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POCT Haemoglobin A1c Performance

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Chair IFCC- EUBD

The role of HbA1c in diabetes care

Long standing role for monitoring diabetes

Since 2011 WHO have advocated for its use for diagnosis of type 2 diabetes

Organisations such as the ADA have aligned with this

Advantages of HbA1c

- No fasting required
- No refrigeration required
- Wealth of data on clinical outcomes for people with diabetes
- Provides insight into the glycaemic control over the previous weeks rather than a ‘spot check’

Disadvantages of HbA1c

- Interferences, in particular from Hb Variants
- Doesn’t provide real time data for assessment of glycaemia
- Doesn’t show impact of wide ranges in glycaemic values
- Cost
- Availability
- Cannot be used in certain conditions

HbA1c interferences

- **Analytical** (Laboratory)
  - Heterozygous Hb variants: most commonly Hbs S, C, D and E
  - Don’t forget there will be no HbA1c in homozygous cases
  - Hereditary persistence of Hb F (up to ~30%)
  - Carbamylated Hb (in renal failure)

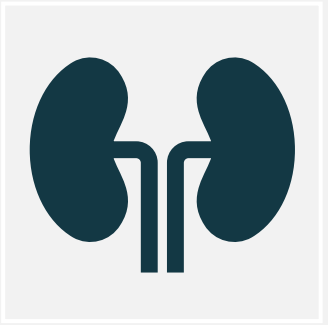
- **Biological:** any condition or disease state that affects erythrocyte lifespan or glycation of hemoglobin
  - Diseases due to homozygous Hb variants (e.g. sickle cell disease)
  - Iron deficiency anemia
  - Renal failure
  - HIV/Aids

Haemoglobin variants

Analytical:

Changes the charge of the Hb

Changes the antibody binding site on Hb

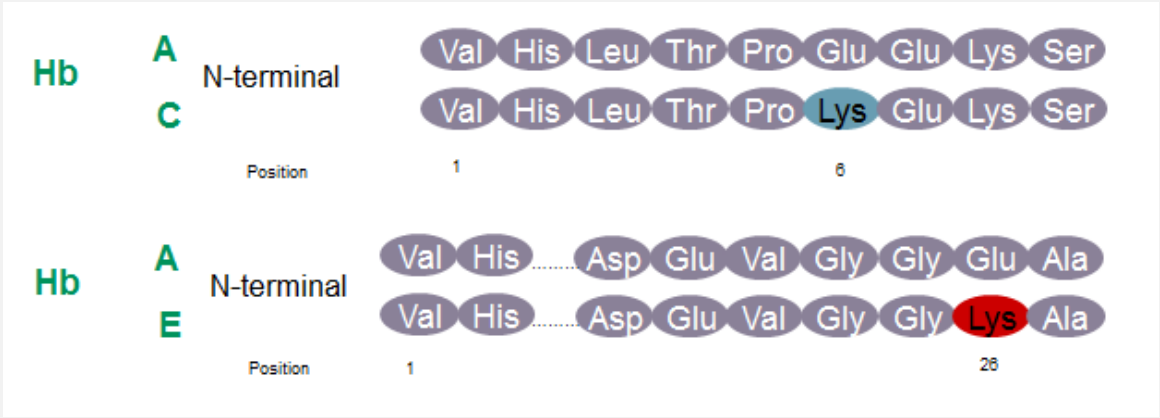


Biological:

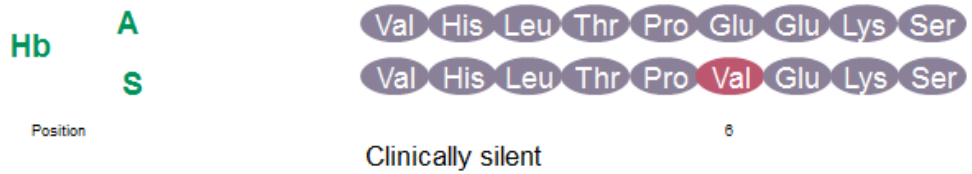
Alters the red cell lifespan (e.g. HbSS or CC)

Alters hemoglobin glycation rate

Haemoglobin variants – β chain

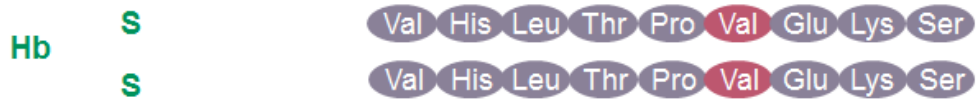


Sickle cell trait (heterozygous) – on normal gene (A) and one sickle cell gene (S)



Clinically silent

Sickle cell disease (homozygous)– both genes are sickle cell genes (S)



Sickle cell disease –
suffer from an severe anemia

What to consider with Hb variants

- Are you only interested in a reliable HbA1c result?
- Do you also want information about a possible Hb-variant?
  - If yes, what do you do with the information?
  - Do you use the information for genetic counselling?

- You cannot make a diagnosis just based on a peak in a chromatogram
  - “Whole picture” should be takin into account
  - (Hb, rbc, mcv, iron-status, HPLC chromatogram, Thal mode, DNA analysis)
  - Confirmation Hb-variant on DNA level

Finding out about variants

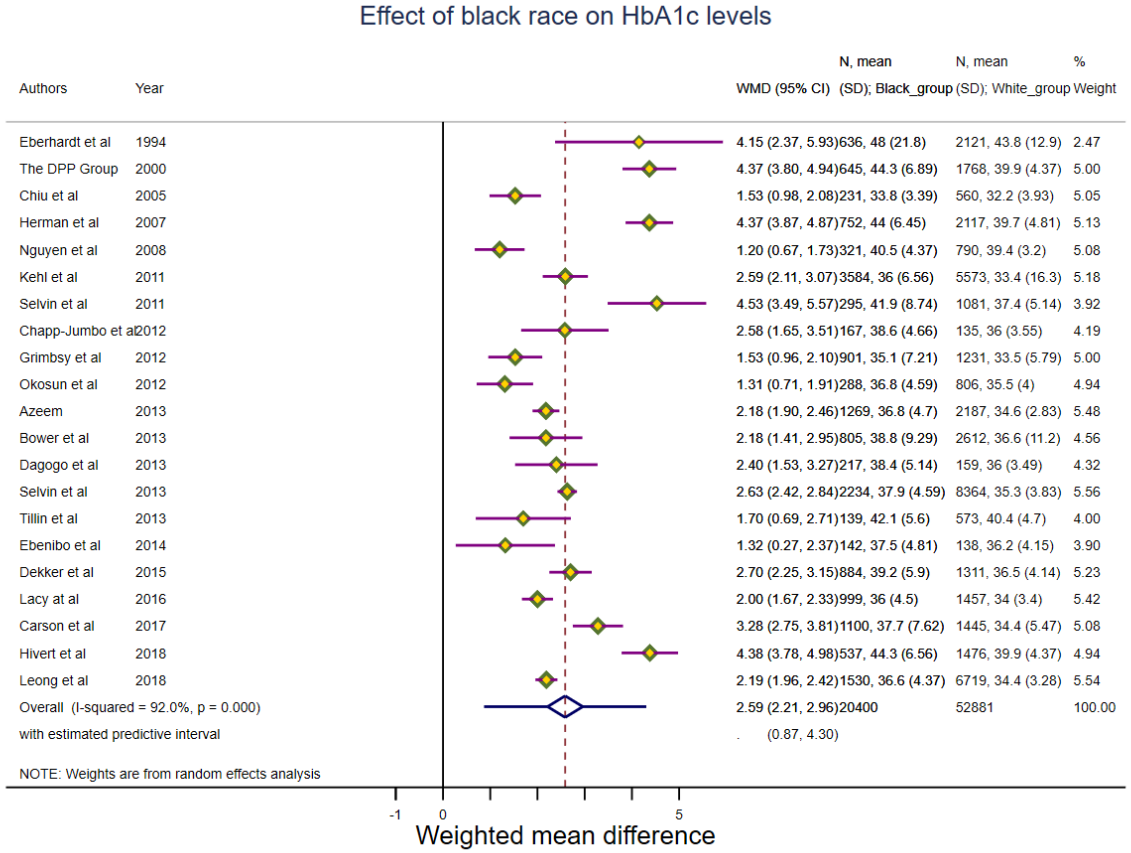
- Common variants: http://www.ngsp.org/interf.asp
- Common and rare variants: Journal of Diabetes Science and Technology 2015, Vol. 9(4) 849–856

More recent data suggests on a population basis this is not a significant effect but it can be on an individual basis

- CPRD data – approx. 230,000 events and 130,000 participants
- FBC, Fer, SCr, FPG, HbA1c in all
- Likely only affects results in severe anaemia (Hb <80 g/L)

DOI: 10.1007/s00125-015-3599-3
Pubmed ID: 25994072

Ethnicity



- **Systematic review**
- (55 studies) and meta-analyses of 34 studies involving 114 592 participants without diabetes
- HbA1c was consistently higher in ethnic or racial groups when compared to White participants
- South Asian and White group, estimated at 3·00 mmol/mol (0·27%) [95%CI, 2·32-3·68].
- HbA1c levels were higher for Black people by 2·59 mmol/mol (0·24%) [95% CI, 2·21-2·96],
- East Asian by 1·73 mmol/mol (0·17%) [95% CI,1·15-2·32],
- Hispanic people by 1·05 mmol/mol (0·10%) [95% CI, 0·79-1·31].

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Should we use POCT HbA1c for monitoring diabetes in routine clinical settings?

Please vote

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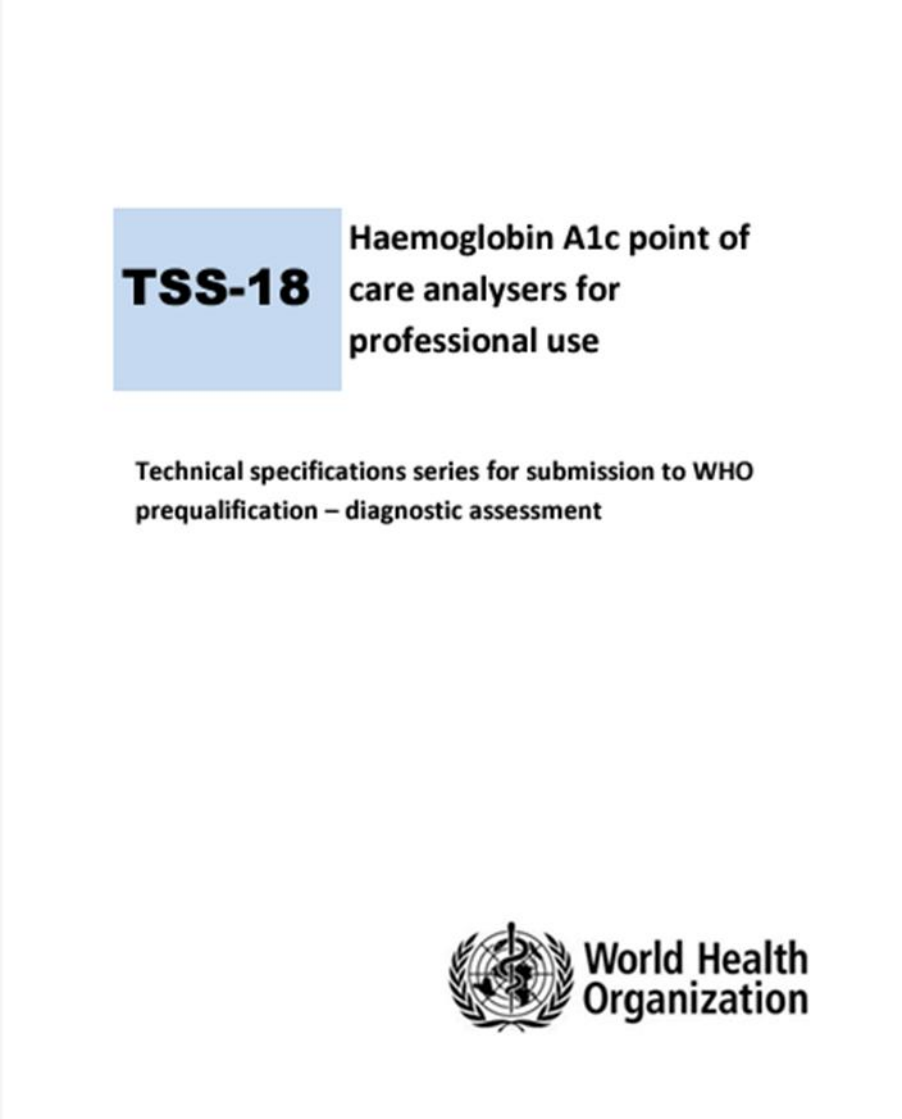
Should we use POCT HbA1c for diagnosis of type 2 diabetes?

Please vote

POCT HbA1c for diagnosis?

- Mixed opinion on whether it should be used for diagnosis
- TSS hints that this is possible….



World Health Organization

Prequalification of Medical Products

IVDs, Medicines, Vaccines and Immunization Devices, Vector Control

What is prequalification?

- The aim of WHO prequalification of in vitro diagnostics (IVDs) is to promote and facilitate access to safe, appropriate and affordable in vitro diagnostics of good quality in an equitable manner. The focus is on IVDs for priority diseases that are appropriate for use in resource-limited settings.

- https://extranet.who.int/prequal/vitro-diagnostics/what-we-do

Steps to achieve pre-qualification

WHO IVD prequalification incorporates comprehensive assessment of individual IVDs through a standardized procedure, to determine whether the product meets WHO prequalification requirements. Assessment has three components:

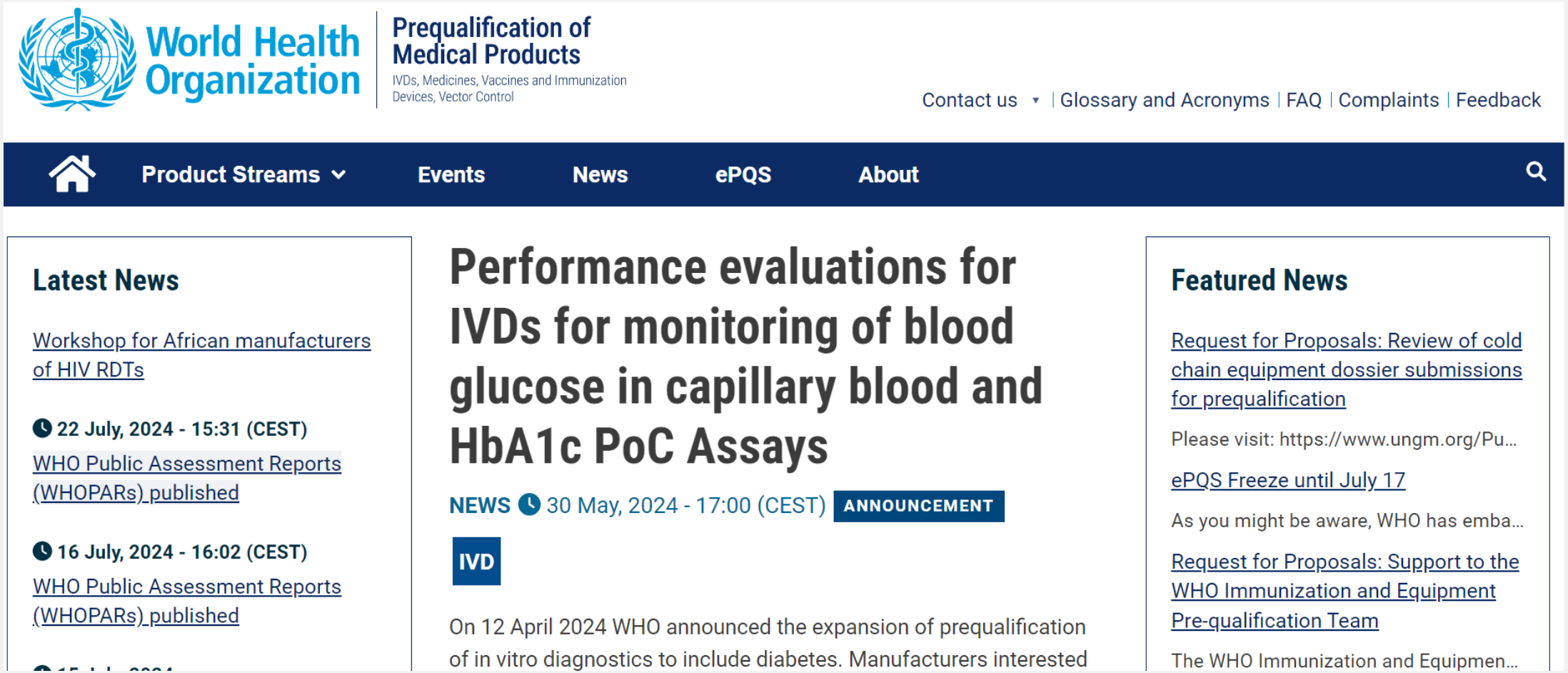
REVIEW OF A PRODUCT DOSSIER

LABORATORY EVALUATION OF PERFORMANCE AND OPERATIONAL CHARACTERISTICS

MANUFACTURING SITE(S) INSPECTION

FOLLOWING PREQUALIFICATION POST-MARKET SURVEILLANCE IS UNDERTAKEN

However


World Health Organization
Prequalification of Medical Products
IVDs, Medicines, Vaccines and Immunization Devices, Vector Control
Contact us | Glossary and Acronyms | FAQ | Complaints | Feedback
Product Streams
Events
News
ePQS
About
Latest News
Workshop for African manufacturers of HIV RDTs
22 July, 2024 - 15:31 (CEST)
WHO Public Assessment Reports (WHOPARs) published
16 July, 2024 - 16:02 (CEST)
WHO Public Assessment Reports (WHOPARs) published
Performance evaluations for IVDs for monitoring of blood glucose in capillary blood and HbA1c PoC Assays
NEWS 30 May, 2024 - 17:00 (CEST) ANNOUNCEMENT
IVD
On 12 April 2024 WHO announced the expansion of prequalification of in vitro diagnostics to include diabetes. Manufacturers interested
Featured News
Request for Proposals: Review of cold chain equipment dossier submissions for prequalification
Please visit: https://www.ungm.org/Pu...
ePQS Freeze until July 17
As you might be aware, WHO has emba...
Request for Proposals: Support to the WHO Immunization and Equipment Pre-qualification Team
The WHO Immunization and Equipmen...

Looking at the evidence

DE GRUYTER

Clin Chem Lab Med 2017; 55(2): 167–180

Review **Open Access**

Jennifer A. Hirst*, Julie H. McLellan, Christopher P. Price, Emma English, Benjamin G. Feakins, Richard J. Stevens and Andrew J. Farmer

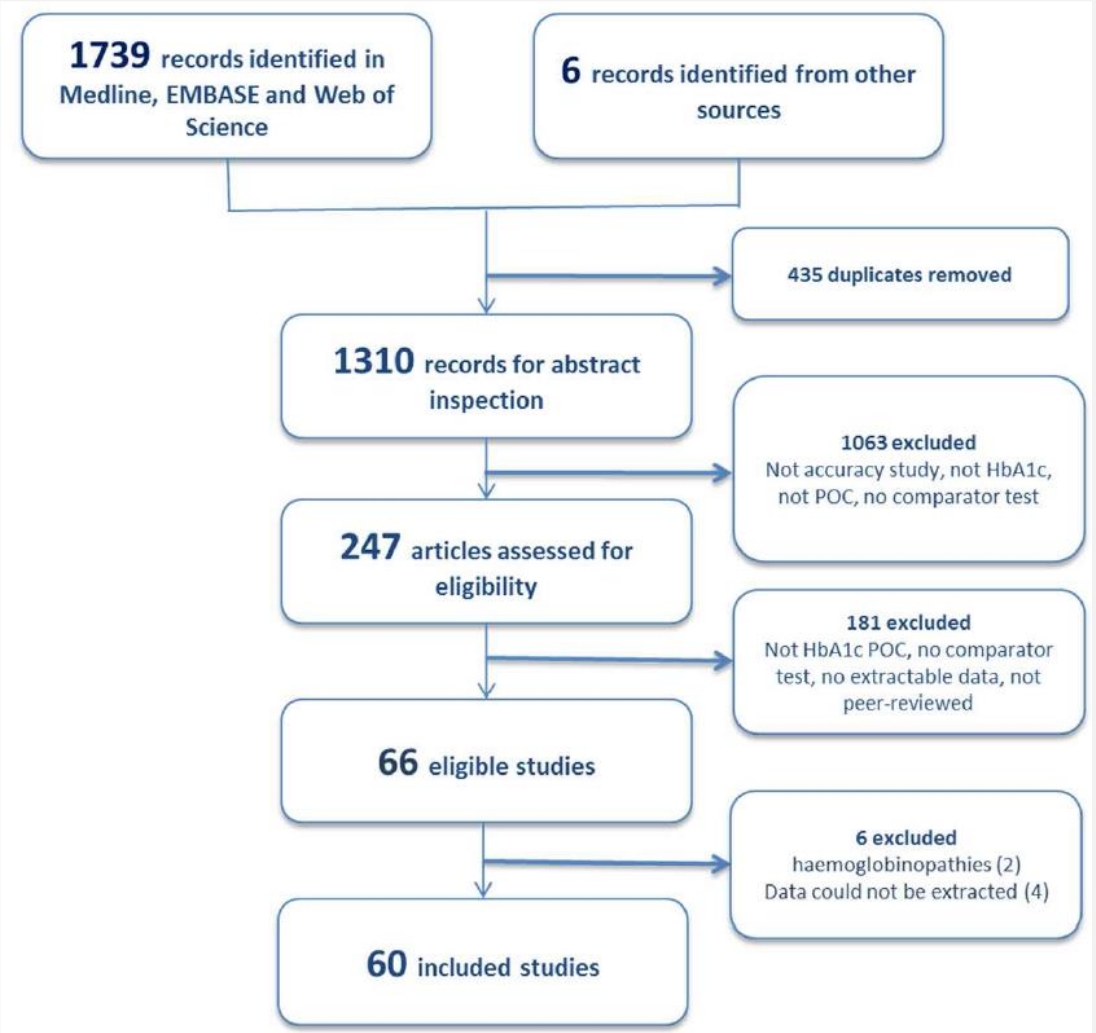
Performance of point-of-care HbA_{1c} test devices: implications for use in clinical practice – a systematic review and meta-analysis

DOI 10.1515/cclm-2016-0303
Received April 12, 2016; accepted July 19, 2016; previously published online September 22, 2016

Quo-Lab, Quo-Test and SDA1cCare. Nine devices had a negative mean bias which was significant for three devices. There was substantial variability in bias within

POCT systematic review

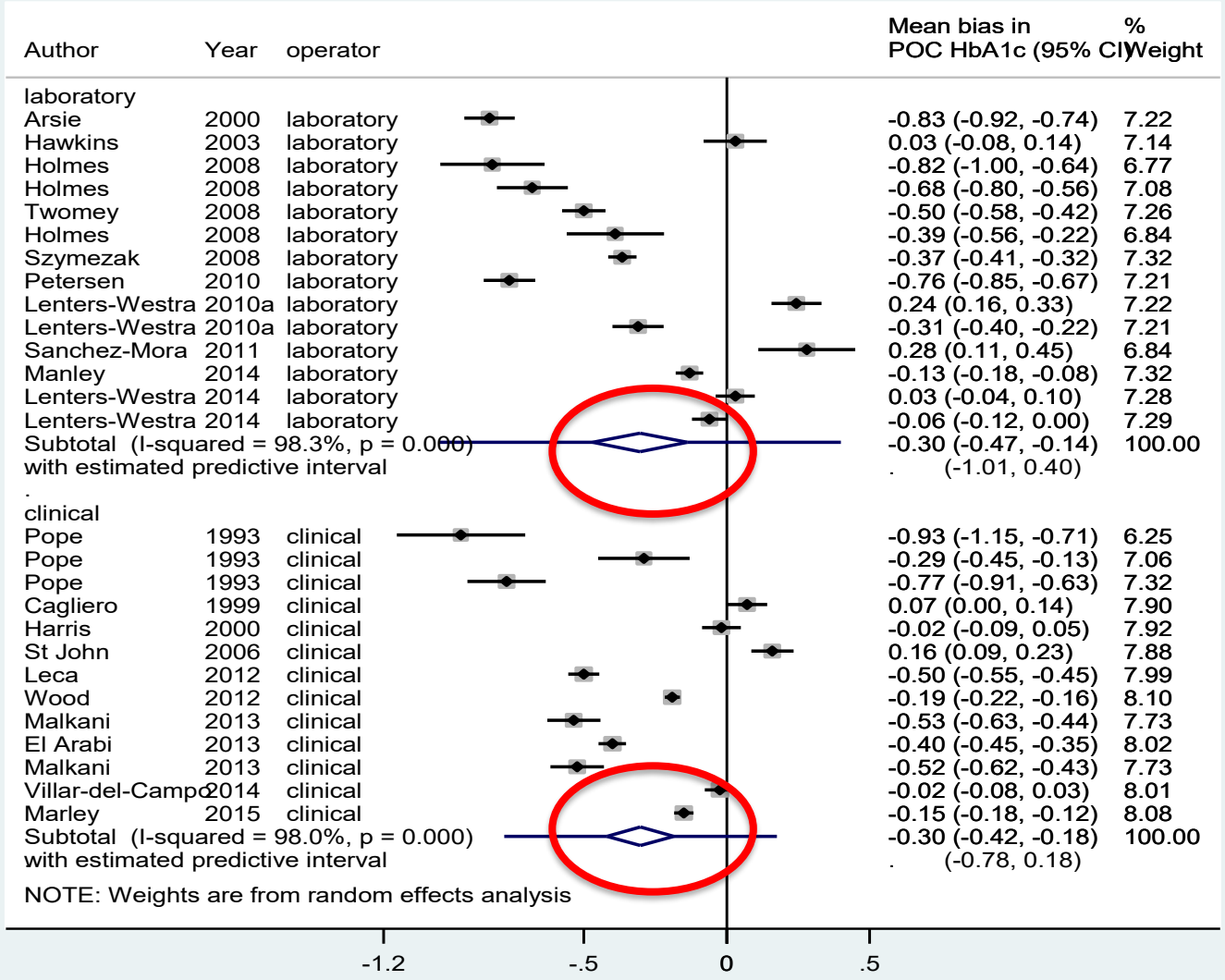
- 19 Laboratory Evaluations
- 21 POC settings – 12 with clinical staff undertaking analysis with POC device
- Comparator methods generally routine laboratory methods
- 9 studies used IFCC or NGSP reference laboratories



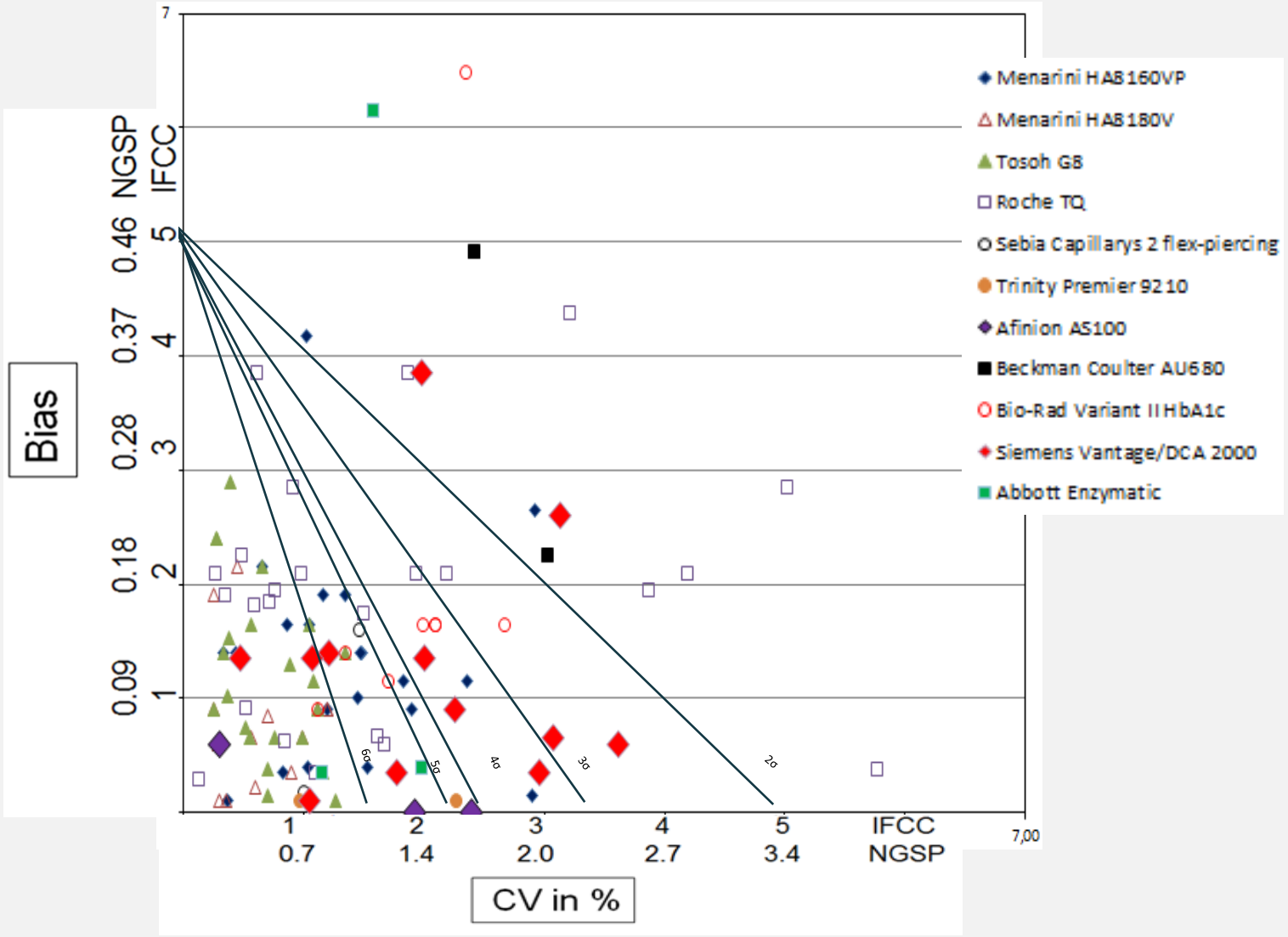
Key points

- Majority of devices had mean negative bias when compared to the laboratory comparison method
- Differences between POC HbA1c and comparator methods can vary considerably within a single device across all the included studies with POC values ranging from as much as 1.5% HbA1c below to 1.5% HbA1c above the comparator method HbA1c across all devices
- Large variation in mean bias with large variations in SD within in single device
- High imprecision levels
- Some evidence of decreased variation and bias over time
- Decreased variability in studies by IFCC and NGSP laboratories

Performance by setting



What does EQA tell us? Results from 134 labs



Lenters-Westra E, English E. Understanding the use of sigma metrics in HbA1c analysis. Clin Lab Med. 2017 Mar;37(1):57-71.

EurA1c data

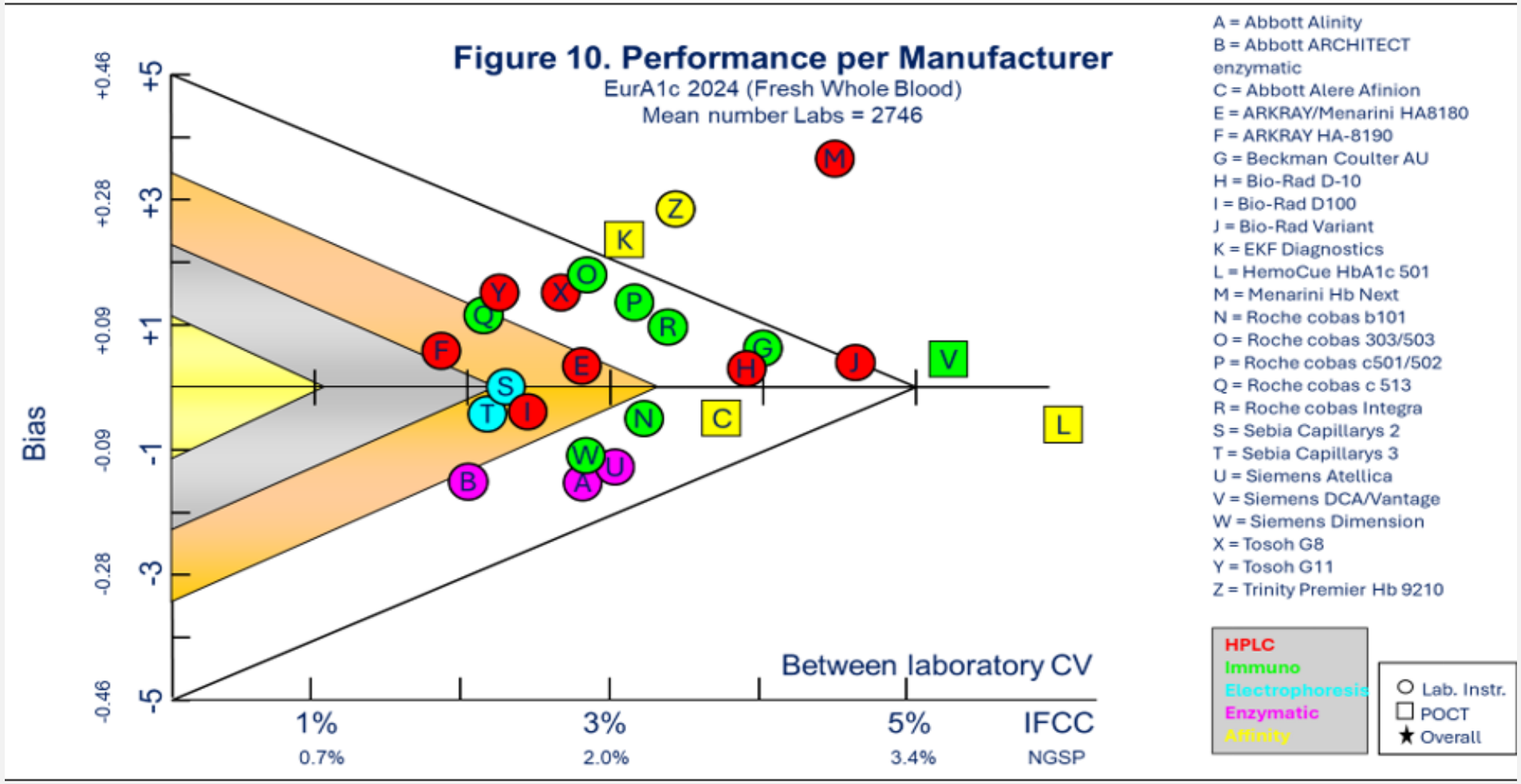


Figure 10. Performance per Manufacturer
EurA1c 2024 (Fresh Whole Blood)
Mean number Labs = 2746
Bias
+0.46
+0.28
+0.09
-0.09
-0.28
-0.46
+5
+3
+1
-1
-3
-5
Between laboratory CV
1%
0.7%
3%
2.0%
5%
3.4%
IFCC
NGSP
A = Abbott Alinity
B = Abbott ARCHITECT enzymatic
C = Abbott Alere Afinion
E = ARKRAY/Menarini HA8180
F = ARKRAY HA-8190
G = Beckman Coulter AU
H = Bio-Rad D-10
I = Bio-Rad D100
J = Bio-Rad Variant
K = EKF Diagnostics
L = HemoCue HbA1c 501
M = Menarini Hb Next
N = Roche cobas b101
O = Roche cobas 303/503
P = Roche cobas c501/502
Q = Roche cobas c 513
R = Roche cobas Integra
S = Sebia Capillarys 2
T = Sebia Capillarys 3
U = Siemens Atellica
V = Siemens DCA/Vantage
W = Siemens Dimension
X = Tosoh G8
Y = Tosoh G11
Z = Trinity Premier Hb 9210
HPLC
Immuno
Electrophoresis
Enzymatic
Affinity
Lab. Instr.
POCT
Overall

Head to Head evaluation of 19 POC HbA1c Devices

Funded by FIND Diagnostics NGO

- EP-15- A3 based protocol to verify manufacturers claims for CV
- EP-9-A3 based protocol to determine bias
- Assessment of interference from common Hb Variants
- Usability assessment
- Performance using IFCC sigma metrics criteria
- Performance using NGSP certification criteria

Clinical Chemistry 71:7
775–788 (2025)

Article

Challenges in Hb A_{1c} Point-of-Care Testing: Only 5 of 19 Hb A_{1c} Point-of-Care Devices Meet IFCC and NGSP Certification Criteria on Independent Evaluation

Erna Lenters-Westra,[a,b] Priyanka Singh,[c] Beatrice Vetter,[c] and Emma English[d,*]

BACKGROUND: Access to Hb A_{1c} testing in low- and middle-income countries (LMICs) can be limited, especially in rural areas. This has led to an increased interest in the potential role of point-of-care testing (POCT) for Hb A_{1c}. The analytical performance of many of these devices is poorly understood but accurate and precise measurement is essential for effective diabetes management.

were performed under ideal conditions; performance may worsen further when used in a clinical setting.

Introduction

The worldwide prevalence of diabetes continues to rise,

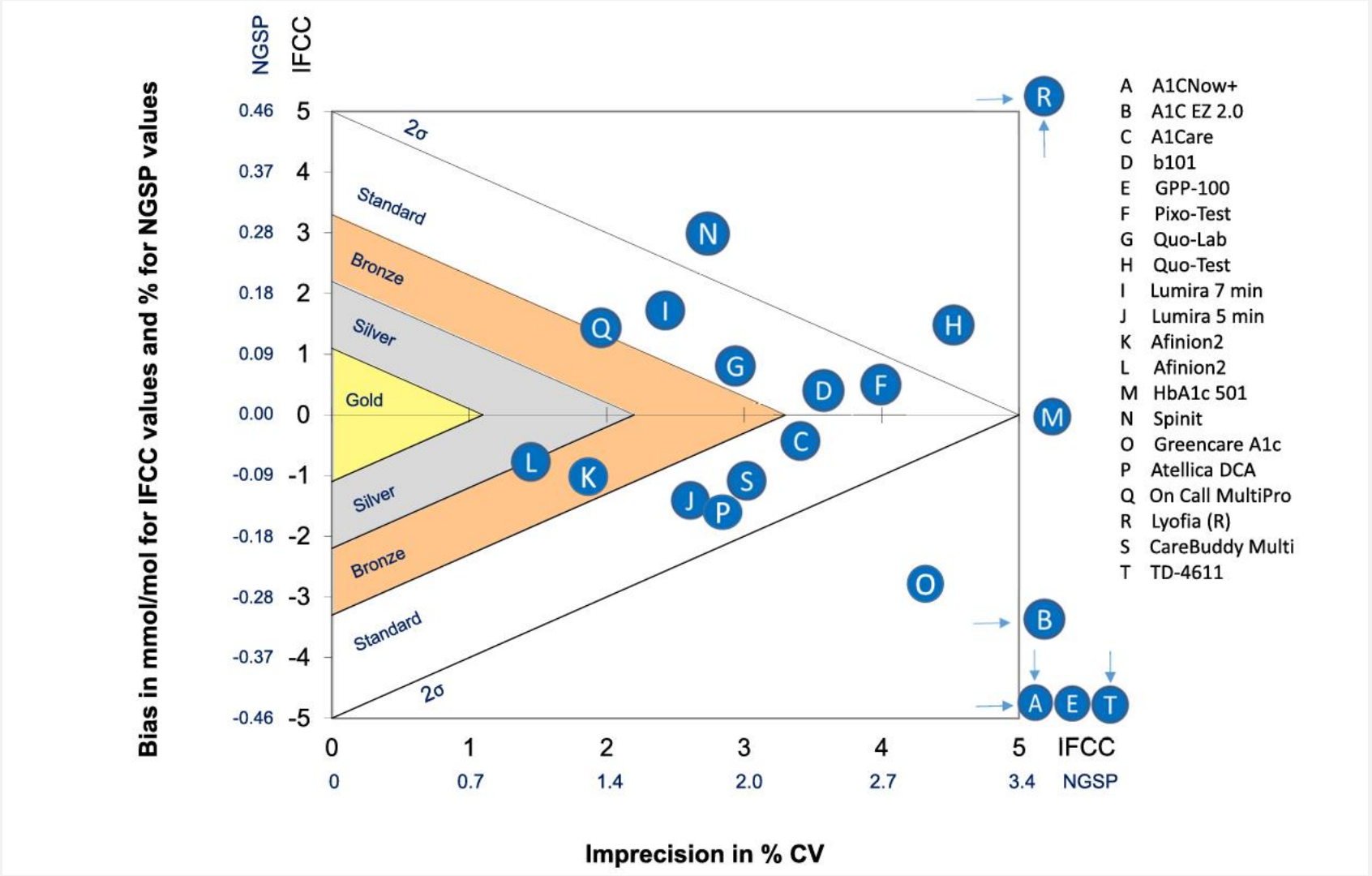

Bias in mmol/mol for IFCC values and % for NGSP values
NGSP
IFCC
0.46 5
0.37 4
0.28 3
0.18 2
0.09 1
0.00 0
-0.09 -1
-0.18 -2
-0.28 -3
-0.37 -4
-0.46 -5
2σ
Standard
Bronze
Silver
Gold
Silver
Bronze
Standard
2σ
0 1 2 3 4 5 IFCC
0 0.7 1.4 2.0 2.7 3.4 NGSP
Imprecision in % CV
A A1CNow+
B A1C EZ 2.0
C A1Care
D b101
E GPP-100
F Pixo-Test
G Quo-Lab
H Quo-Test
I Lumira 7 min
J Lumira 5 min
K Afinion2
L Afinion2
M HbA1c 501
N Spinit
O Greencare A1c
P Atellica DCA
Q On Call MultiPro
R Lyofia (R)
S CareBuddy Multi
T TD-4611

Table 5. (continued)

Device	NGSP criteria: Premier Hb9210	NGSP criteria: Roche TQ	NGSP criteria: Tosoh G11	NGSP criteria: Abbott	IFCC criteria: Sigma (pass/fail)	Precision CV (%) NGSP units (CV (%) SI units): 5.1% 33 mmol/mol	6.3% 46 mmol/mol	9.2% 77 mmol/mol	Dupl. EP-9	Interferences: Hb variant
Spinit	fail	fail	fail	fail	1.4 (fail)	2.1[b] (3.4[b])	**1.9 (2.6)**	2.4 (3.1)	2.4 (3.3)	Hb F > 6.9%
Greencare A1c	fail	fail	fail	fail	0.9 (fail)	2.7[b] (4.4[b])	2.6 (4.4)	**2.0[b]** (2.5[b])	3.7	Hb F > 6.9%
Atellica DCA	fail	fail	fail	**pass**	**2.1 (pass)**	**1.6 (2.9)**	**1.9[b] (2.9[b])**	**1.9 (2.5)**	**1.6 (2.3)**	Hb F > 5.1%
On Call MultiPro	fail	**pass**	**pass**	fail	**3.4 (pass)**	**1.9 (3.3)**	**1.4 (2.0)**	**1.6 (2.1)**	**1.2 (1.8)**	Hb F > 6.8%
Lyofia	fail	fail	fail	fail	<0 (fail)	6.0 (10.4)	11.3[b] (15.9[b])	8.6 (11.0)	11.6 (15.8)	Inconclusive
CareBuddy Multi	fail	fail	fail	fail	**2.4 (pass)**	**1.3 (2.2)**	2.1 (3.1)	2.4[b] (3.2[b])	2.4 (3.5)	Hb F > 6.9%
TD-4611	fail	fail	fail	fail	<0 (fail)	7.7[b] (15.2[b])	3.7[b] (5.5[b])	4.5[b] (5.8[b])	9.6 (14.2)	Inconclusive
LumiraDx (5 min)	fail	fail	fail	fail	**2.4 (pass)**	2.5 (4.5)	**1.7 (2.6)**	**1.6 (2.1)**	**1.9 (2.7)**	Inconclusive

Pass IFCC/NGSP criteria and CV ≤2% in NGSP units and CV ≤3% in SI units in bold.
[a]EDTA has a negative bias with this method.
[b]Claimed CV not met.

Key messages

Consider if there really is a clinical need for POCT

The analytical performance criteria for HbA1c POCT and lab method for monitoring and diagnosis of DM should be the same

Proficiency testing should be mandated for users of POC assays to ensure quality

Analytical performance of POCT instruments is variable – instruments choice needs careful consideration

It is essential to have oversight of POC devices with a quality framework in place BEFORE you start to use them

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Should we use POCT HbA1c for monitoring diabetes in routine clinical settings?

Please vote

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Should we use POCT HbA1c for diagnosis of type 2 diabetes?

Please vote

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Thank you - any questions

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