

Evaluation of the Quo-Test A1C Assay at the John Radcliffe Hospital, Oxford, UK

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1. SUMMARY

An evaluation of the Quo-Test A1C assay was carried out in the Biochemistry department of the John Radcliffe Hospital in Oxford by an independent evaluator. Forty venous samples were run on two Quo-Test Analyzers and the results were compared with the Hospital's Menarini HA-8160 system. Results were compared for accuracy, precision and bias. The results of the study indicated that the Quo-Test Analyzer gave results which were substantially equivalent to the Menarini HA-8160 analyzer in accuracy ($r=0.987$, 95% limits of agreement -0.71 to 0.56%) and with no significant bias (-0.07 for the combined instruments). In conclusion, although the two systems use different methodologies for the measurement of HbA1c, the agreement between the two analyzers was excellent.

2. INTRODUCTION

The analytical performance of the Quo-Test A1C assay was assessed by running patient samples in the Biochemistry Department of the John Radcliffe Hospital, Oxford. The John Radcliffe Hospital was opened in the 1970s and is Oxfordshire's main accident and emergency site. It also provides acute medical and surgical services, trauma, intensive care, cardiac services, diabetes services and women's services. The John Radcliffe Hospital has over 700 inpatient

beds and nearly 100 day case beds (including the West Wing and Children's Hospital). It is the largest of the Trust's hospitals. It houses many departments of Oxford University Medical School, and is the base for most medical students who are trained throughout the Trust.

The primary intended use for the Quo-Test A1C assay is for use by Physician Office Laboratory (POL) staff (or equivalent), who will test patients using finger-stick or venous blood samples. The purpose of this evaluation was to establish the performance characteristics of the Quo-Test System when used by an independent evaluator. To that end, forty patient samples were analysed on two Quo-Test Analyzers. The results were compared with those reported by the Menarini HA-8160 analyzer, which is the system used by the hospital laboratory. The results were then analyzed for accuracy, precision and bias.

When comparing two (or more) systems for the measurement of A1C, it is important to consider the methodological variability which is derived from the type of assay used to measure the patient samples^{1,2}. There are four main methods commonly used in the measurement of A1C; Electrophoresis, HPLC, antibody affinity and boronate affinity. Whilst all of these methods are accepted and standardised for the measurement of A1C^{3,4}, it is also accepted that small discrepancies will be found between these methods when measuring A1C values in a patient population. The Menarini HA-8160 uses HPLC with reverse phase cation exchange chromatography to separate HbA1c from other types of haemoglobin. The Quo-Test A1C assay is a boronate affinity method.

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The acceptance criteria for the study were that the Coefficient of Variation (CV) for duplicate testing of the Quo-Test Assay on two separate Analyzers should be less than 5%. The mean bias between the two analyzers should be +/- 0.3 % A1c. The Correlation coefficient for all samples compared with the predicate device should be greater than $r = 0.95$. The 95 % limits of Agreement for the overall bias of the Quo-Test duplicate tests compared with the predicate assay should be within +/- 0.85 % A1c, this is according to guidelines issued by the National Glycohemoglobin Standardisation Program (NGSP)⁵, when comparing a device with a secondary reference method.

3. MATERIALS AND METHODS

Two Quo-Test Analyzers and a single lot (n° 13) of Quo-Test A1c test cartridges were used in the study. Forty venous blood samples were obtained from the Biochemistry department with blinded results obtained on the Hospital's Menarini HA-8160 analyzer.

The 40 blood samples were run in singlicate on each of the two Quo-Test analyzers. The results from each analyzer were then compared with the results of the Menarini HA-8160 for accuracy and bias. The Quo-Test results for both analyzers were then pooled and all 80 results were compared with the Menarini results and finally the results from the two Quo-Test analyzers were compared with each other to determine inter-analyzer variation.

4. RESULTS

The results obtained with Analyzer 1 (Figure 1a and 1b) and 2 (Figure 2a and 2b) were in first instance compared individually with the results from the Menarini HA-8160 for accuracy and bias using a scatter diagram and a Bland Altman plot.

For Analyzer 1, the Pearson's correlation coefficient was $r = 0.987$, the bias was -0.09 % A1c and the 95 % limits of agreement for the bias were -0.72 % to +0.55 % A1c. Similarly for Analyzer 2, the Pearson's correlation coefficient was $r = 0.987$, the bias was -0.06 % A1c and the 95 % limits of agreement for the bias were -0.7 % to +0.58 % A1c. All the results were within acceptable limits.

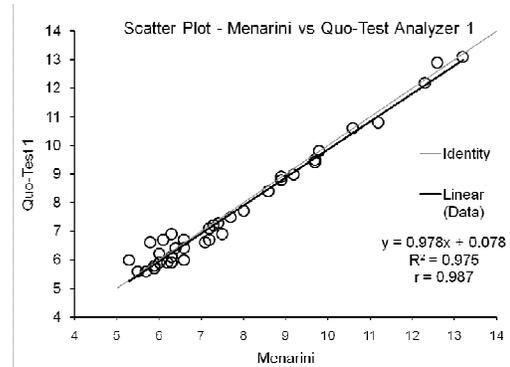


Figure 1a: Scatter Diagram for Quo-Test Analyzer 1 versus the laboratory reference method, Menarini HA-8160.

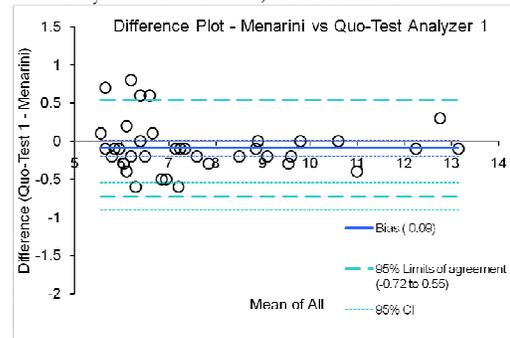


Figure 1b: Bland Altman plot for Quo-Test Analyzer 1 versus the laboratory reference method, Menarini HA-8160.

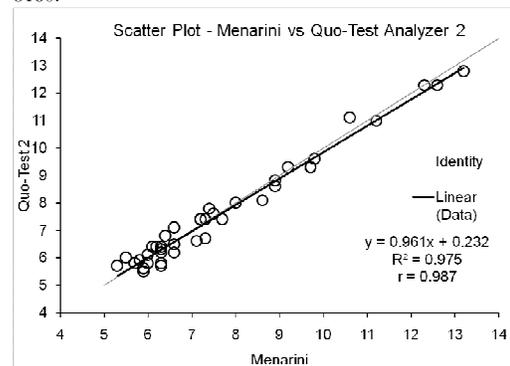


Figure 2a: Scatter Diagram for Quo-Test Analyzer 2 versus the laboratory reference method, Menarini HA-8160.

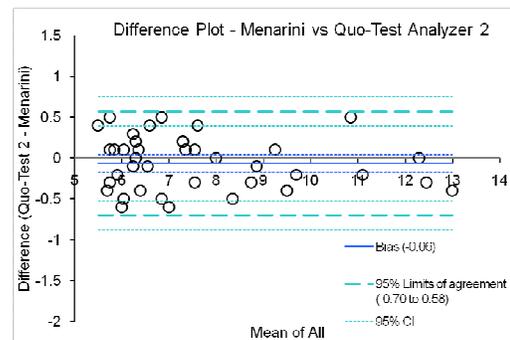


Figure 2b: Bland Altman plot for Quo-Test Analyzer 2 versus the laboratory reference method, Menarini HA-8160.

5. Discussion

Combined Quo-Test Results: The results for Analyzers 1 and 2 were combined and were compared with the results from the Menarini HA-8160 for accuracy and bias (see Figures 3a and 3b). The results were combined to give an indication of the level of performance observed if a laboratory were running two Quo-Test Analyzers in the same or different laboratories. It can be seen that the Pearson's correlation coefficient was $r = 0.987$, the bias was -0.07% A1c and the 95% limits of agreement for the bias were -0.71% to $+0.56\%$ A1c. All the results were within acceptable limits, indicating that running two Analyzers still produced excellent results.

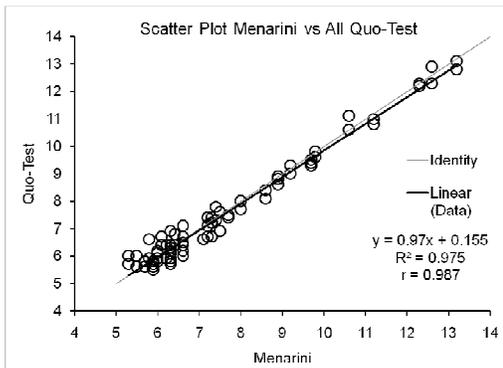


Figure 3a: Scatter diagram of combined analyzer results versus laboratory reference results.

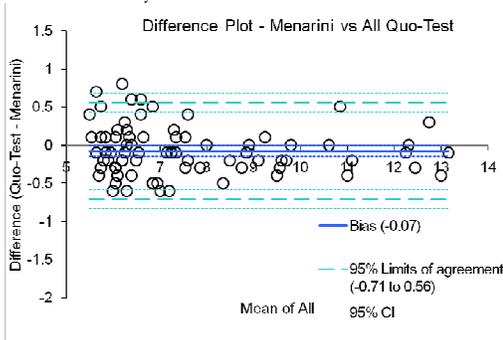


Figure 3b: Bland Altman plot for combined analyzer results versus laboratory reference results.

Comparison between the Quo-Test Analyzers:

When the two Analyzers were compared between themselves, no significant instrument to instrument variation was found. From Figures 4a and 4b, it can be seen that the mean bias (Quo-Test Analyzer 1 result – Analyzer 2 result) was $+0.03\%$ A1c. In addition, the 95% confidence intervals for the bias include zero. Therefore the difference between the two

Analyzers was not statistically significant thus indicating that the results produced by the two Analyzers were indistinguishable from each other.

The co-efficient of variation (CV) for the duplicate results was then calculated for each pair. The overall CV was found to be 3.21% , which was acceptable.

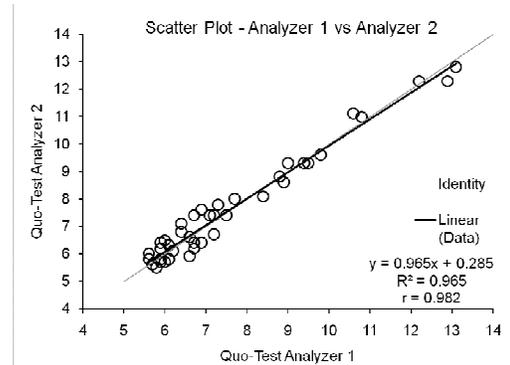


Figure 4a: Scatter plot for the comparison between the two Quo-Test analyzers.

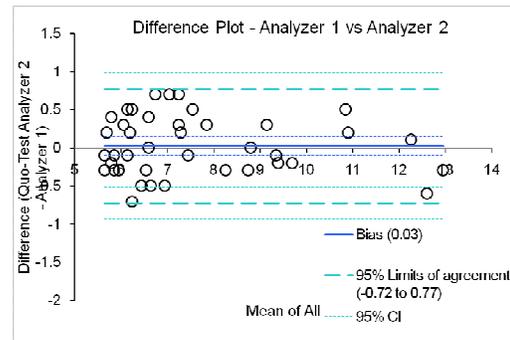


Figure 4b: Bland-Altman plot for the comparison between the two Quo-Test Analyzers.

6. Conclusion

Although the two systems use different methodologies for the measurement of HbA1c, the agreement between the two analyzers was excellent. A summary of the results can be seen in the Table below.

	Quo-Test Analyzer 1	Quo-Test Analyzer 2	Quo-Test Combined
Number of Samples	40	40	80
Pearson's Correlation	$r = 0.987$	$r = 0.987$	$r = 0.987$
Bias (% A1c)	-0.09	0.06	-0.07
95 % Limits of Agreement	-0.72 to 0.55%	-0.7 to 0.58%	-0.71 to 0.56%

The results of the study indicated that the Quo-Test Analyzer gave results which were substantially equivalent to the Menarini HA-8160 analyzer in accuracy and with no significant bias. In addition, even when the results of the two Quo-Test Analyzers were compared with the Hospital's method, the total error was within the exacting performance criteria of the National Glycohemoglobin Standardisation Program (NGSP).

7. References

1. Evaluation of HbA1c determination methods in patients with haemoglobinopathies. W. Schnedl *et al.* Diabetes Care 23:339-344 2000.
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4. Little RR, Wiedmeyer HM, England JD, *et al.* Interlaboratory standardization of measurements of glycated hemoglobin. Clin Chem 38:2472-78 1992.
5. Website of the National Glycohemoglobin Standardisation Program (NGSP):
<http://www.ngsp.org/prog/index.html>