

9th International Scientific Meeting
**STRUCTURING EQAS FOR MEETING
METROLOGICAL CRITERIA:
READY FOR PRIME TIME**

MILANO, ITALY
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AULA MAGNA - SETTORE DIDATTICO COLOMBO
Università degli Studi
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*The SIBioC experience

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*Outline

1. Actual requirements for obtaining and assessing HbA_{1c} standardization in Italy
2. SIBioC 2014 EQAS
3. Future perspectives

1. Actual requirements for obtaining and assessing HbA_{1c} standardization in Italy
2. SIBioC 2014 EQAS
3. Future perspectives

Recommendations for the implementation of international standardization of glycated hemoglobin in Italy¹⁾

Recommendation no. 1

1. The goal of the total allowable error is $\pm 6.7\%$ (as a percentage fraction of the absolute HbA_{1c} value).
2. The long-term imprecision of the method should be no more than 2%.
3. Participating in EQAS programs, in which commutable materials are used, and adopting HbA_{1c} values assigned using the IFCC reference measurement procedure, are the best way to establish whether measurements that are obtained meet the standards for total error stated above.

Recommendation no. 3

1. HbA_{1c} should be measured using methods calibrated to the IFCC reference system.
2. The result should be reported in mmol/mol and % units derived using the conversion equation described above.
3. For a limited period of time, the HbA_{1c} value will be expressed in laboratory reports using conventional units (%) followed by the IFCC units (mmol/mol). The conventional units will subsequently be omitted.

Table 1. Biological variation in Hb A_{1c} and estimated analytical goals related to the NGSP and IFCC measurement systems, as expressed in the Hb A_{1c} concentration unit of measure (percentage and millimoles per mole, respectively) and as a percentage of the Hb A_{1c} measured.

Parameter	NGSP system		IFCC system	
	Unit of measure, %	Percentage	Unit of measure, mmol/mol	Percentage
Biological variation				
Mean Hb A _{1c}	4.90		30.0	
Intraindividual variation	0.08 (as SD)	1.6%	0.88 (as SD)	2.9%
Interindividual variation	0.20 (as SD)	4.1%	2.20 (as SD)	7.3%
Reference interval (95% central interval)	4.50–5.30	92%–108%	25.6–34.4	85%–115%
Analytical goals (biological variation)^a				
Imprecision	0.04	0.8%	0.44	1.5%
Bias	0.05	1.1%	0.59	2.0%
Total error	0.12	2.4%	1.32	4.4%
Analytical goals (outcome based)^b				
Imprecision	0.15	2.0%	1.6	2.8%
Total error	0.50	6.7%	5.0	8.6%

^a Calculated according to Fraser et al. (5).

^b Calculated according to Mosca et al. (4).

Linee guida per la gestione dei programmi di Valutazione Esterna di Qualità

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ABSTRACT

Guidelines for External Quality Assessment Scheme organization. This document describes a model for EQAS organization based on the following principles: 1) education, i.e. EQAS should be intended more for quality improvement than for surveillance of laboratory proficiency, even if they should require corrective actions in case of poor performance, 2) organization by a third party, independent of manufacturers producing reagents or analytical systems and operating according to the ISO 17043 standard, and 3) use of commutable materials to provide information on the trueness of measurements. Optimal characteristics, structure, and organization EQAS shall have to be recognised by SIBioC are described. Special schemes for pre- and post-analytical phases are also considered.

1. Actual requirements for obtaining and assessing HbA_{1c} standardization in Italy
2. **SIBioC 2014 EQAS**
3. Future perspectives

Principal EQAS exercises for HbA_{1c}

<i>Program</i>	<i>Country</i>	<i>Sample</i>	<i>HbA_{1c} title</i>
CRB Castelfranco V.	Italy	Lyophilized	Target
Regional (Careggi)	Italy	Lyophilized	Consensus mean
CAP	USA	Blood	Target
CTCB	France	Blood	Consensus mean
EQAS Bio-Rad	USA	Lyophilized	Consensus mean
Equalis	Sweden	Blood	Target
ERL	The Netherlands	Lyophilized	Target
Probioqual	France	Lyophilized	Consensus mean
UKNEQAS	UK	Blood	Target

Feasibility of an EQAS for HbA_{1c} in Italy using fresh blood samples

Clin Chem Lab Med 2014;52(7): e151-e153

1 fresh blood sample
10 laboratories

- Shipment, room temperature
 - ~~priority mail~~
 - courier **OK** (within 4 days)



- Checking the stability at room temperature

Table 1 Stability of HbA_{1c} (mmol/mol) during storage at room temperature.

Method	Basal	After 4 days	After 7 days
Menarini 8180 V	44.3±0.5	43.7±0.7	41.9±0.9 ^a
Trinity Premier 9210	45.0±0.7	44.2±0.8	42.0±0.6
Sebia Capillarys	45.5±0.8	44.7±0.7	42.5±0.8 ^a
Mean±SD	44.9±0.6	44.2±0.5	42.1±0.3 ^b

^aAbnormal peaks appearing in the chromatograms and in the electropherograms; ^bp=0.002 respect to basal (t-test).

4 days at room temperature

➤ Results (10 selected Italian laboratories)

<i>Method</i>	<i>HbA_{1c} mmol/mol</i>	<i>DS mmol/mol</i>	<i>n</i>
Tosoh G8	46.2	1.3	5
Bio-Rad Variant II	44.3	1.5	3
Roche Tina-quant	44.0	--	1

No abnormalities in the chromatograms

➤ Conclusions

➔ EQAS with fresh blood is feasible



EQAS SIBioC 2014 for HbA_{1c}

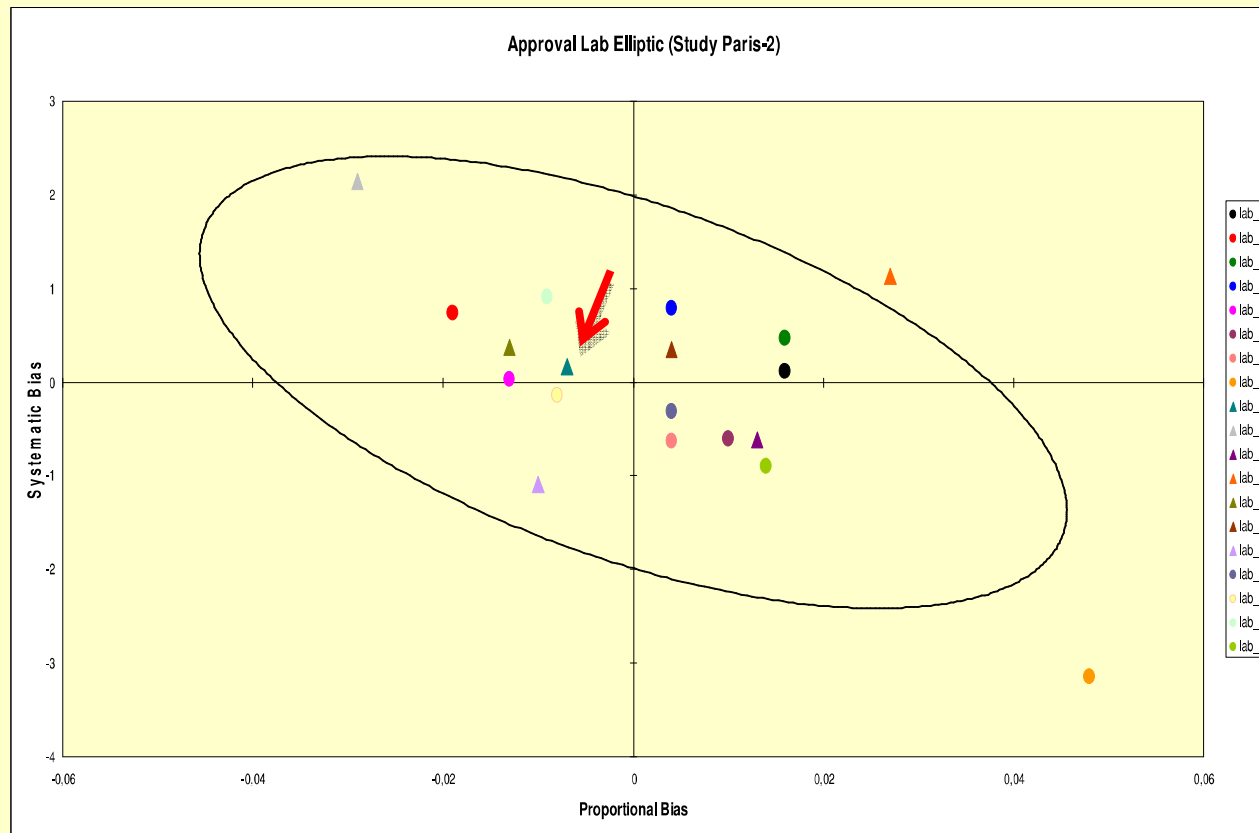


- December 2014
- 2 samples of fresh blood 500 μ L (single donation)
- Shipment by courier at room temperature
- 206 laboratorists
- Main actual methods well represented (Bio-Rad, Menarini, Roche, Sebia, Tosoh)
- Measurements within a few days after receiving the samples
- Survey on the Internal Quality Control data of the last month



➤ Target HbA_{1c} values

Assigned by the IFCC reference measurement procedure (HPLC-CE).



➤ Limits of acceptability

1. TE calculated from clinical needs ($\pm 8.6\%$)
2. TE calculated with more stringent criteria ($\pm 6.0\%$)

Results

❖ Shipment

Total No. of shipments: 206

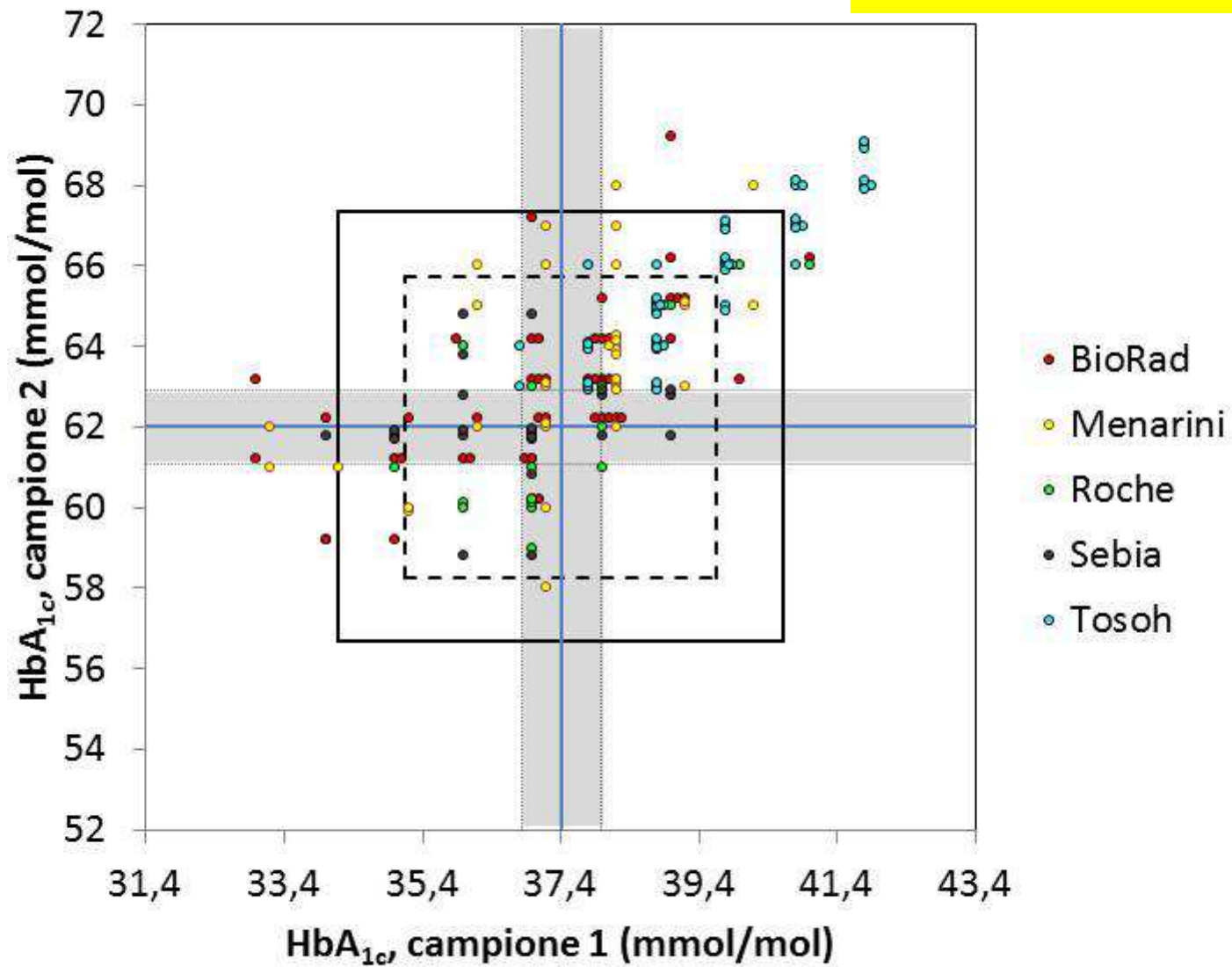
Total provided data: 193 → **93.7 % of all shipments**

❖ Global variability

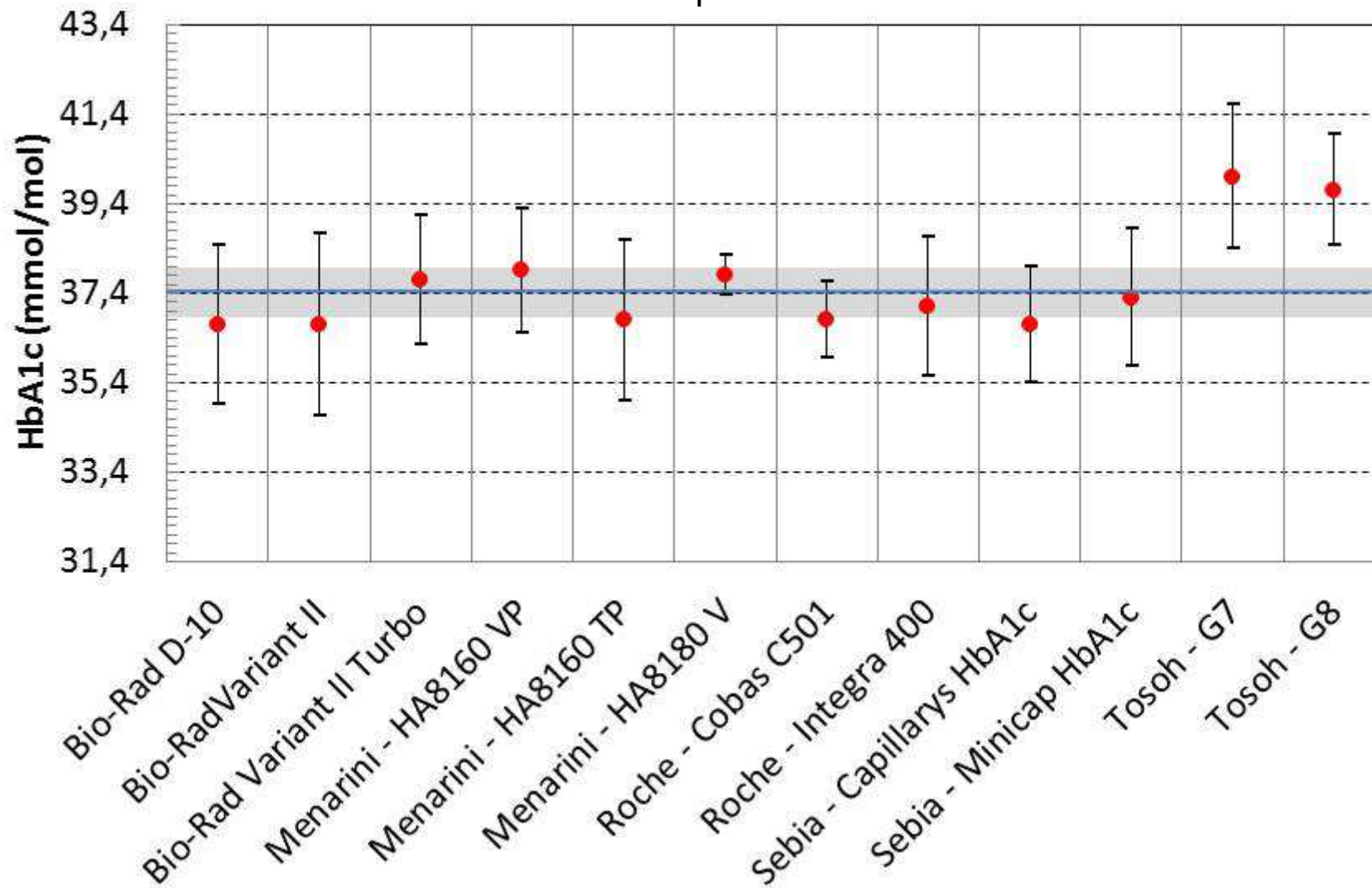
	Mean <i>mmol/mol</i>	SD <i>mmol/mol</i>	CV %	n	Valore Met. Rif.	Bias %
Sample 1	37.9	2.0	5.3	191	37.4 ±	1.3
Sample 2	63.7	2.4	3.8	189	62.0 ±	2.7

0.83

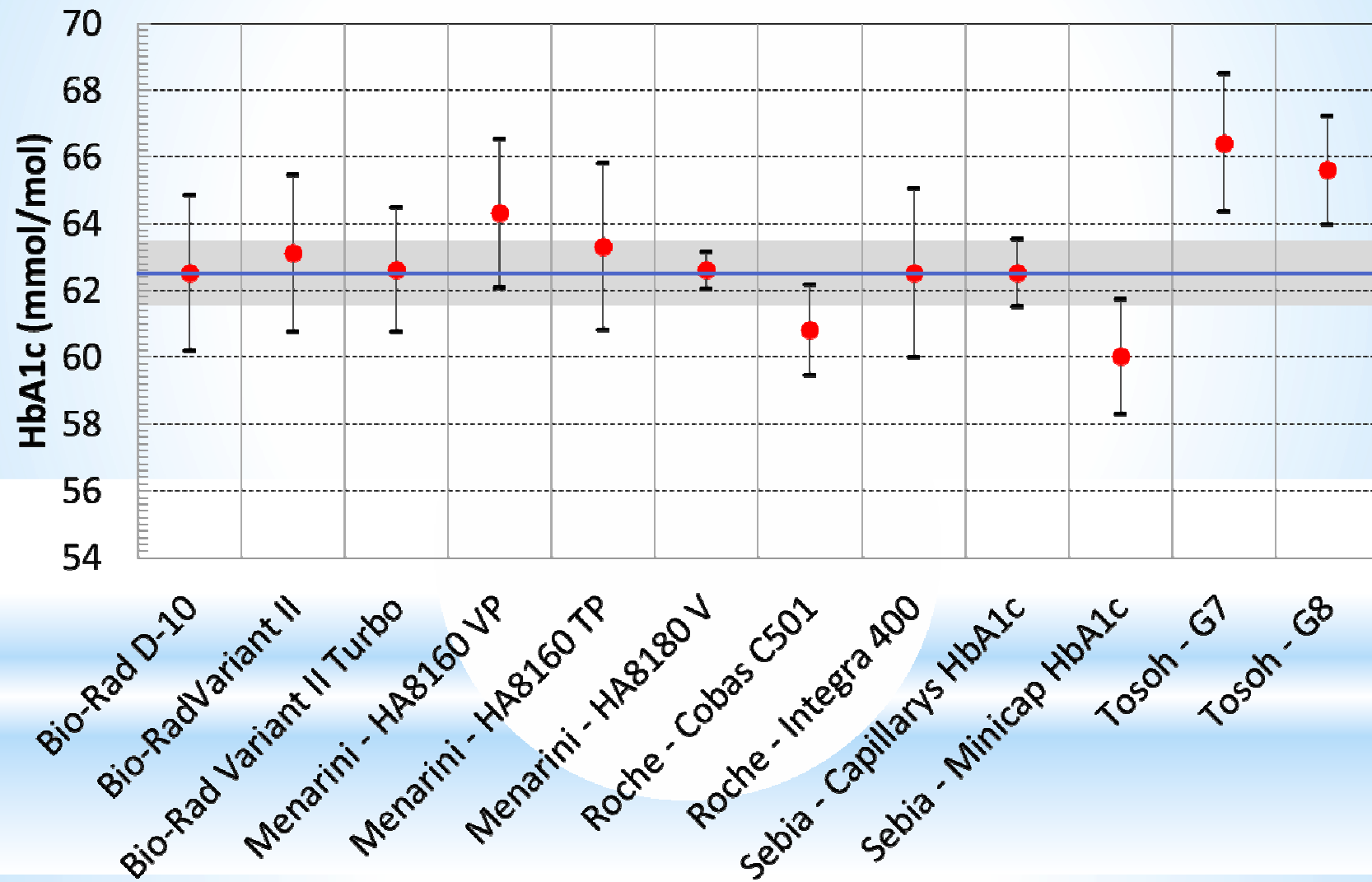
Youden plot

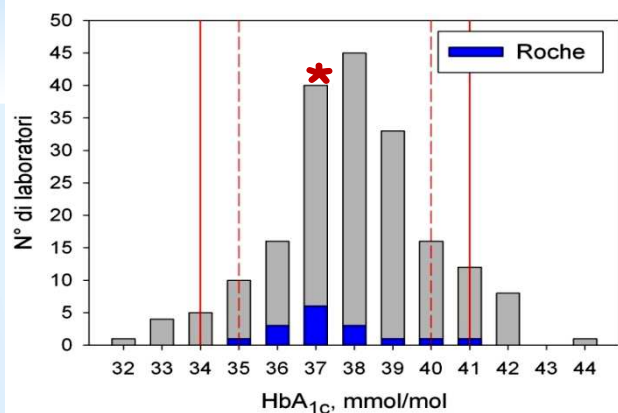
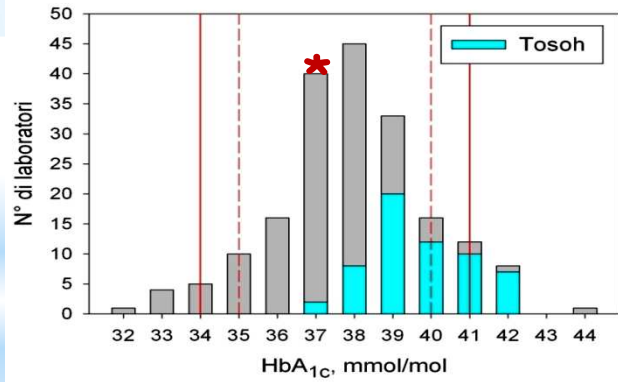
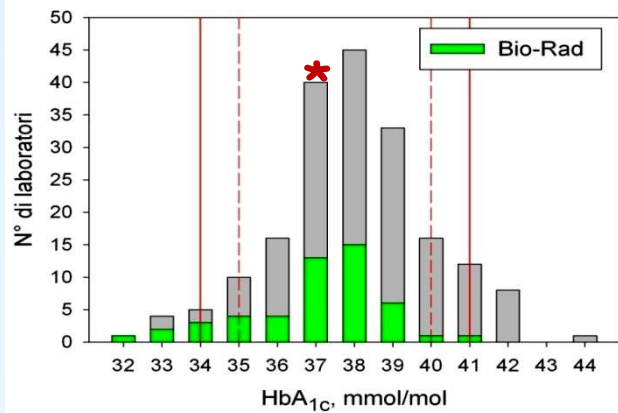


Sample 1

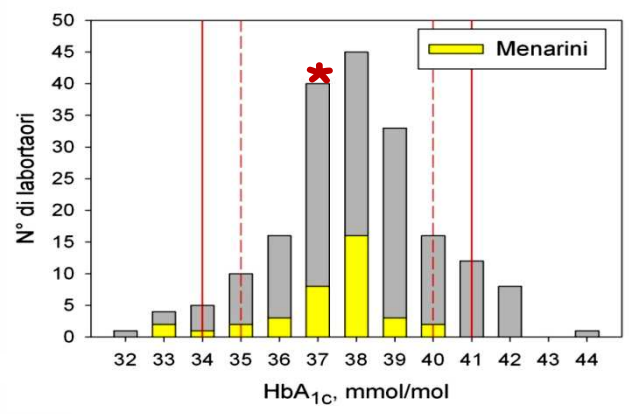


Sample 2

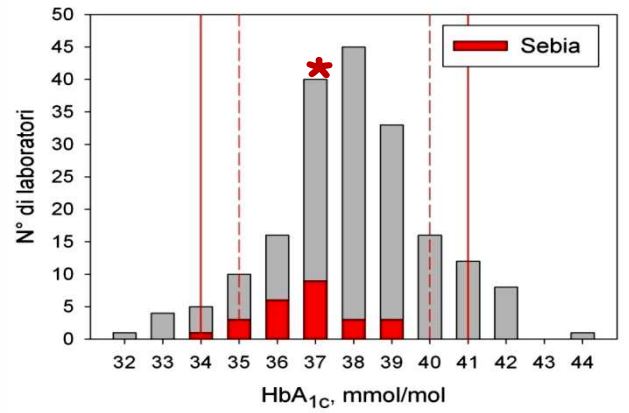


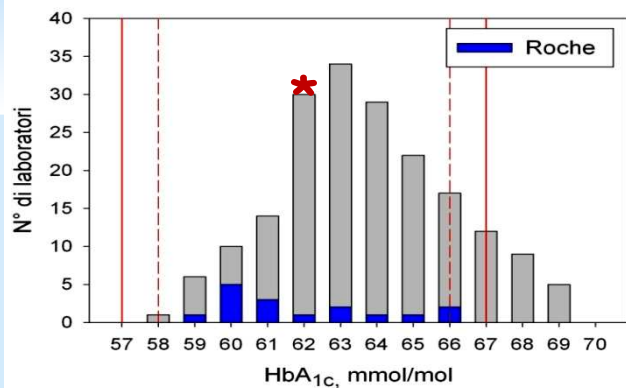
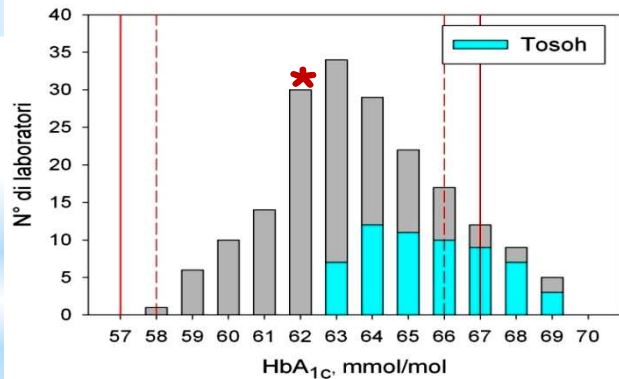
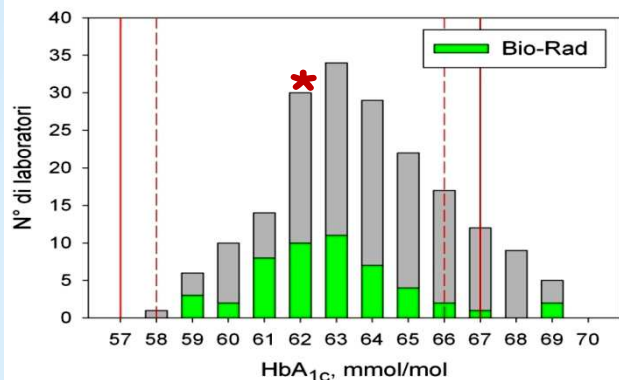


——— TE = ±8.6%
- - - TE = ±6.0%

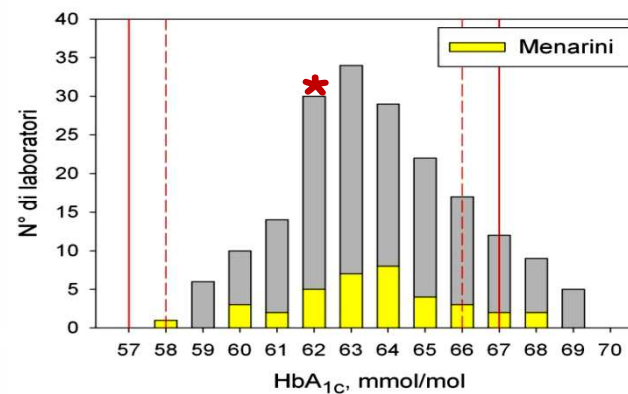


Sample 1

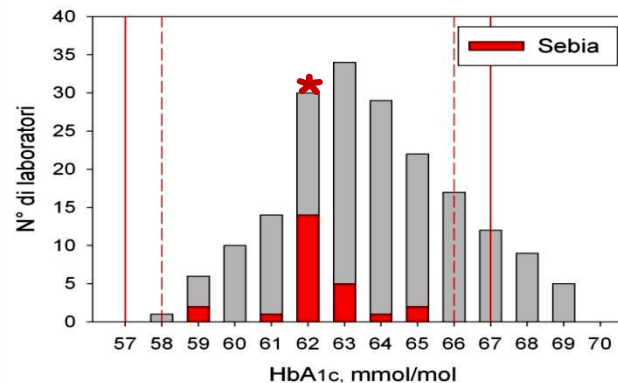




————— TE = ±8.6%
 - - - - - TE = ±6.0%



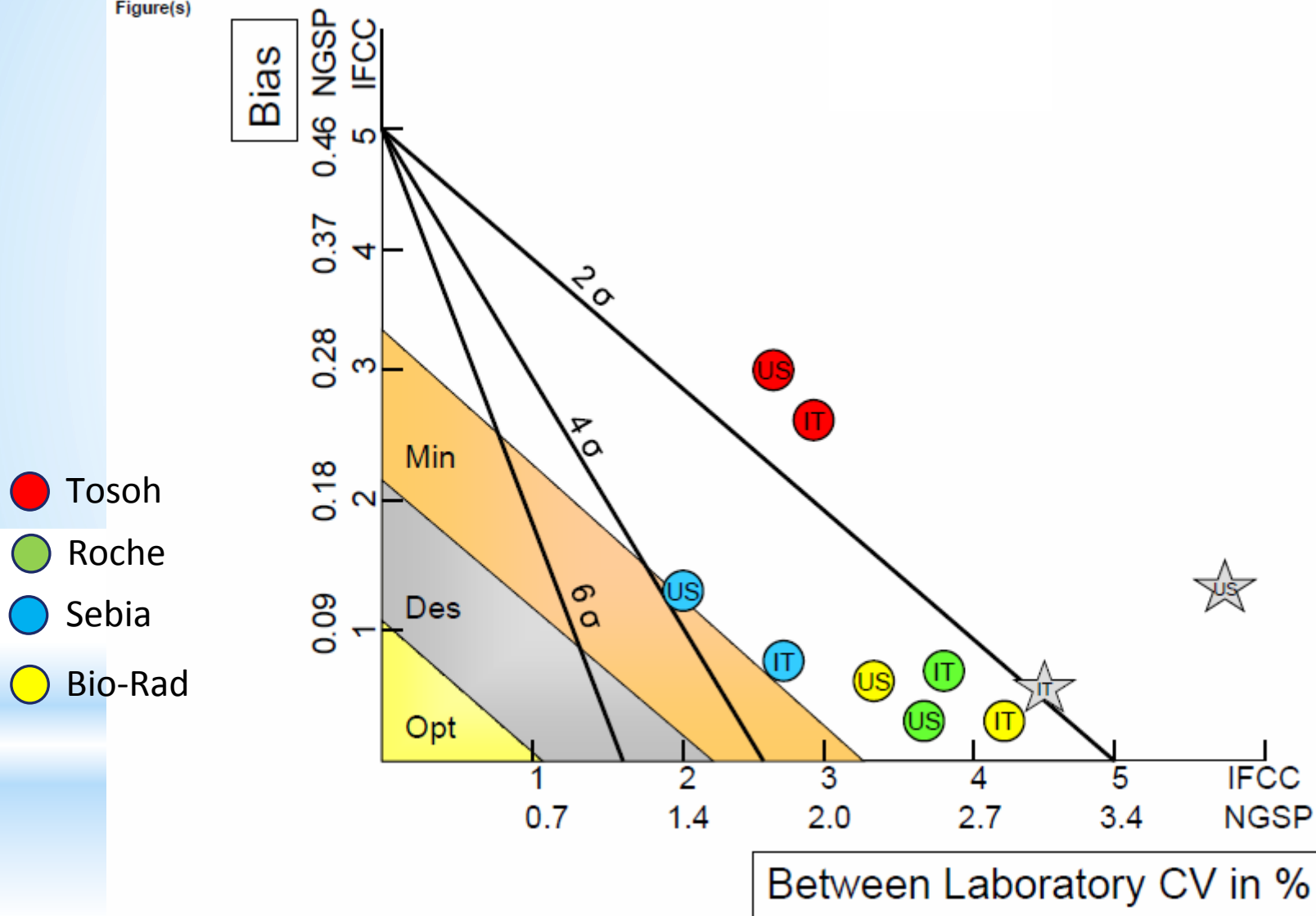
Sample 2



Tab.1. Results of the study grouped by method and instruments

Methods and Instruments	Sample 1					Sample 2				
	<i>N° labs (outliers)</i>	<i>Mean mmol/mol</i>	<i>SD mmol/mol</i>	<i>CV %</i>	<i>N° labs within TAE 6.0 %</i>	<i>N°labs (outliers)</i>	<i>Mean mmol/mol</i>	<i>SD mmol/mol</i>	<i>CV %</i>	<i>N° labs within TAE 6.0 %</i>
Abbott Architect c4000	1 (0)	37.0	--	--	1 (100)	1 (0)	63.0	--	--	1 (100)
B-Analyst	1 (0)	37.0	--	--	1 (100)	1 (0)	63.0	--	--	1 (100)
Bio-Rad D-10	11 (2)	36.7	1.79	4.9	9 (82)	11 (2)	62.5	2.34	3.7	10 (91)
Bio-Rad Variant II	25 (1)	36.7	2.03	5.5	19 (76)	25 (1)	63.1	2.35	3.7	22 (88)
Bio-Rad Variant IITurbo	14(0)	37.7	1.44	3.8	12 (86)	14 (0)	62.6	1.86	3.0	13 (93)
Menarini - HA8160 VP	12 (0)	37.9	1.38	3.6	9 (75)	12 (0)	64.3	2.23	3.5	8 (67)
Menarini - HA8160 TP	20 (0)	36.8	1.80	4.9	17(85)	20 (0)	63.3	2.49	3.9	16 (80)
Menarini - HA8180 V	5 (0)	37.8	0.45	1.2	5 (100)	5 (0)	62.6	0.55	0.9	5 (100)
Roche - Cobas C501	11(0)	36.8	0.84	2.3	10 (91)	11 (0)	60.8	1.36	2.2	11 (100)
Roche - Integra 400	3 (0)	37.1	1.55	4.2	3 (100)	3 (0)	62.5	2.53	4.0	3 (100)
Roche - Modular	2 (0)	40.5	--	--	0 (0)	2 (0)	66.0	--	--	0 (0)
Sebia - Capillarys HbA1c	22 (0)	36.7	1.29	3.5	18 (82)	22 (0)	62.5	1.01	1.6	22 (100)
Sebia - Minicap HbA1c	3 (0)	37.3	1.53	4.1	3 (100)	3 (0)	60.0	1.73	2.9	3 (100)
Tosoh - G7	8 (0)	40.0	1.60	4.0	3 (38)	8 (0)	66.4	2.07	3.1	3 (38)
Tosoh - G8	49 (0)	39.7	1.24	3.1	25 (51)	49 (0)	65.6	1.63	2.5	25 (51)
Tosoh - GX	2 (0)	37.5	--	--	0 (0)	2 (0)	63.0	--	--	2 (100)
Other	1 (0)	42.0	--	--	0 (0)	0 (1)				

Figure(s)





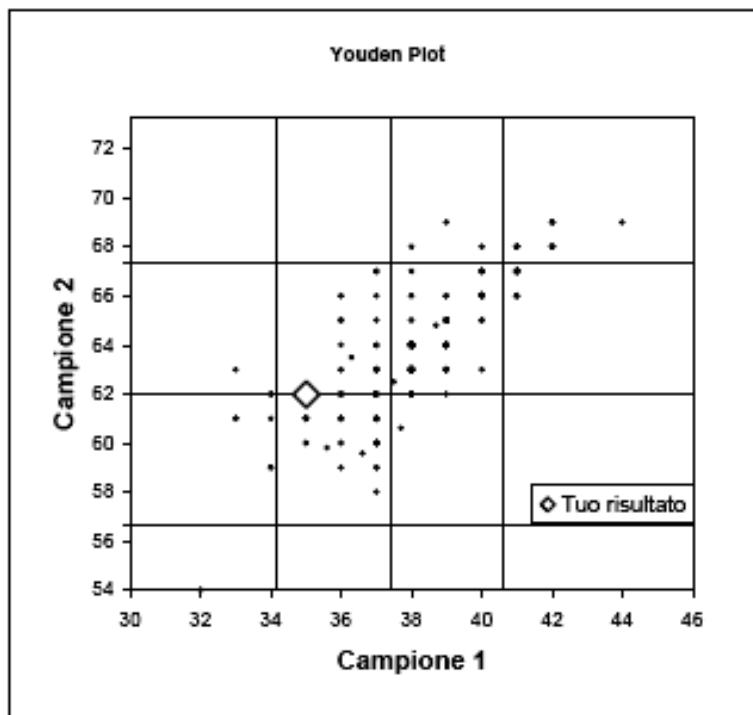
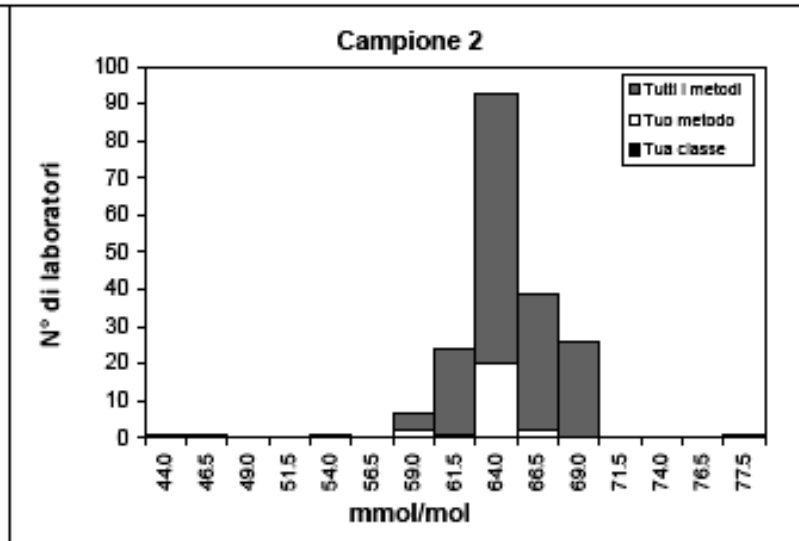
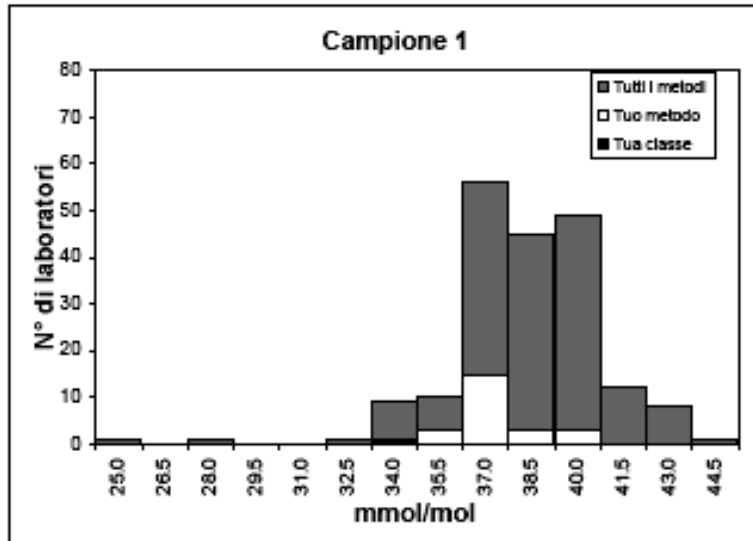
VEQ HbA_{1c} SIBioC 2014

Lab	Servizio di Medicina di Laboratorio Ospedale San Raffaele - Milano
Lab ID	14007
Data dell'esercizio	Ottobre 2014

Analita	HbA _{1c}
Unità	mmol/mol
Gruppo di metodo	SEBIA
Analizzatore	Sebia - Capillarys HbA _{1c}

	Tuo risultato	Valore Metodo Riferimento	Media di Gruppo	Errore Totale della misura	ET _a	Score
Campione 1	35	37.4	36.8	-6.4%	± 8.6%	75
Campione 2	62	62.0	62.2	0.0%	± 8.6%	0

Gruppo di Metodo	Campione 1					Campione 2				
	N (outliers)	Media mmol/mol	DS mmol/mol	CV%	Tuo z	N (outliers)	Media	DS	CV%	Tuo z
Tutti i dati (outliers esclusi)	193 (2)	37.9	2.03	5.3%		191 (4)	63.6	2.40	3.8%	
BIORAD	50 (3)	37.0	1.85	5.0%		50 (3)	62.9	2.19	3.5%	
MENARINI	37 (0)	37.3	1.63	4.4%		37 (0)	63.5	2.28	3.6%	
ROCHE	18 (0)	37.2	1.55	4.2%		18 (0)	61.7	2.16	3.5%	
SEBIA	25 (0)	36.8	1.30	3.5%	1.4	25 (0)	62.2	1.36	2.2%	0.2
TOSOH	59 (0)	39.7	1.33	3.3%		59 (0)	65.6	1.74	2.7%	
Altri metodi	3 (0)	38.6				3 (0)	67.7			



A.

Internal Quality control

n = 193 IQC expected

n = 176 IQC received (91 %)

- 19 HbA_{1c} expressed in %

- 3 difficult to be interpreted

n = 15 IQC analyzed (80 %)

Methods	CV 1, %			CV 2, %		
	<i>n</i>	<i>median</i>	<i>min - max</i>	<i>n</i>	<i>median</i>	<i>min - max</i>
All	153	2.0	0.0 - 7.4	151	1.4	0.0 - 10.0
Bio-Rad	39	2.0	0.1 - 5.0	39	1.8	0.1 - 10.0
Menarini	30	1.3	0.0 - 4.6	29	1.1	0.0 - 4.4
Roche	12	2.2	0.4 - 5.8	10	2.1	1.0 - 6.9
Sebia	18	3.4	1.9 - 4.8	18	2.2	1.0 - 4.7
Tosoh	52	1.8	0.0 - 7.4	53	1.0	0.0 - 3.4
Altri	2	1.7	0.2 - 3.2	2	0.5	0.2 - 0.8

Conclusions

- * Most of the Italian laboratories meet the allowable TE of 8.9%, not that of 6 %.
- * Global inter-laboratory variation (CV 3-5%) is well below respect to the 1997 exercise.
- * Most of the analytical methods meet the desirable bias goal.
 - * Corrective actions for some methods/laboratories are expected.
- * The results on the internal quality control need further attention.



Biochimica Clinica

Biochimica Clinica è indicizzata
in Scopus, EMBASE,
Engineering Village e Reaxys

1 Il progetto pilota SIBioC di VEQ della misura dell'emoglobina glicata¹

2

3 Andrea Mosca¹, Renata Paleari¹, Anna Carobene², Ferruccio Ceriotti² per il Gruppo di Studio
4 SIBioC Diabete Mellito.

5

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22

23 Titolo in inglese

24 **Pilot SIBioC EQAS project on glyated hemoglobin measurement**

25

1 Pilot SIBioC EQAS project on glyated hemoglobin measurements: a manufacturer's
2 viewpoint

3 Il progetto pilota SIBioC di VEQ della misura dell'emoglobina glicata: il punto di vista
4 di un produttore

5

6

7 Stefaan Marivoet¹, Nancy Van Bijlen¹, Stefano Frediani², Paola Bellati²

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9 ¹ Tosoh Bioscience N.V./S.A., Tessenderlo (Belgium)

10 ² Tosoh Bioscience srl, Rivoli, Torino (IT)

11

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Performance of glyated hemoglobin (HbA_{1c}) methods evaluated with
EQAS studies using fresh blood samples: Still space for improvements

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1. Actual requirements for obtaining and assessing HbA_{1c} standardization in Italy
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- 3. Future perspectives**

Future perspectives

- * EurA1c trial 2016
 - * More than 800 laboratories (BE – DE – NL)
 - * Fresh blood samples only
 - * 3 shipments (January – June - November)
 - * Probably embedded within our main National EQAS (Careggi, CRB)

- * Similar EQAS could be also organized for other measurands (not only red cell components)

- * Improvements only if all stakeholders (governments and international organizations, scientific societies, manufacturers and specialists in laboratory medicine) will act in a coordinated way.

- * SIBioC (Progetti di Ricerca 2014)
- * All laboratories who took part to the study
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- * Cas Weykamp, Carla Siebelder
- * Fabio Agostara (A.Menarini Diagnostici), Gianni Bertoli (Bio-Rad Laboratories), Stefano Frediani (Tosoh Bioscience), Giovanni Magni (Roche Diagnostici) and Sauro Maoggi (Sebia Italia)

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