glucose values ≥5.55 mmol/L) 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 EN ISO 15197:2015 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 contrived in the laboratory.

Table 2. EN ISO 15197:2015 Glucose Distribution for Blood Glucose System Accuracy[4]

ISO category	Glucose concentration	Proportion of samples for clinical evaluation
	mmol/L	%
1	≤2.77	5
2	>2.77-4.44	15
3	>4.44-6.66	20
4	>6.66-11.10	30
5	>11.10-16.65	15
6	>16.65-22.20	10
7	>22.20	5

Data Collection

All testing and data collection were consistent with the EN ISO 15197:2015 standard.[4] 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 three 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 EN ISO 15197:2015 accuracy standard are shown in **Table 3**.[4] 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. EN ISO 15197:2015 Defined Limits for Blood Glucose System Accuracy[4]

Glucose concentration	ISO limits	Criteria for accuracy
<5.55 mmol/L	±0.83 mmol/L	95% of all results must be within ISO limits[a]
≥5.55 mmol/L	±15%	
99% of measured glucose values shall fall within Zones A and B of the Parkes Error Grid.		

[a]EN ISO 15197:2015 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 five 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

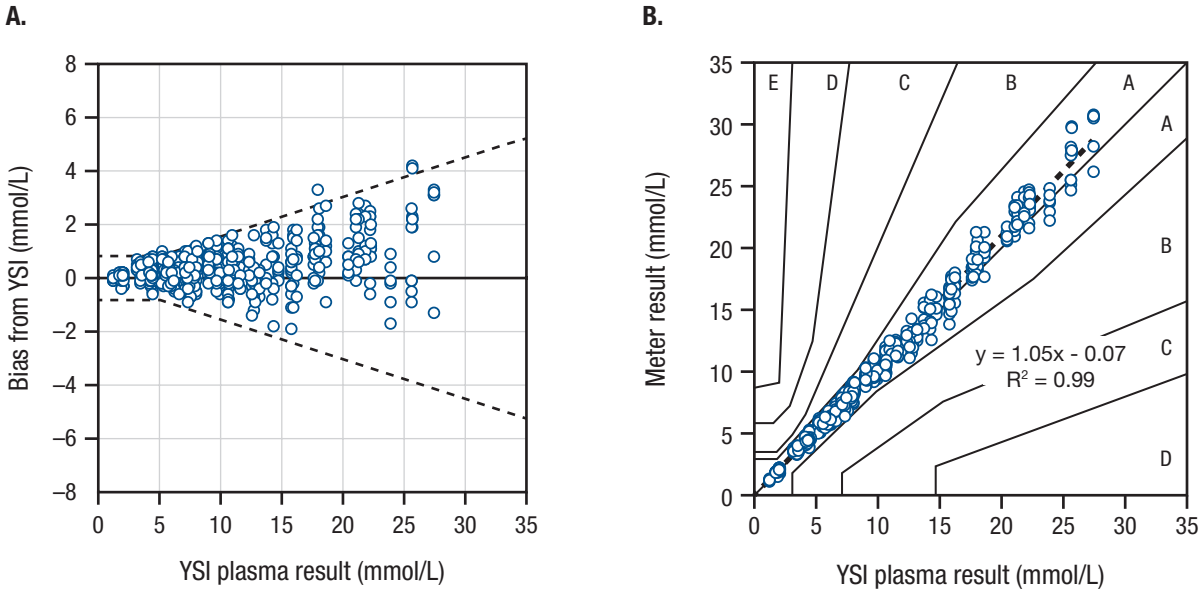
A total of 109 patients being treated for diabetes or with a recent diagnosis of diabetes were enrolled in the study, and 100 of these (34% male; 62% female) were included in the patient evaluation. The mean patient age was 58 years (range, 26-77 years). Sixty-seven percent of patients were African American, 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 EN ISO 15197:2015 glucose distribution for accuracy evaluation were included in the healthcare provider accuracy analysis; an additional 11 samples contrived 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 EN ISO 15197:2015 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 y-intercept was –0.07 (SE ± 0.05) mmol/L. 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. EN ISO 15197:2015 Accuracy Results for Healthcare Professionals Using TRUE METRIX Versus YSI Reference Instrument

	Within ±0.28 mmol/L	Within ±0.56 mmol/L	Within ±0.83 mmol/L
Results <5.55 mmol/L	99/156 (63.5%)	135/156 (86.5%)	155/156 (99.4%)
	Within ±5%	**Within ±10%**	**Within ±15%**
Results ≥5.55 mmol/L	207/444 (46.6%)	364/444 (82%)	441/444 (99.3%)



A, Bias plot of all TRUE METRIX results versus YSI reference instrument results analyzed per the EN ISO 15197:2015 accuracy standard.
B, Parkes Error Grid of TRUE METRIX results versus YSI reference instrument results.

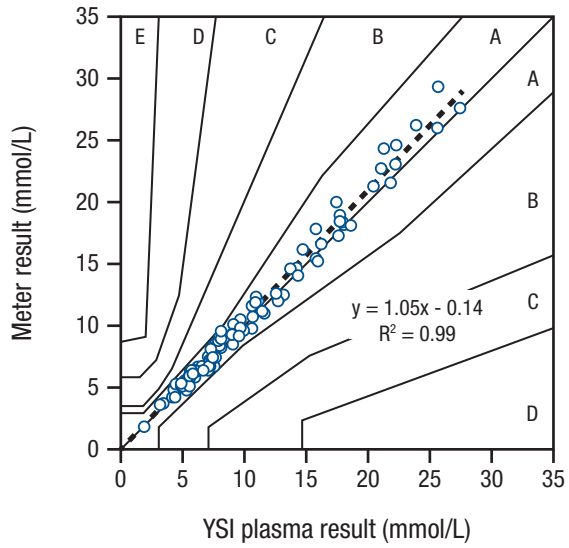
Figure 2. EN ISO 15197:2015 Accuracy Results for Healthcare Professionals Using TRUE METRIX Versus YSI Reference Instrument

User Evaluation

TRUE METRIX patient results also exceeded the minimum EN ISO 15197:2015 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 y-intercept was –0.14 (SE ± 0.15) mmol/L. 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. EN ISO 15197:2015 Accuracy Results for Patients Using TRUE METRIX Versus YSI Reference Instrument

	Within ±0.28 mmol/L	Within ±0.56 mmol/L	Within ±0.83 mmol/L
Results <5.55 mmol/L	9/18 (50%)	17/18 (94.4%)	18/18 (100%)
	Within ±5%	**Within ±10%**	**Within ±15%**
Results ≥5.55 mmol/L	39/82 (47.6%)	65/82 (79.3%)	81/82 (98.8%)



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

Figure 3. EN ISO 15197:2015 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 Blood Glucose Monitoring System, from Trividia Health, Inc., meets the accuracy criteria of the EN ISO 15197:2015 standard for self-testing blood glucose monitoring systems. Clinical study results demonstrate that both healthcare professionals and first-time patient users are able to achieve clinically 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 use by healthcare professionals and for self-testing by diabetes patients.

REFERENCES

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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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