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HbA_{1c} point-of-care testing: analytical performance in the EurA1c external quality assessment trial involving 40 centers in Italy

Glycated hemoglobin (HbA_{1c}) has been the gold standard for assessing glycemic control in patients with diabetes for many years. Since 2011, the World Health Organization has also promoted its use for the diagnosis of type 2 diabetes mellitus.[1] This indication has subsequently been incorporated into major international recommendations, including the American Diabetes Association's Standards of Care, consolidating the role of HbA_{1c} in both therapeutic monitoring and diagnosis.

In this context, point-of-care testing (POCT) systems are a technology of growing interest, as they allow rapid measurements to be performed close to the patient. The claimed ease of use makes them suitable for use in community settings and peripheral healthcare facilities, where they can support decentralized care models and facilitate access to diabetes monitoring. However, the key issue remains the analytical quality of POCT systems.

Previous studies have evaluated HbA_{1c} POCT performances and compared different models, using external quality assessment schemes (EQAS) based mainly on lyophilized matrix;[2, 3] however, data obtained within EQAS using fresh whole blood samples assigned by IFCC reference methods remain relatively limited.[4] In order to be considered clinically reliable, these instruments must meet quality criteria agreed upon by the scientific community. This Letter aims to contribute to further evidence on the reliability of the POCT systems for HbA_{1c}.

The Committee on Education in the Use of Biomarkers in Diabetes (C-EUBD) defined a total allowable error criterion of ±5 mmol/mol at a value of 50 mmol/mol. This threshold is based on the assumption that a change in therapy will only be considered if there is a change in HbA_{1c}≥5 mmol/mol in closely spaced measurements. However, it has been claimed that this level of performance is insufficient for the diagnostic use of HbA_{1c}[5] and a value of 3 mmol/mol has been proposed.[6]

EQAS programs are a fundamental tool for verifying analytical performances and enabling comparison between analytical platforms and laboratories. Since 2016, the Tuscany Regional Reference Centre for EQA (CRRVEQ) has been participating in the international IFCC/EUBD EurA1c trial, which in one of the study arms distributes fresh whole blood samples with HbA_{1c} values assigned.[7]

The samples are prepared from blood donations and distributed under controlled conditions to participating laboratories. The HbA_{1c} value is assigned by reference measurement procedures performed in laboratories belonging to the IFCC reference network.[8]

In the 2025 cycle, in addition to the established group of participating laboratories (N.=48), the CRRVEQ recruited 40 non-hospital facilities equipped with POCT systems for HbA_{1c} measurement.

In accordance with the trial protocol, these facilities received two fresh blood samples, one with an HbA_{1c} concentration close to the diagnostic decision limit (Sample 1, HbA_{1c}=45.9 mmol/mol) and the other with an HbA_{1c} concentration close to the therapeutic target for diabetes (Sample 2, HbA_{1c}=58.8 mmol/mol). The measurements were performed within the defined time window to guarantee sample stability, and the results were transmitted to the trial manager. While awaiting the comprehensive international report, including data from all participants and scheduled for October 2026, the CRRVEQ conducted a preliminary analysis of the available results.

This preliminary assessment examined the distribution of the data, as well as the analytical accuracy and precision of the measurements, and the ability of the methods to meet the predefined quality criteria in both the POCT and High Performance Liquid Chromatography/Capillary Electrophoresis (HPLC/CE) groups.

Particular attention was given to the POCT systems, with the aim of highlighting possible differences compared with laboratory-based methods and of evaluating the analytical accuracy of the results obtained with these devices.

The distribution of all results obtained by the different analytical platforms was assessed using the Shapiro-Wilk Test to evaluate the assumption of normality. Overall, 170 results were included in the analysis. The analytical systems (N.>7) showed normally distributed results ($p>0.05$). Subsequently, the analytical performances of the systems were evaluated in terms of imprecision and accuracy.

When imprecision was evaluated, we found that for the two target values (45.9 mmol/mol sample 1 and 58.8 mmol/mol sample 2), the coefficient of variation ranged from 3.2% (sample 1) and 2.3% (sample 2) (TOSOH G11, Tosoh Bioscience, Tokyo, Japan) to 5.1% (sample 1) and 3.9% (sample 2) (POCT Roche Cobas b101, Roche Diagnostics, Mannheim, Germany), respectively. The Feltz–Miller test did not show statistically significant differences in imprecision between these two platforms for either target value (χ^2=1.02, $p=0.31$ for sample 1; χ^2=1.27, $p=0.26$ for sample 2).

However, this observation was not confirmed when the entire group of POCT systems recruited by CRRVEQ was considered. The Feltz and Miller asymptotic test for equality of Coefficient of variation (CV) yielded a statistically significant difference between POCT (N.=40) and laboratory instruments (N.=48) for both samples (sample 1: χ^2=12.46 and $p<0.001$; Sample 2: χ^2=11.03 and $p=0.0009$), suggesting higher analytical variability in POCT systems.

Regarding accuracy, we observed for Tosoh G11 fairly differ-

TABLE I.—*Number and percentage of acceptable (YES) and unacceptable (NO) results obtained with different analytical systems, on the two blood samples analyzed within the 2025 cycle of the EurA1c trial. The acceptability of the results was assessed based on a total allowable error (TEa) of 5 mmol/mol and 3 mmol/mol.*

Analytical system	N.	TEa=5 mmol/mol				TEa=3 mmol/mol			
		Sample 1 45.9 mmol/mol		Sample 2 58.8 mmol/mol		Sample 1 45.9 mmol/mol		Sample 2 58.8 mmol/mol	
		Yes	No	Yes	No	Yes	No	Yes	No
POCT									
Abbott/Alere Afinion	1	1	0	1	0	1	0	0	1
AFIAS-1 Menarrini	2	1	1	1	1	0	2	1	1
Boditech I-Chroma	1	0	1	0	1	0	1	0	1
Callegari Clini 5	2	1	1	0	2	1	1	0	2
Roche Cobas b 101	27	24	3	24	3	15	12	19	8
Simplex TAS 101 (enzymatic)	1	1	0	0	1	1	0	0	1
Voden Vchemys	4	1	3	3	1	0	4	2	2
Wondfo Finecare FIA Meter	2	1	1	1	1	1	1	0	2
All (%)	40 (100)	30 (75)	10 (25)	30 (75)	10 (25)	19 (47.5)	21 (52.5)	22 (55)	18 (45)
Other Systems									
Abbott Alinity	1	1	0	1	0	1	0	1	0
Arkray Adams HA-8380 series	1	1	0	1	0	1	0	1	0
Bio-Rad D-10 series	3	3	0	2	1	2	1	0	3
Bio-Rad Variant series	1	1	0	1	0	1	0	1	0
Menarini (Arkray) HA-8160 series	1	1	0	1	0	1	0	0	1
Menarini HbNEXT	4	4	0	4	0	4	0	4	0
Roche Cobas c 501/502 (6000/8000)	7	7	0	7	0	7	0	5	2
SEBIA Capillarys 2	2	2	0	2	0	2	0	2	0
SEBIA Capillarys 3	11	10	1	11	0	10	1	11	0
SEBIA Minicap	3	3	0	3	0	3	0	3	0
Siemens Atellica CH (enzymatic)	1	1	0	1	0	1	0	1	0
Tosoh G11	8	8	0	8	0	8	0	5	3
Tosoh G8	4	3	1	3	1	3	1	3	1
Trinity Biotech Premier Hb9210	1	1	0	1	0	1	0	1	0
All (%)	48 (100)	46 (95.8)	2 (4.2)	46 (95.8)	2 (4.2)	45 (93.8)	3 (6.3)	38 (79.2)	10 (20.8)

ent biases for the two samples (-0.05% for sample 1 and 5.9% for sample 2), while POCT Roche Cobas b101 showed a marked negative bias (-4.3% for both samples). For SEBIA Capillarys 2 and 3, the estimated biases were -1.4% for sample 1 and -0.4% for sample 2, although the small sample sizes preclude a robust evaluation.

Using a descriptive statistical analysis, the ability of the analytical systems to meet predefined quality criteria was evaluated. When considering a Total Allowable Error (TEa) of ±5 mmol/mol, POCT systems showed, overall, a percentage of acceptable results equal to 75%. HPLC/CE systems, applying the same TEa, showed a higher percentage of acceptability, reaching 95.8%.

When the evaluation was repeated using the more stringent criterion of TEa (±3 mmol/mol, the percentage of acceptable results in POCT systems was markedly reduced, setting overall at around 48-55%, although differences between instruments were observed. A decline in performance was also observed in HPLC/CE systems, albeit to a lesser extent, with the overall percentage of acceptable results ranging between 79-94%, confirming however greater analytical robustness compared with POCT even under more restrictive evaluation conditions (Table I).

Given the relatively limited number of users for some analytical systems, these estimates should be interpreted with caution and primarily considered as indicative of overall analytical trends, particularly in light of the fact that the POCT group was largely dominated by the Roche Cobas b101 system (27 out of 40 determinations), while other devices were represented by very small sample sizes. As a consequence, the aggregated POCT results are strongly influenced by this system and should be interpreted with caution when generalizing to the entire POCT category. However, the results suggest that the Cobas b101 may exhibit a systematic negative bias, consistent across the evaluated HbA_{1c} levels, and a lower analytical accuracy compared with non POCT platforms. This negative bias may be related to matrix effects or other analytical factors, which should be further investigated.

Factors such as operator-dependent variability, environmental conditions, or limitations in the instrument's analytical range could contribute to the high variability observed across the POCT group.

In conclusion, the use of some POCT analytical systems for measuring HbA_{1c} may appear adequate for monitoring diabetes in specific settings, when current TEa criteria are applied. However, general statements regarding the analytical performance of HbA_{1c} POCT systems should be made with caution, given the high variability observed and the possible bias. Furthermore, the application of more stringent quality criteria, such as TEa=3 mmol/mol, highlights significant limitations not just for POCT, but also for several laboratory-based instruments.

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Conflicts of interest
The authors certify that there is no conflict of interest.

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