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Weqas | GLOBAL PROVIDER OF QUALITY IN DIAGNOSTIC MEDICINE

EXTERNAL QUALITY ASSESSMENT

INTERNAL QUALITY CONTROL

REFERENCE MEASUREMENT SERVICES

EDUCATION & TRAINING

POCT Performance Update

Gareth Davies / Ceri Parfitt

Overview

- APS
- HbA1c (for Monitoring)
- INR
- Glucose
- Ketones

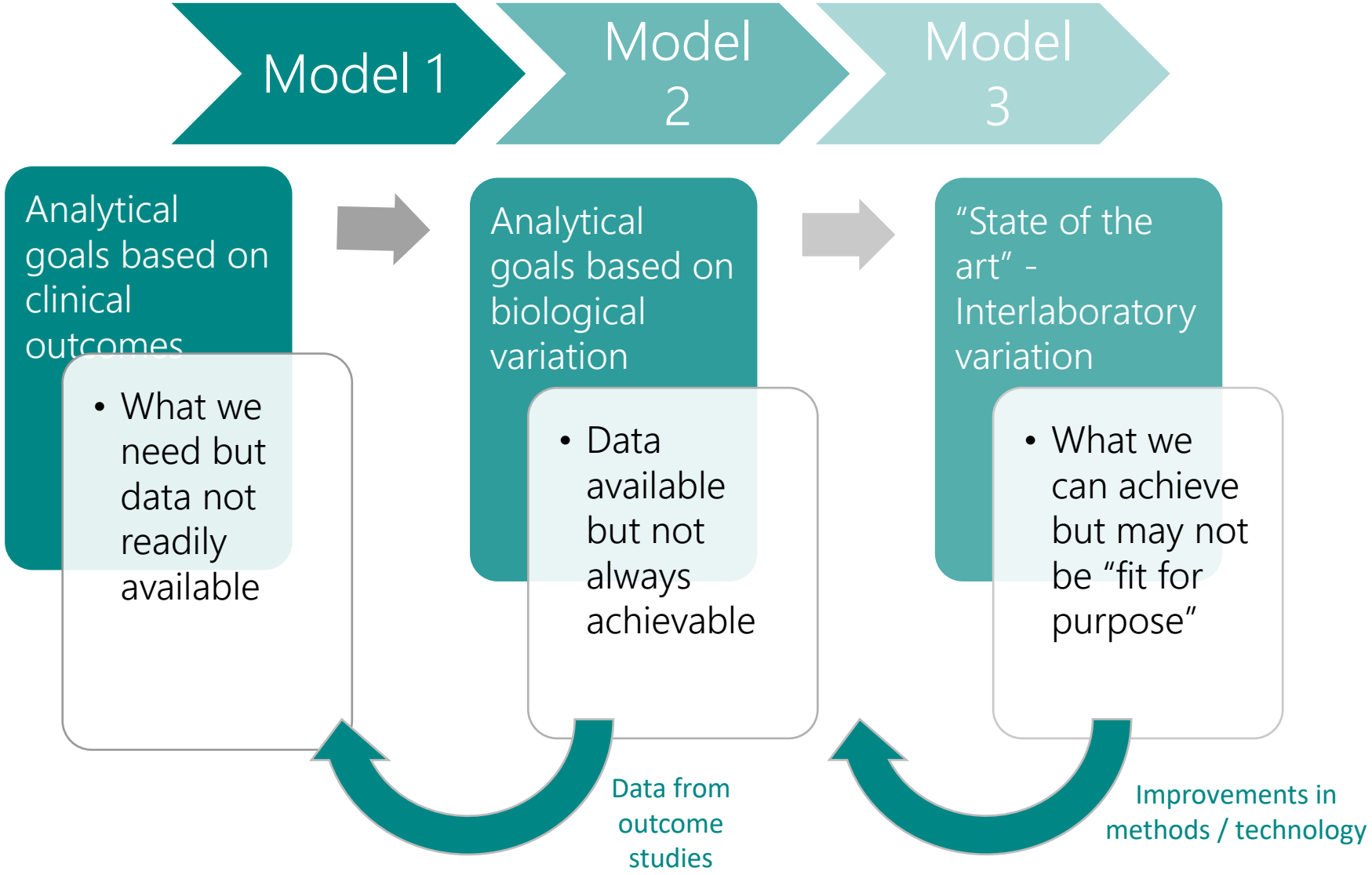
What is APS?

- APS is defined as a range of values around the target which is considered acceptable for the performance of that test.
- A result outside the acceptable range should alert the laboratory that that their assay may produce results that are at risk of detrimentally affecting clinical decision making.
- It provides a simple tool to allow a rapid, standardized assessment of EQA results in both numerical and graphical report formats.
- Laboratories and Point of Care (POCT) users must ensure that the analytical quality attained for that test is appropriate for the needs of the clinical service and the clinical utility of the test.
- It is therefore essential that EQA performance specification also reflect the clinical need and utility of the test.
- Various strategies have been proposed over the last 25 years, including the Consensus hierarchy from the Stockholm Conference in 1999, and the simpler EFLM Milan strategy in 2014.

Defining APS

- **Model 1. Based on the effect of analytical performance on clinical outcomes.** This model is the most rational since it is based on the actual clinical outcome; however, in practice it is applicable only to a few tests since it is difficult to show the direct effect of laboratory tests on medical outcome.
- **Model 2. Based on components of biological variation of the measurand.** This model seeks to minimize the ratio of the analytical noise to the biological signal. Its applicability can however be limited by the validity and robustness of the data on biological variation.
- **Model 3. Based on the state of the art.** This model is the one where data is most easily available. It is linked to the highest level of analytical quality achievable with the currently available techniques**.**

Clinically Relevant Performance Specification



Strategy for HbA1c
What is the clinical utility of the test?

- Monitoring:
  - For individual patient monitoring over time - analytical variance is by far the major contributor to the performance characteristic – low between batch variance needed.
  - DCCT and UKPDS studies established the central role of HbA1c as the index for the long-term control of the glycaemic state – stable method over time.

- Diagnosis:
  - Global diagnostic goals (WHO diagnosis – 48mmol/mol) - bias becomes an essential characteristic. Monitor bias of method (lab performance) to standardised procedure (IFCC method).
  - NICE guidelines – HbA1c targets 48-58 mmol/mol , patients monitored 2 – 6 monthly.

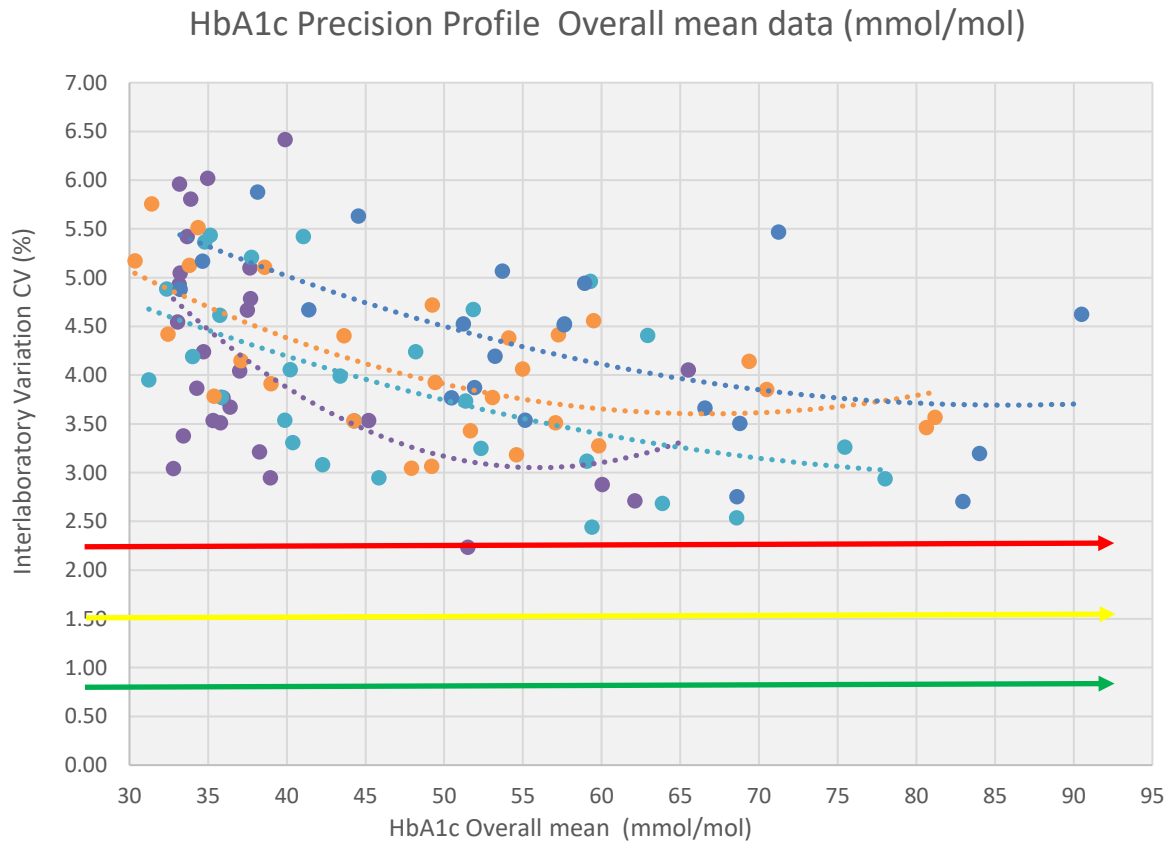
Specific treatment goals have been established based on HbA1c measurements. For HbA1c both strategies are therefore important factors.

Comparison of Performance Specification for HbA1c

APS - Total Allowable Error, TEa%							
IFCC MQT	NGSP cert for manufacturers	RCPA (Aus)	CLIA (US)	CAP (US)	WEQAS (UK)	UKNEQAS (UK)	Rilibak Germany
	± 5.0%$_{NGSP}$		± 8.0%$_{NGSP}$	± 6.0%$_{NGSP}$			
± 5 mmol/mol 10.4% @48mmol/mol	± 6.8% $_{IFCC}$	± 4 or ± 8% >45 mmol/mol	± 10.4% $_{IFCC}$	± 8.3% $_{IFCC}$	± 6.3%	± 5 %	± 8.0%

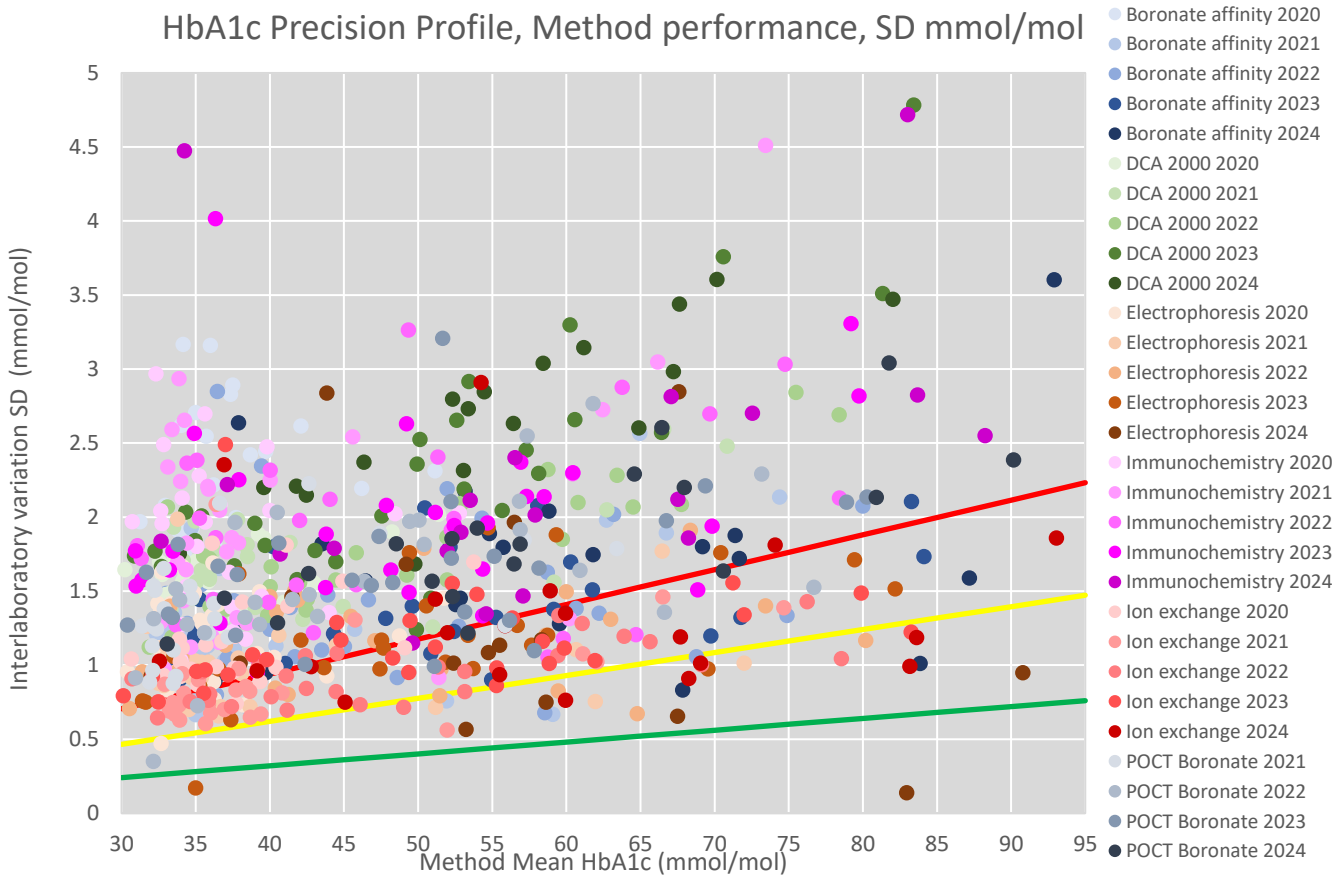
HbA1c Precision Profile

Overall data also includes affects of bias. Data includes laboratory and POCT methods
Can we use universal APS based on biological variation? – NO



HbA1c Precision Profile

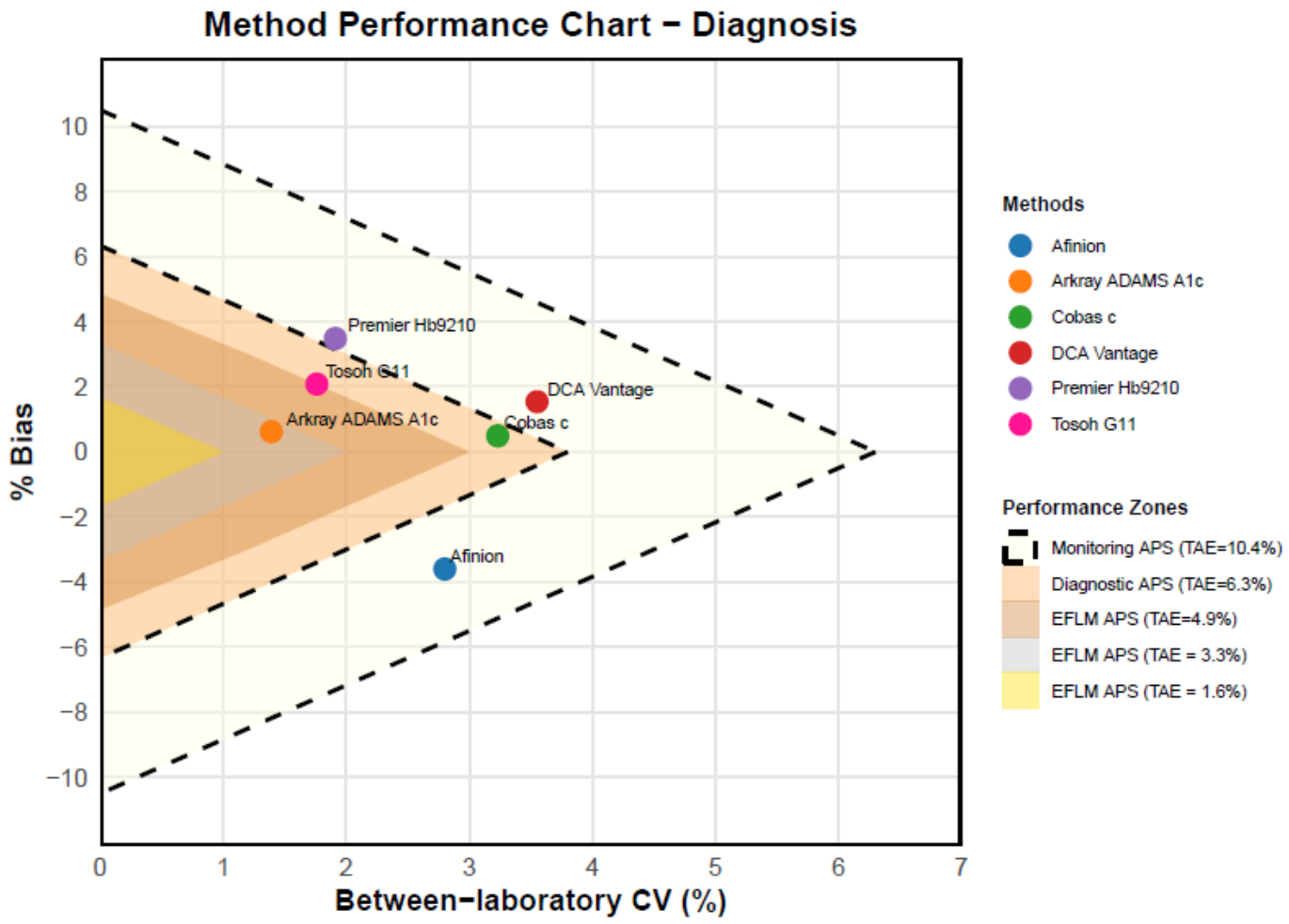
Should we use different APS for laboratory and POCT methods? - **YES**
Most laboratory electrophoresis and Ion exchange methods can achieve **Minimum**



Proposed model for Monitoring and Diagnosis

Monitoring	Diagnosis	Quality Improvement		
± 10.4%	± 6.3%	± 4.9%	± 3.3%	±1.6%
Represents ± a change of 5 mmol/mol @48 mmol/mol	Represents ± a change of 3 mmol/mol @48 mmol/mol	EFLM Minimum	EFLM Desirable	EFLM Optimal

Proposed model for Monitoring and Diagnosis

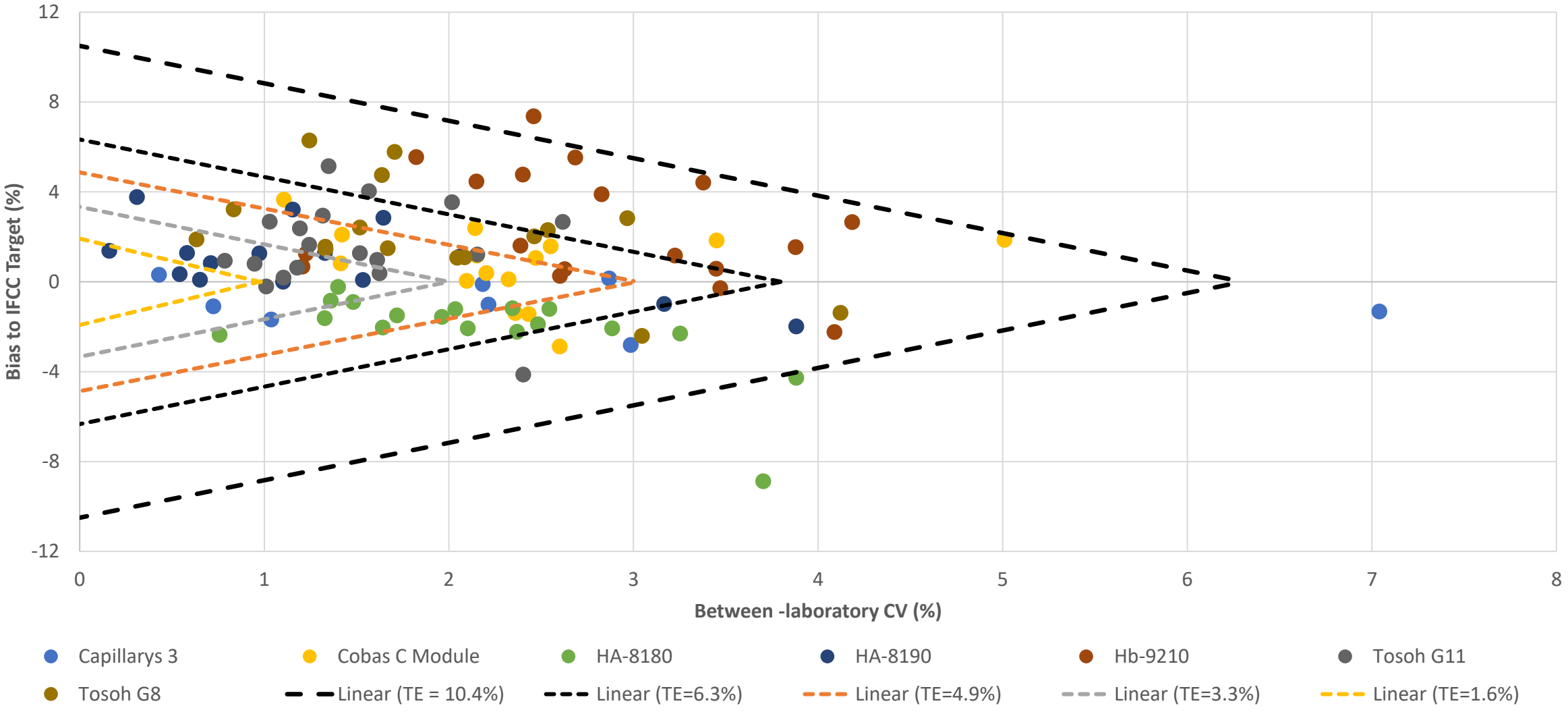


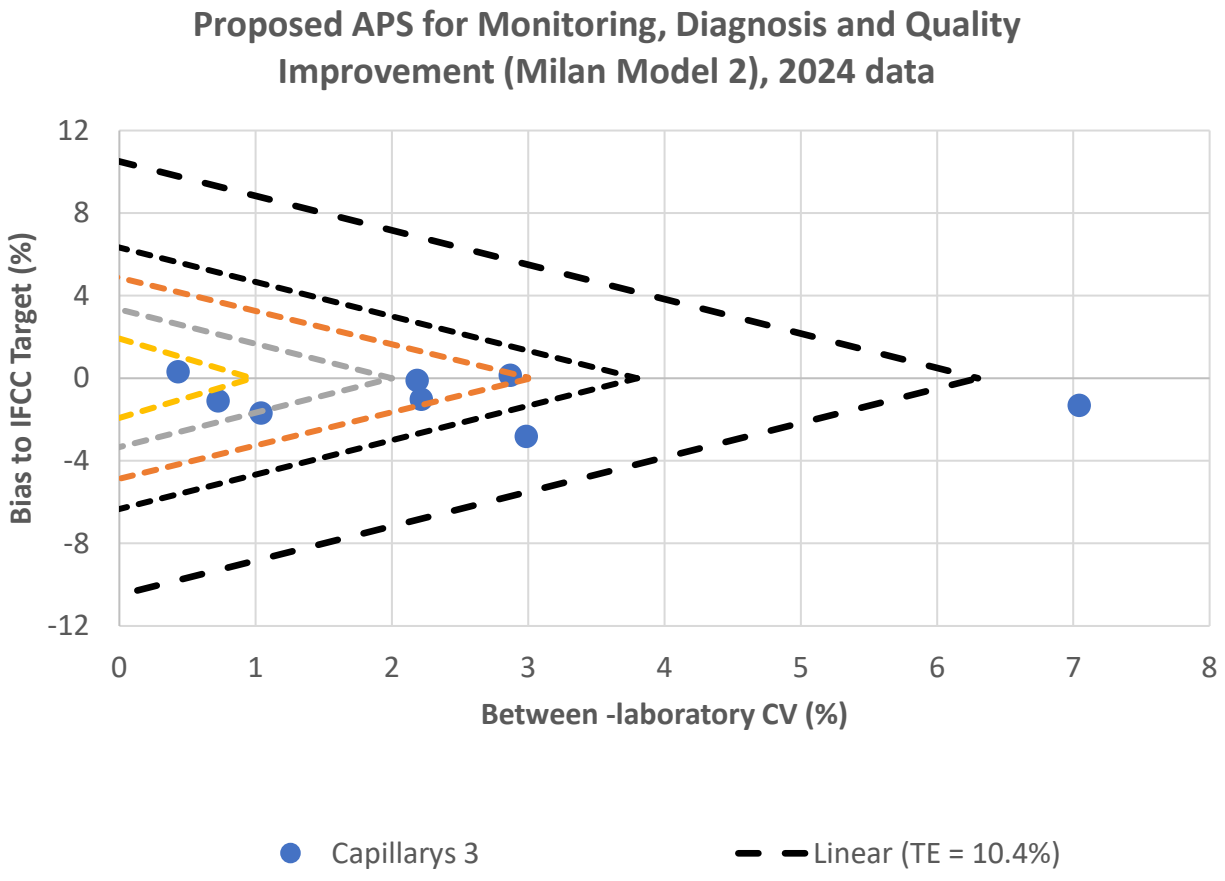
HbA1c Methods within the outer triangle may be considered as meeting the current APS for the analysis of HbA1c to aid in the **monitoring** of diabetes.

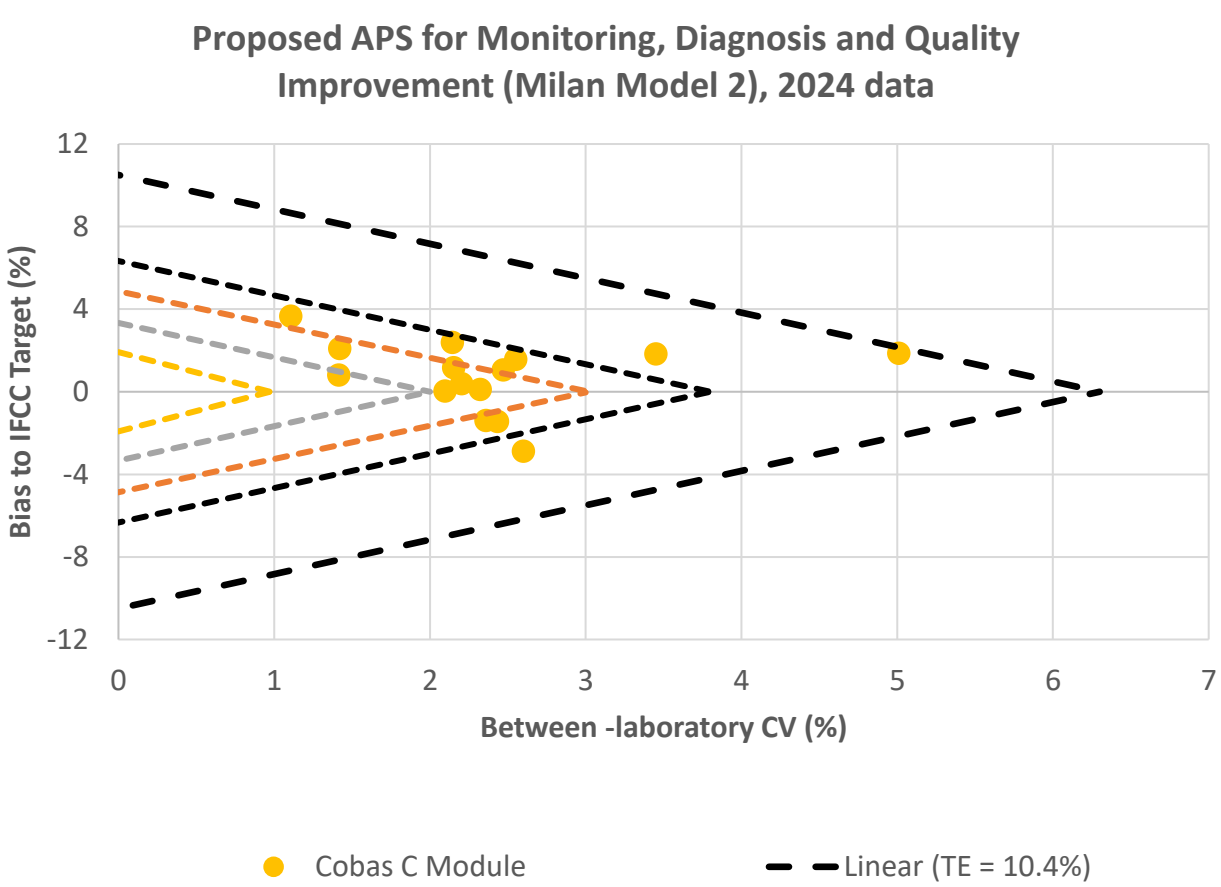
Methods within any of the 4 inner triangles may be considered as meeting the current APS for the analysis of HbA1c to aid in the **diagnosis** of diabetes. However, where possible methods that meet the minimum APS according to EFLM should be encouraged.

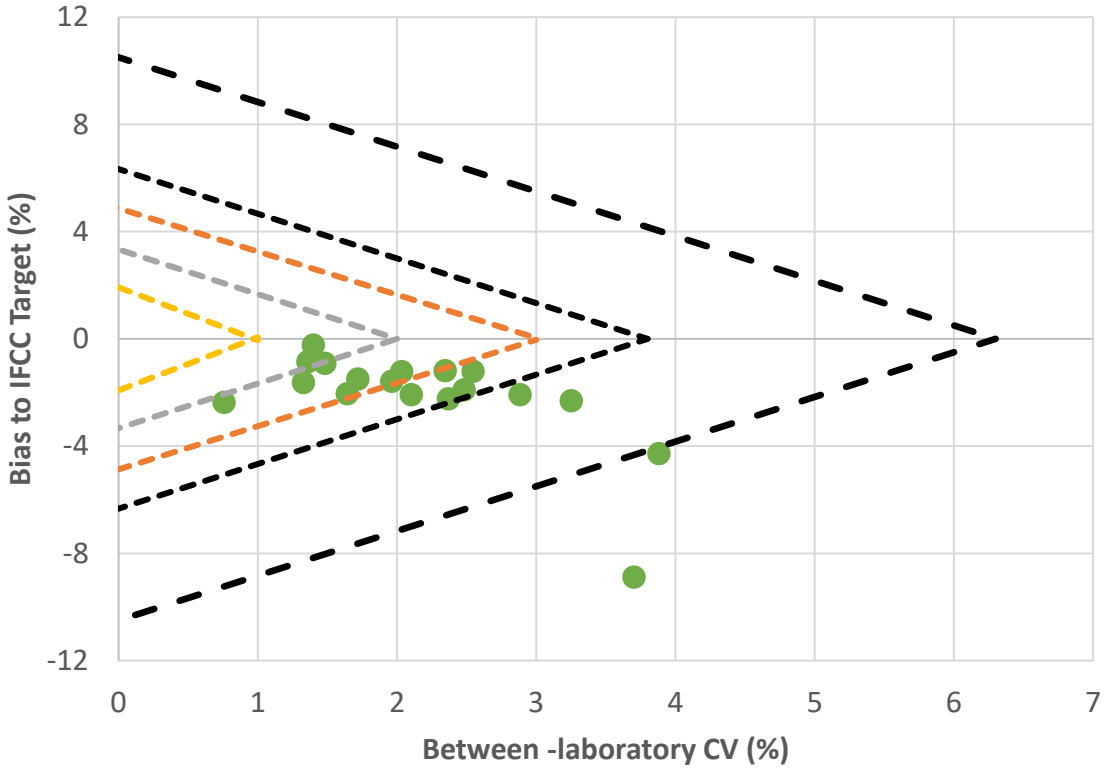
Results are evaluated using a modification of the IFCC Model Quality Targets using Biological Variation. Cas Weykamp et al. Investigation of Two Models to Set and Evaluate Quality Targets for HbA1c: Biological Variation and Sigma−metrics Clin Chem. 2015 Mar 3;61(5):752–759

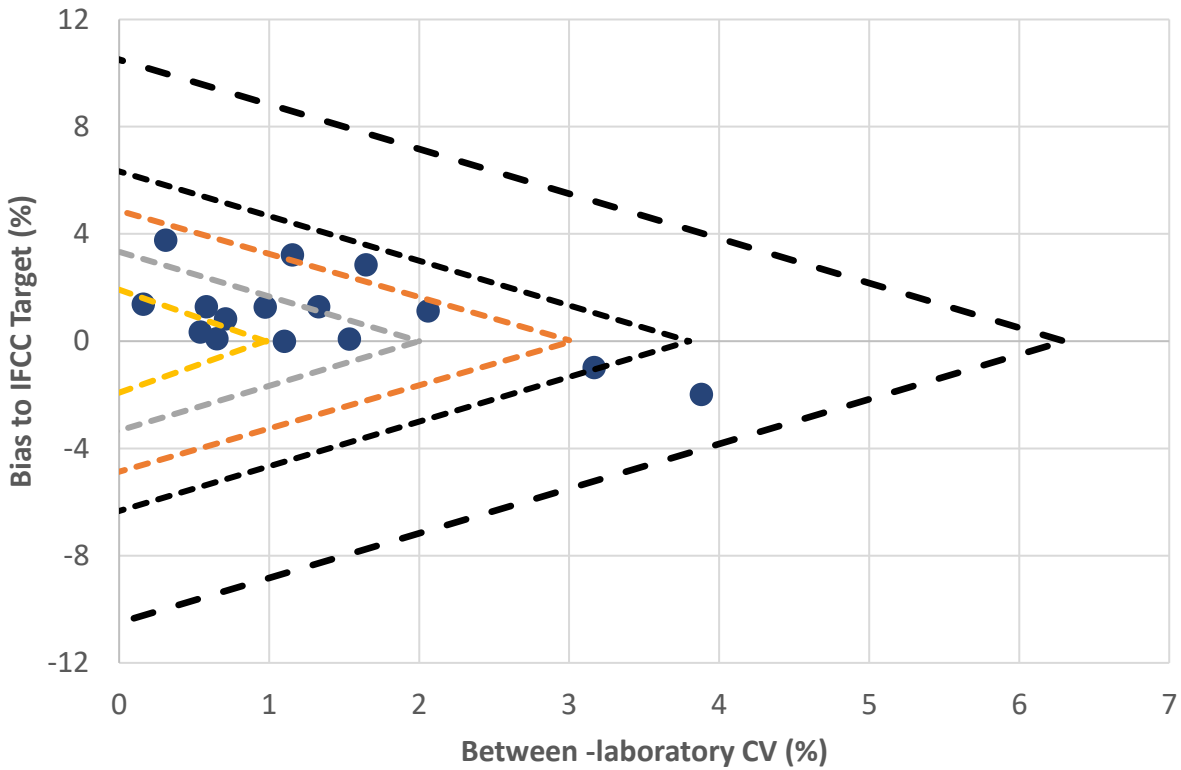
Proposed APS for Monitoring, Diagnosis and Quality Improvement, Jan – Dec 2024

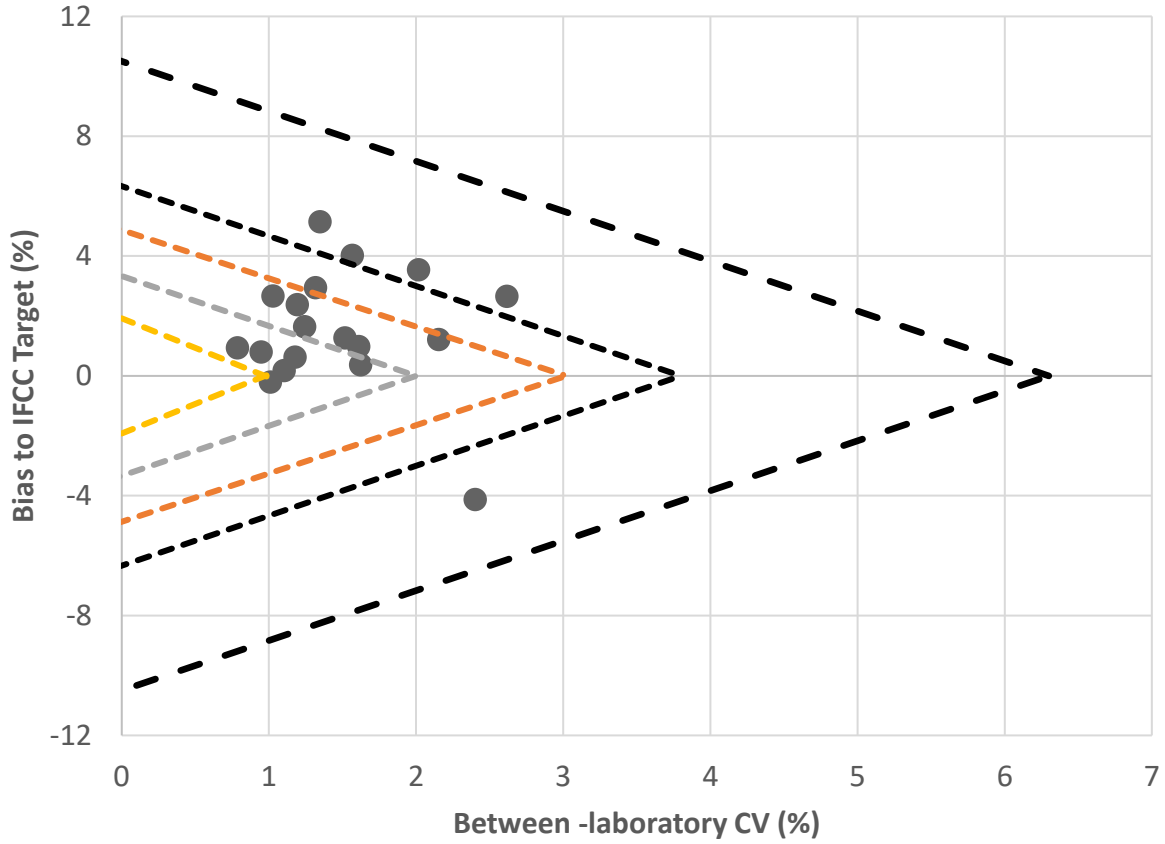


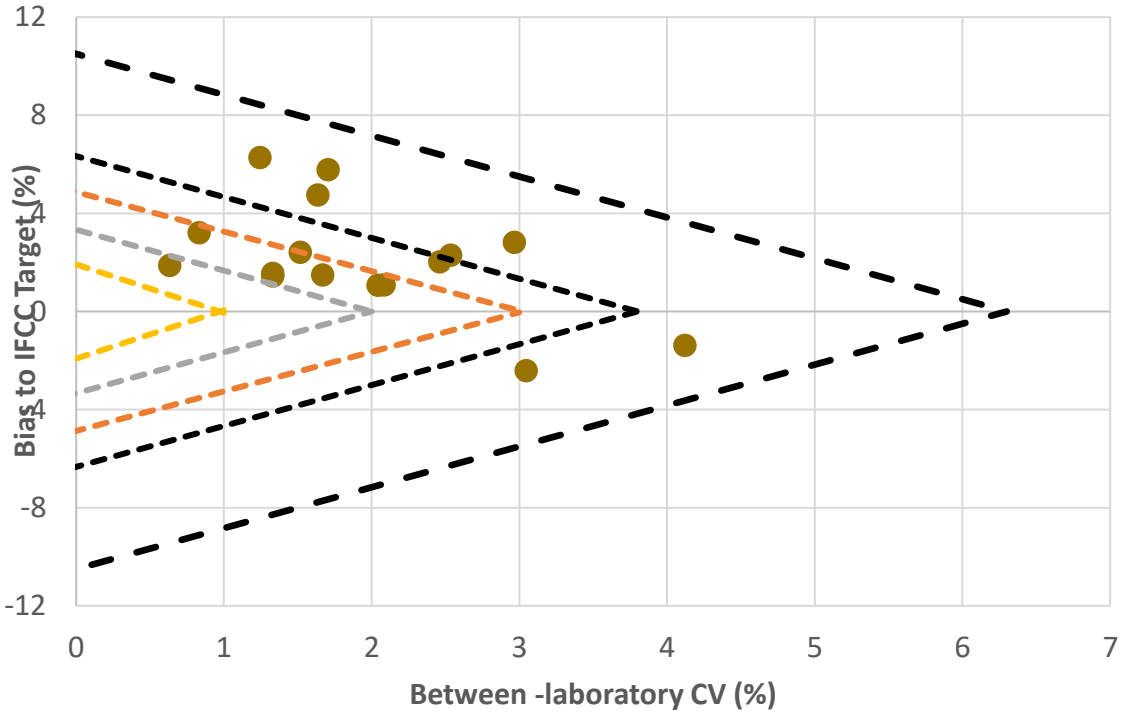

Proposed APS for Monitoring, Diagnosis and Quality Improvement (Milan Model 2), 2024 data
Bias to IFCC Target (%)
12
8
4
0
-4
-8
-12
0
1
2
3
4
5
6
7
8
Between -laboratory CV (%)
Capillarys 3
Linear (TE = 10.4%)


Proposed APS for Monitoring, Diagnosis and Quality Improvement (Milan Model 2), 2024 data
Bias to IFCC Target (%)
12
8
4
0
-4
-8
-12
0
1
2
3
4
5
6
7
Between -laboratory CV (%)
Cobas C Module
Linear (TE = 10.4%)


12
8
4
0
-4
-8
-12
0
1
2
3
4
5
6
7
Bias to IFCC Target (%)
Between -laboratory CV (%)
HA-8180
Linear (TE = 10.4%)


12
8
4
0
-4
-8
-12
0
1
2
3
4
5
6
7
Bias to IFCC Target (%)
Between -laboratory CV (%)
HA-8190
Linear (TE = 10.4%)

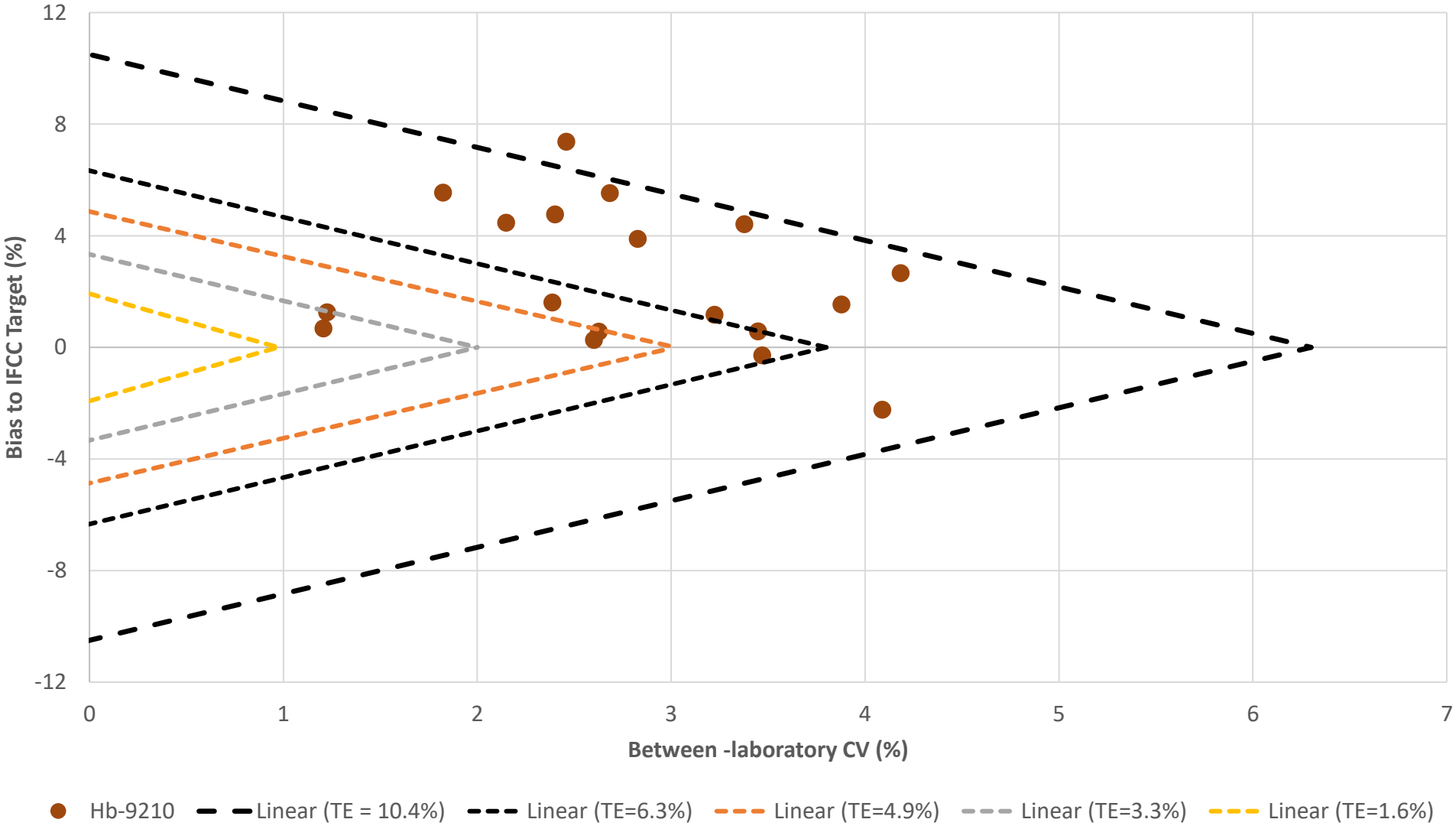




Tosoh G11 — Linear (TE = 10.4%)

Tosoh G8 — Linear (TE = 10.4%)

Would we have picked up the recent issue using the new APS?



Weqas POCT INR programme

- Suitable for most POCT devices, including Abbott iStat, Roche CoaguChek and Siemens Xprecia Stride
- One sample sent bimonthly – at least 6 per year
- Most samples supplied aim to challenge therapeutic targets at INR 2.5 and 3.5
  - Range 1.3 – 4.6 in previous 12 months
- Scoring based on Milan Model 3 performance specification (state of the art)
  - Most recently updated in 2023

POCT INR

- Prothrombin time (PT) - time taken for plasma to form a clot in presence of calcium and tissue thromboplastin
- International normalised ratio (INR) = (Patient PT/control PT)^{ISI}
- Monitoring patients taking vitamin K antagonists e.g. warfarin
  - Narrow therapeutic window
  - Underdosing – risk of excessive clotting
  - Overdose – risk of excessive bleeding
- INR targets depend on underlying condition
  - INR 2.5 – DVT, PE, atrial fibrillation, mitral stenosis, post-MI…
  - INR 3.5 – recurrent DVT or PE

Why use POCT INR?

- Accessibility
  - Community anticoagulation services
  - In clinics without on-site labs – remote/rural sites, prison healthcare
  - Home visits/self-testing – relatively rare at the moment

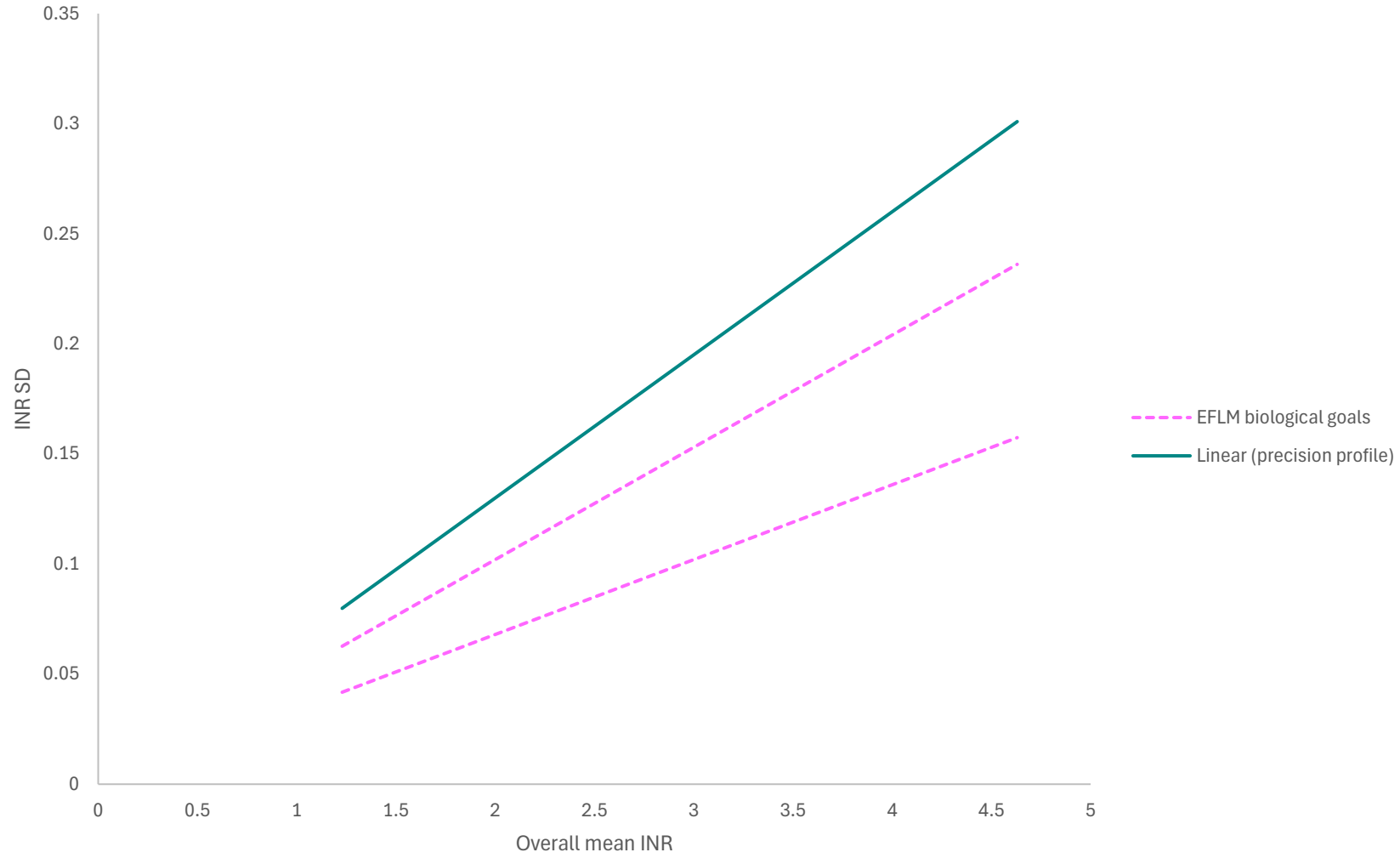
- Immediate results vs lab testing
  - Emergency situations – warfarin overdose/haemorrhage/stroke
  - Pre-operative checks/in-procedure monitoring
  - Most POCT instruments calibrated for INR 1.5-4.5 – not always appropriate

Why use POCT INR?

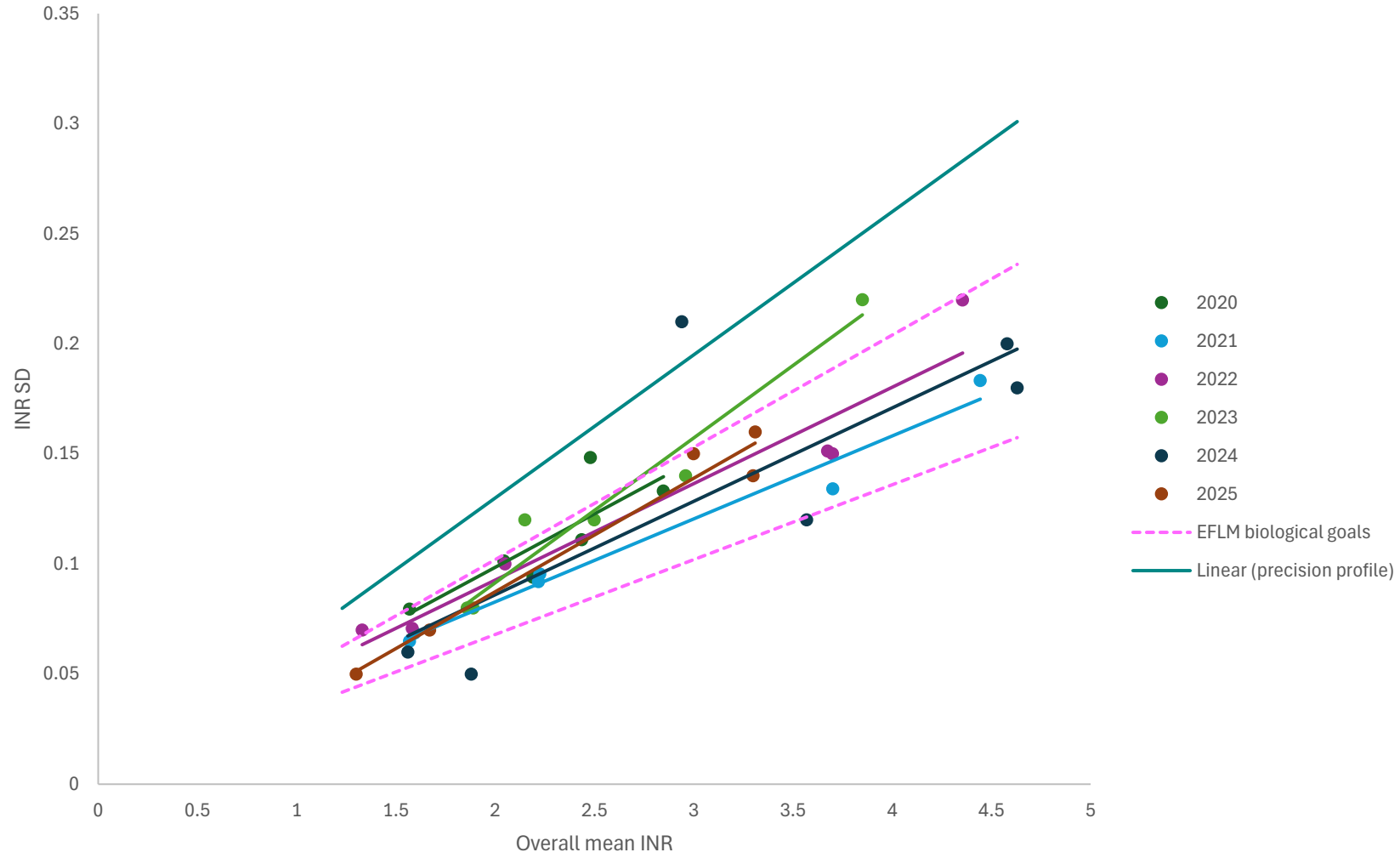
- Benefits
  - Enables real-time dose adjustments
  - Reduces appointment length and frequency
  - Reduces demand on lab services
  - Improved patient satisfaction and adherence
  - Improved anticoagulation control
  - Lab samples rejected if short/wrong tube

- Pitfalls
  - POCT INR more prone to artifacts than conventional testing on plasma
  - Overestimation at low INR/underestimation at high INR
  - Errors from antiphospholipid antibodies
  - Variation between instruments – especially outside INR >4.0

POCT INR - Current performance

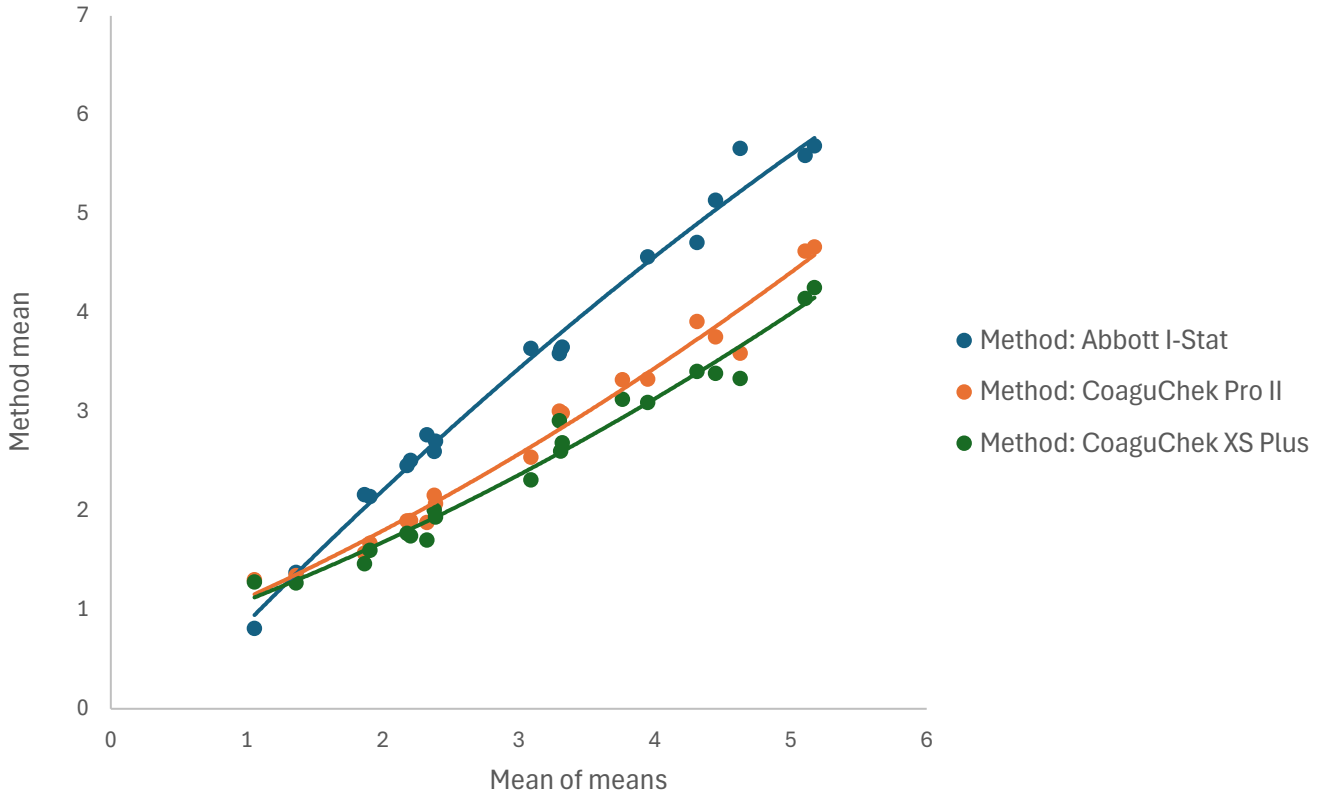


POCT INR - Current performance



INR method comparison

- EQA data over previous 3 years shows variation between instruments
- Consistent with previous studies
- Patients should be managed on only one POCT INR device, given known variation between devices
  - Maintain results within 0.5 units



Clinical Chemistry, Volume 56, Issue 10, 1 October 2010, Pages 1618–1626

Participation rates

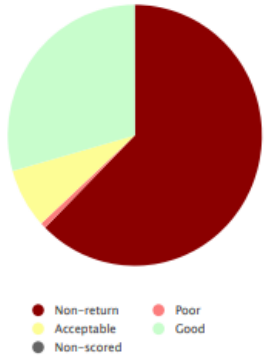
Programme: **POCT INR** • Distribution Code: **IN0925** • Analyte: **INR** • Units: **units**
Distribution Start: 09-Sep-2025 • Distribution End: 30-Sep-2025 • Report Issued: 13-Oct-2025 • Report Status: Final

Overall

	Overall		Sample 1	
	n	%	n	%
Good	75	74.3	75	74.3
Acceptable	24	23.8	24	23.8
Poor	1	1	1	1
Non-Return	1	1	1	1
Non-scored	0	0	0	0
Total	101		101	

Programme: **POCT INR** • Distribution Code: **IN0925** • Analyte: **INR** • Units: **units**
Distribution Start: 09-Sep-2025 • Distribution End: 30-Sep-2025 • Report Issued: 13-Oct-2025 • Report Status: Final

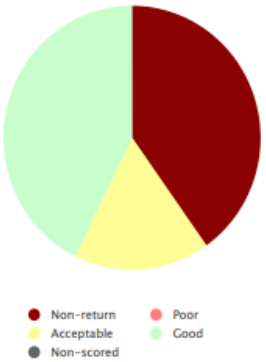
Overall



	Overall		Sample 1	
	n	%	n	%
Good	40	29.4	40	29.4
Acceptable	10	7.4	10	7.4
Poor	1	0.7	1	0.7
Non-Return	85	62.5	85	62.5
Non-scored	0	0	0	0
Total	136		136	

Programme: **POCT INR** • Distribution Code: **IN0925** • Analyte: **INR** • Units: **units**
Distribution Start: 09-Sep-2025 • Distribution End: 30-Sep-2025 • Report Issued: 13-Oct-2025 • Report Status: Final

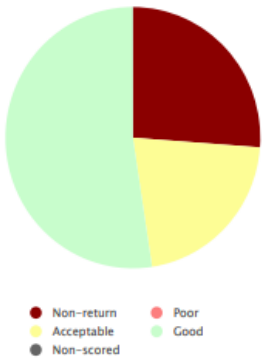
Overall



	Overall		Sample 1	
	n	%	n	%
Good	35	42.7	35	42.7
Acceptable	14	17.1	14	17.1
Poor	0	0	0	0
Non-Return	33	40.2	33	40.2
Non-scored	0	0	0	0
Total	82		82	

Programme: **POCT INR** • Distribution Code: **IN0925** • Analyte: **INR** • Units: **units**
Distribution Start: 09-Sep-2025 • Distribution End: 30-Sep-2025 • Report Issued: 13-Oct-2025 • Report Status: Final

Overall



	Overall		Sample 1	
	n	%	n	%
Good	110	52.4	110	52.4
Acceptable	45	21.4	45	21.4
Poor	0	0	0	0
Non-Return	55	26.2	55	26.2
Non-scored	0	0	0	0
Total	210		210	

Weqas POCT Glucose and Ketones programme

- Designed for healthcare professionals using POCT devices
  - >30 000 samples per month
- Suitable for all POCT devices in current use
- One sample sent monthly/bimonthly/quarterly as required
  - Glucose – 1.8 – 20 mmol/L in past 12 months
  - Ketones – 0.6 – 6.0 mmol/L in past 12 months

POCT Glucose

- Rapid turnaround time
  - Emergencies – hypoglycaemia, DKA, altered mental status, critical illness
  - Immediate bedside decision-making – management during surgery or post-op, dialysis, neonates and paediatrics

- Settings without access to lab services
  - Remote facilities, community clinics, primary care

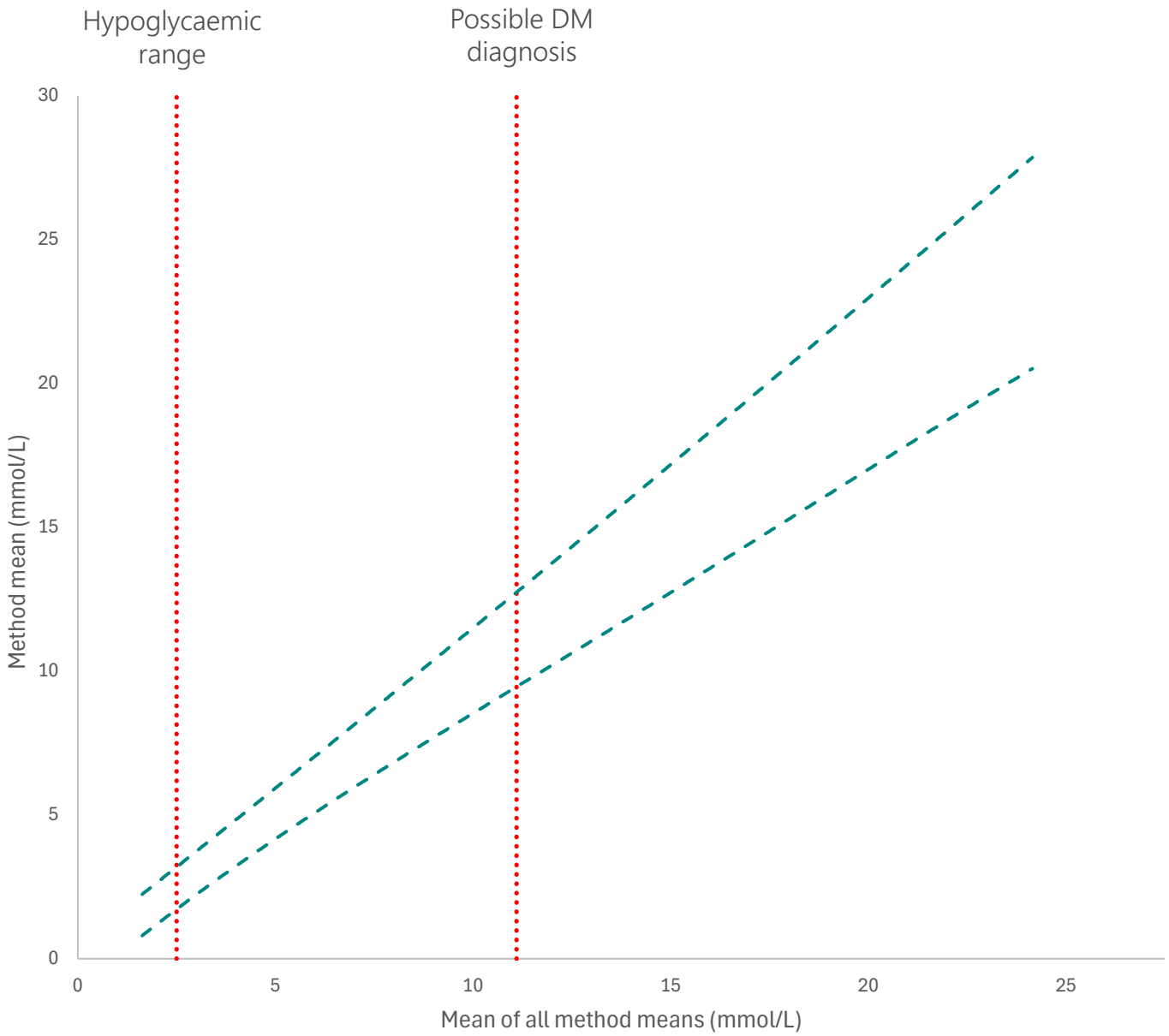
- Patient-centred care
  - Supports self-management of chronic condition e.g. DM
  - Reduces need for repeated venepuncture – paediatrics, long-term care, ICU, behavioural health units

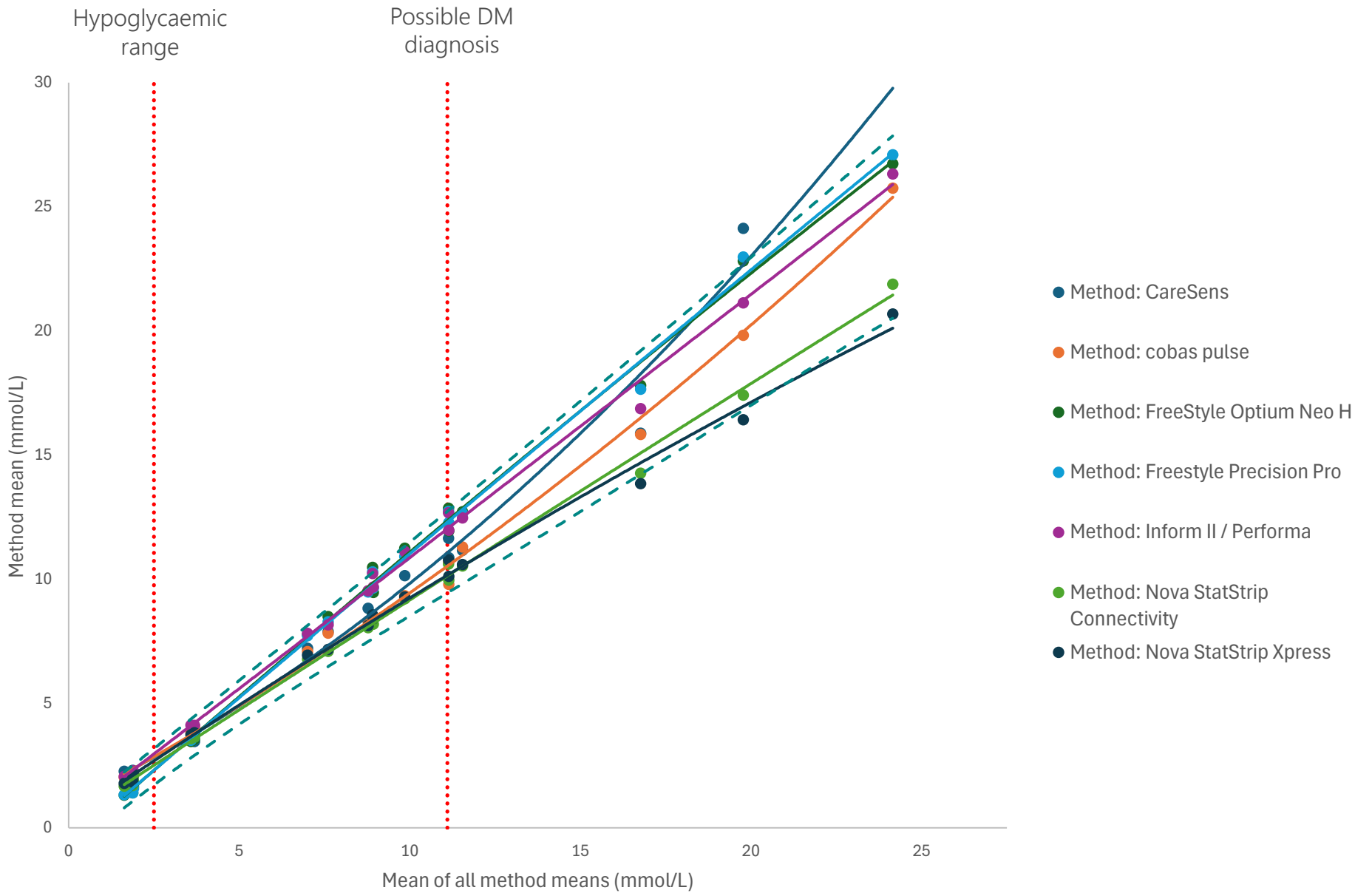
POCT Glucose

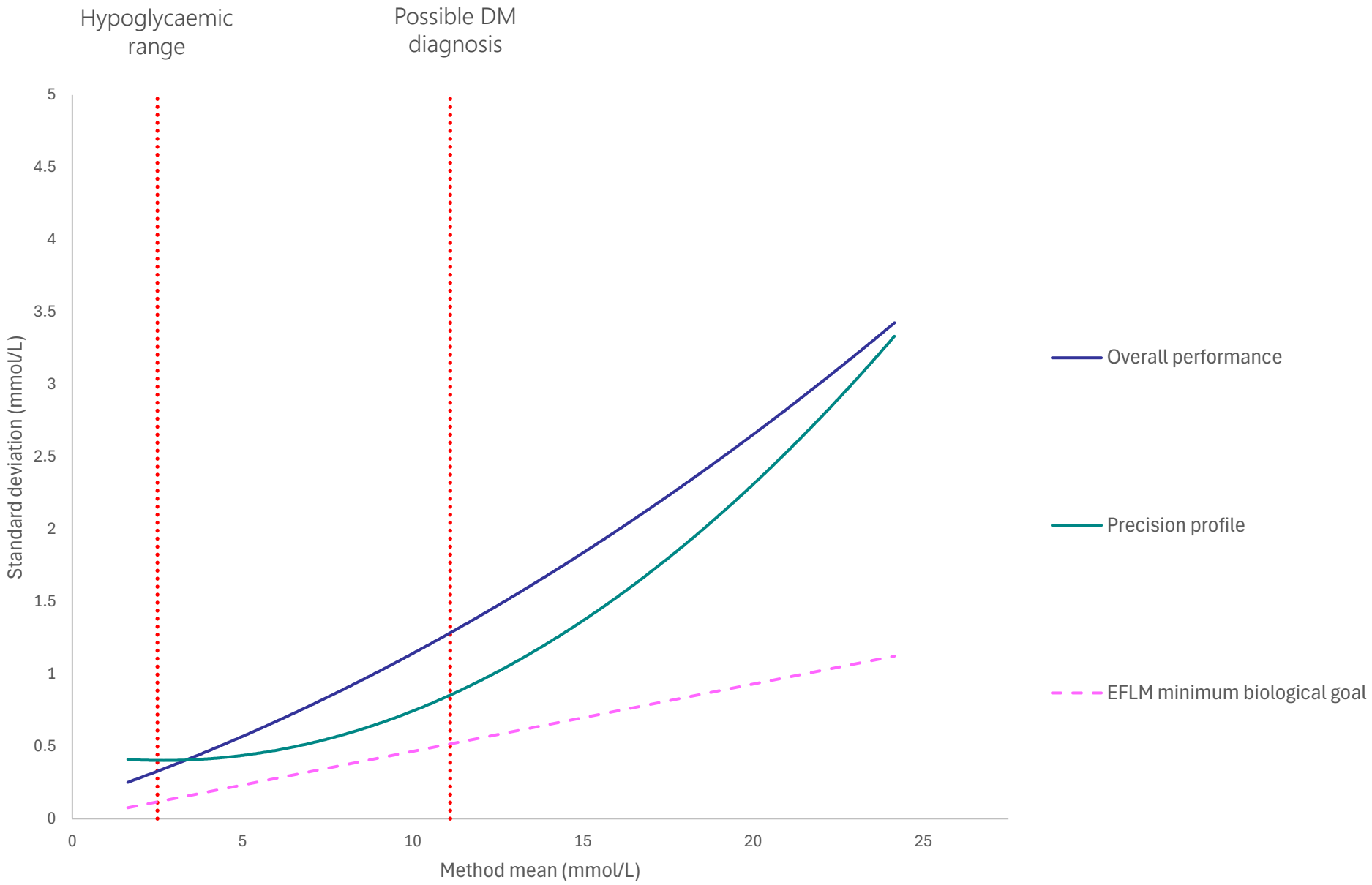
- Potential pitfalls
  - Interferences are common – ascorbic acid, low/high haematocrit, oxygen levels
  - Variation in capillary sample quality – perfusion, dehydration, shock
  - Operator-dependent errors – variation in operator skill, sample contamination, test strip handling

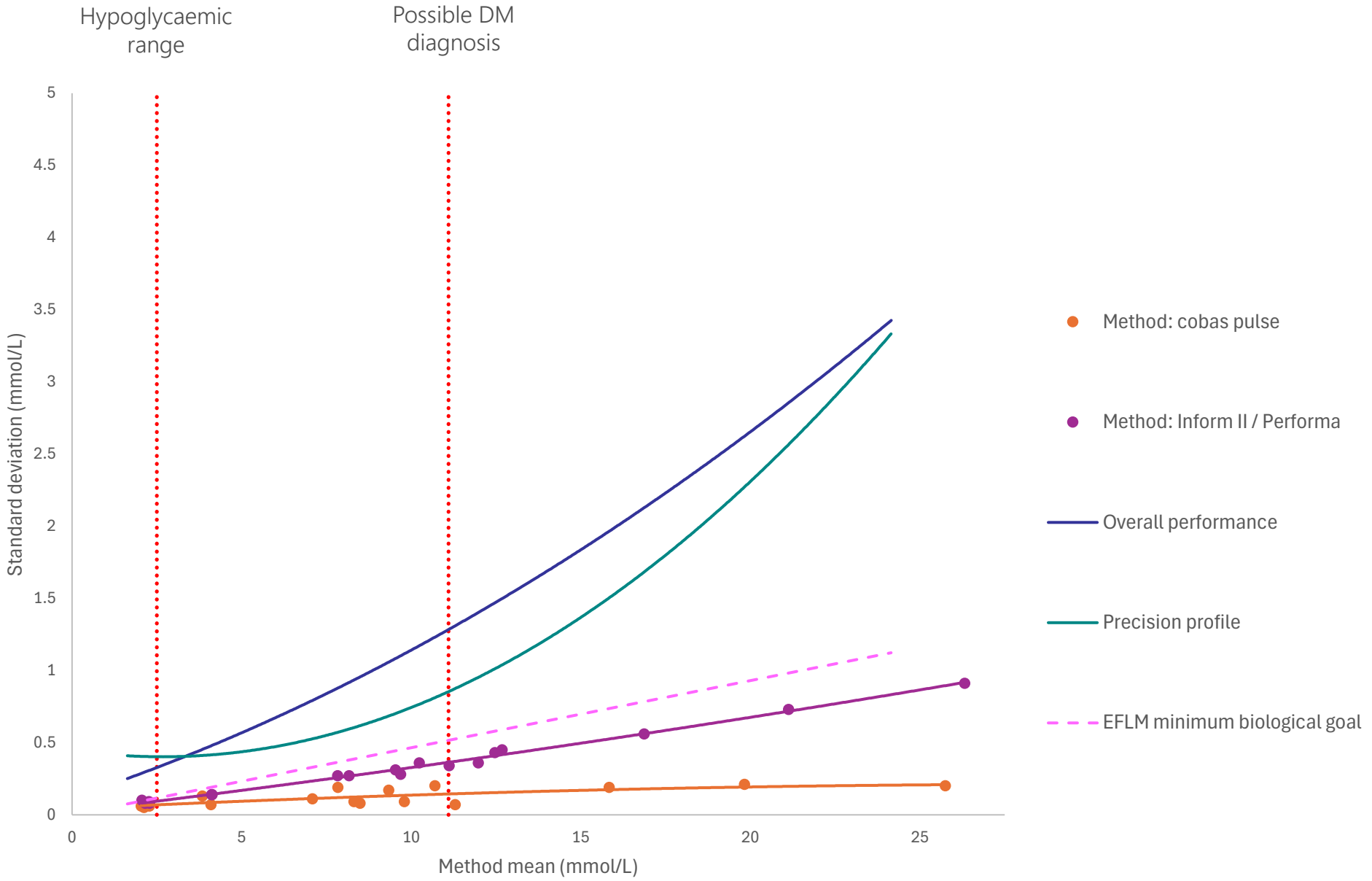
POCT Glucose – performance specifications

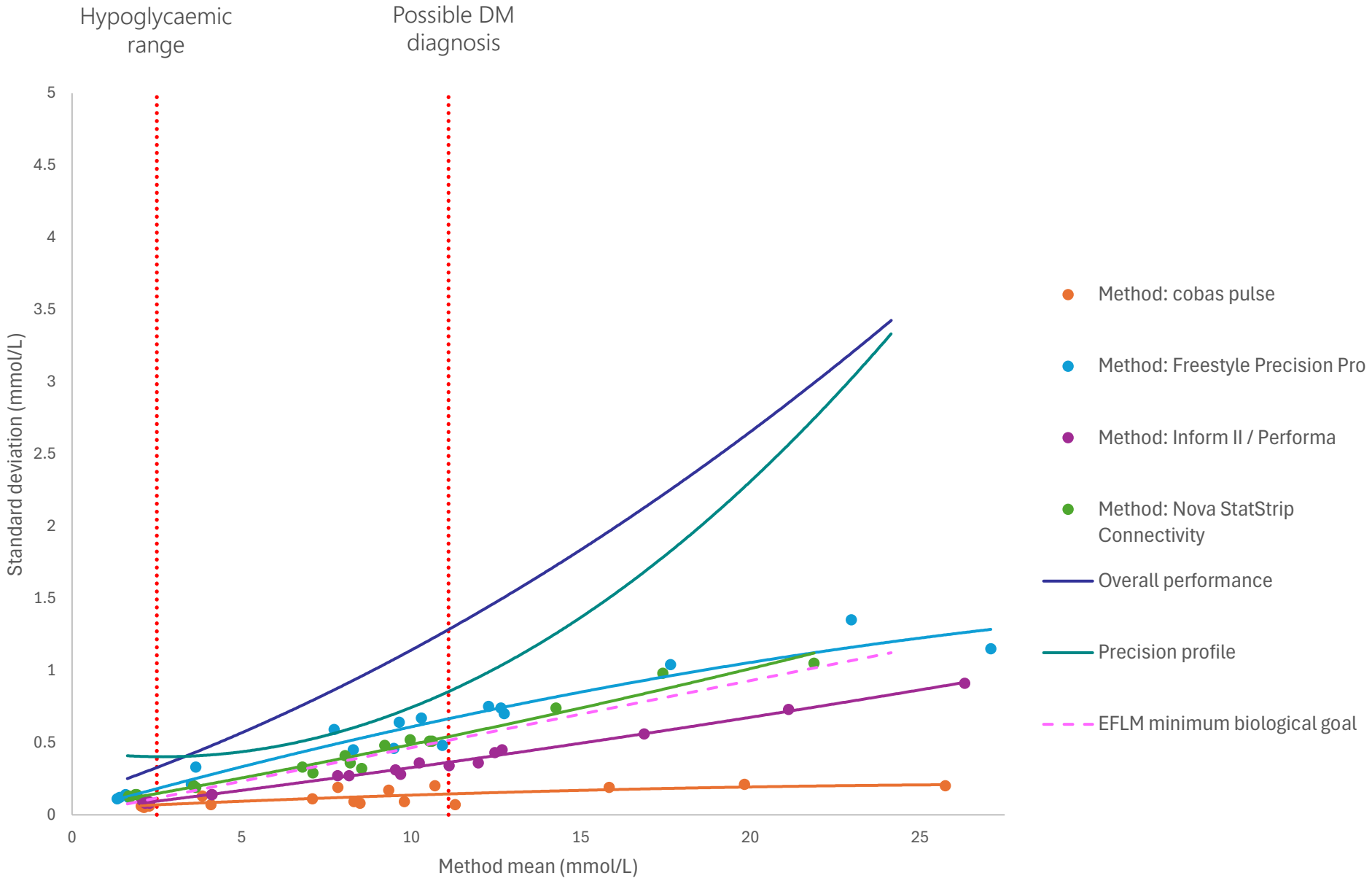
- ISO15197:2013 states glucose meters:
  - 95 % of results within:
    - 0.8 mmol/L of reference value below 5.6 mmol/L
    - 15 % of reference value at 5.6 mmol/L or above

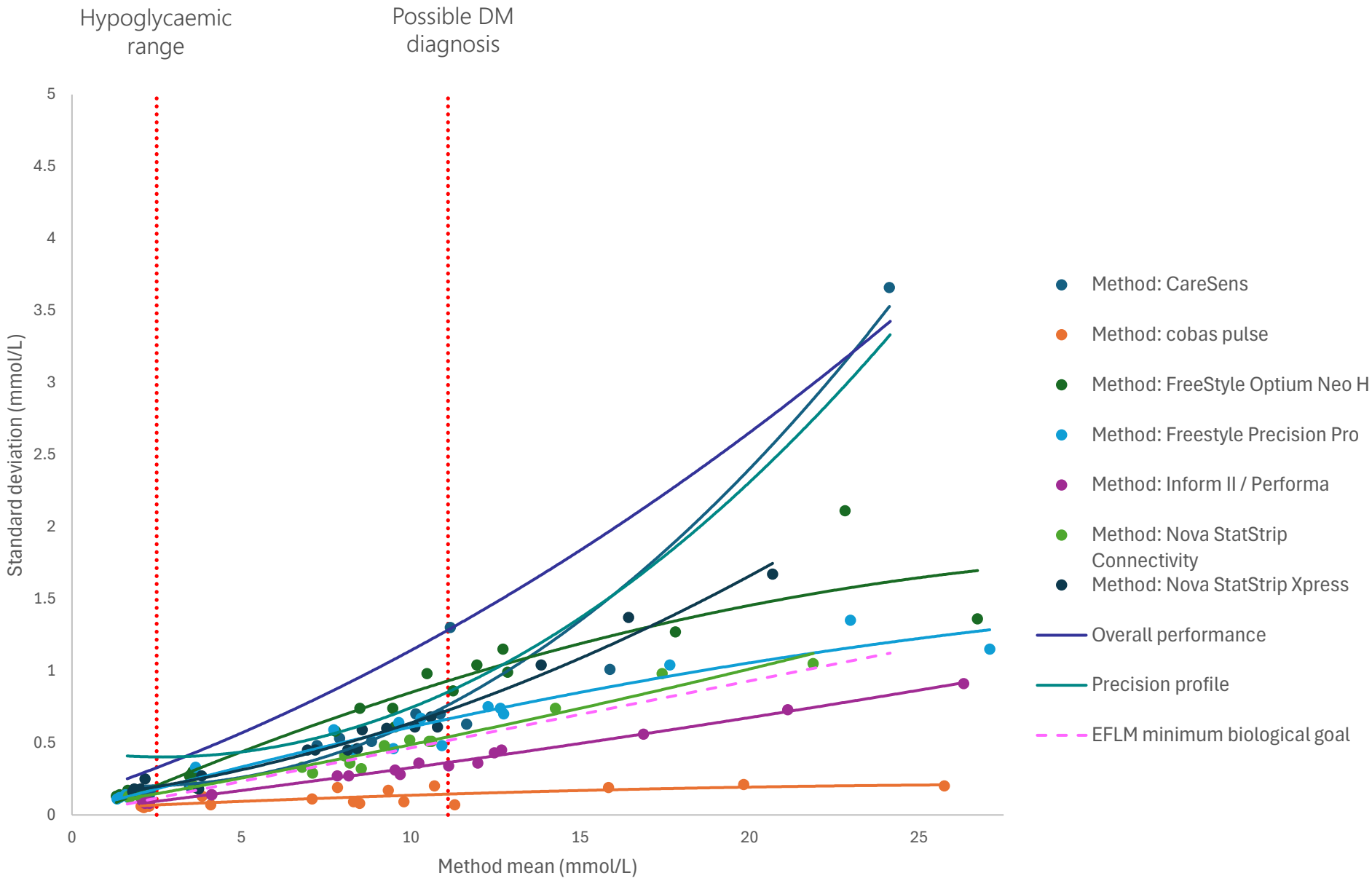

Hypoglycaemic range
Possible DM diagnosis
Method mean (mmol/L)
Mean of all method means (mmol/L)
0
5
10
15
20
25
30


Hypoglycaemic range
Possible DM diagnosis
Method mean (mmol/L)
Mean of all method means (mmol/L)
0
5
10
15
20
25
30
Method: CareSens
Method: cobas pulse
Method: FreeStyle Optium Neo H
Method: Freestyle Precision Pro
Method: Inform II / Performa
Method: Nova StatStrip Connectivity
Method: Nova StatStrip Xpress


Hypoglycaemic range
Possible DM diagnosis
Standard deviation (mmol/L)
Method mean (mmol/L)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
0
5
10
15
20
25
Overall performance
Precision profile
EFLM minimum biological goal


Hypoglycaemic range
Possible DM diagnosis
Standard deviation (mmol/L)
Method mean (mmol/L)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
0
5
10
15
20
25
Method: cobas pulse
Method: Inform II / Performa
Overall performance
Precision profile
EFLM minimum biological goal


Hypoglycaemic range
Possible DM diagnosis
Standard deviation (mmol/L)
Method mean (mmol/L)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
0
5
10
15
20
25
Method: cobas pulse
Method: Freestyle Precision Pro
Method: Inform II / Performa
Method: Nova StatStrip Connectivity
Overall performance
Precision profile
EFLM minimum biological goal


Hypoglycaemic range
Possible DM diagnosis
Standard deviation (mmol/L)
Method mean (mmol/L)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
0
5
10
15
20
25
Method: CareSens
Method: cobas pulse
Method: FreeStyle Optium Neo H
Method: Freestyle Precision Pro
Method: Inform II / Performa
Method: Nova StatStrip Connectivity
Method: Nova StatStrip Xpress
Overall performance
Precision profile
EFLM minimum biological goal

POCT Ketones

- Rapid assessment of emergency situations
  - DKA/hyperglycaemia, vomiting, diarrhoea, dehydration, unexplained illness
  - May be more informative than urine ketones in acute illness

- Detection of ketosis in individuals with T1DM
  - Early detection and treatment of ketosis may improve patient outcomes and reduce hospital admissions

- Assessment of response to treatment
  - Aim for reduction of 0.5 mmol/hour until concentration is <1.0 mmol/L

POCT Ketones

- Pitfalls
  - Variation increases at high ketone concentrations
  - Sampling issues – poor perfusion, dehydration – can affect results
  - Devices are not interchangeable

POCT Ketones – performance specifications

PERSPECTIVES IN CARE | JANUARY 17 2022

Controversies Around the Measurement of Blood Ketones to Diagnose and Manage Diabetic Ketoacidosis

Eric S. Kilpatrick; Alexandra E. Butler; Linda Ostlundh; Stephen L. Atkin; David B. Sacks

Discussing the reliability of meter measurement raises the question of what analytical performance should be regarded as clinically acceptable. There is an opportunity to clinically define how good this should be for optimal patient care (the so-called analytical performance specification [32]), which, if beyond current meter analytical capability, might help drive the development of instruments that can achieve this degree of performance.

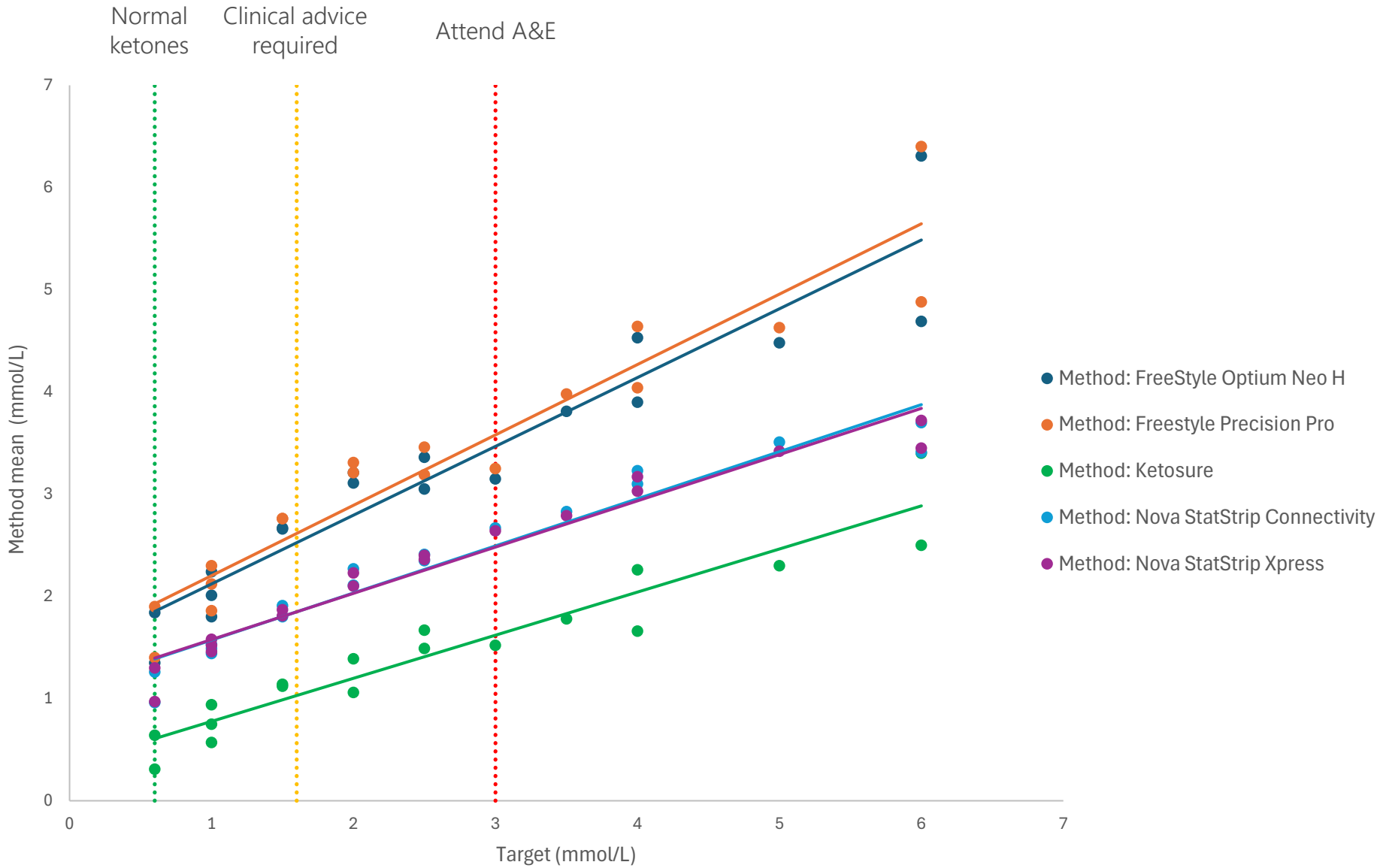
JOURNAL ARTICLE

Establishing Pragmatic Analytical Performance Specifications for Blood Beta-Hydroxybutyrate Testing

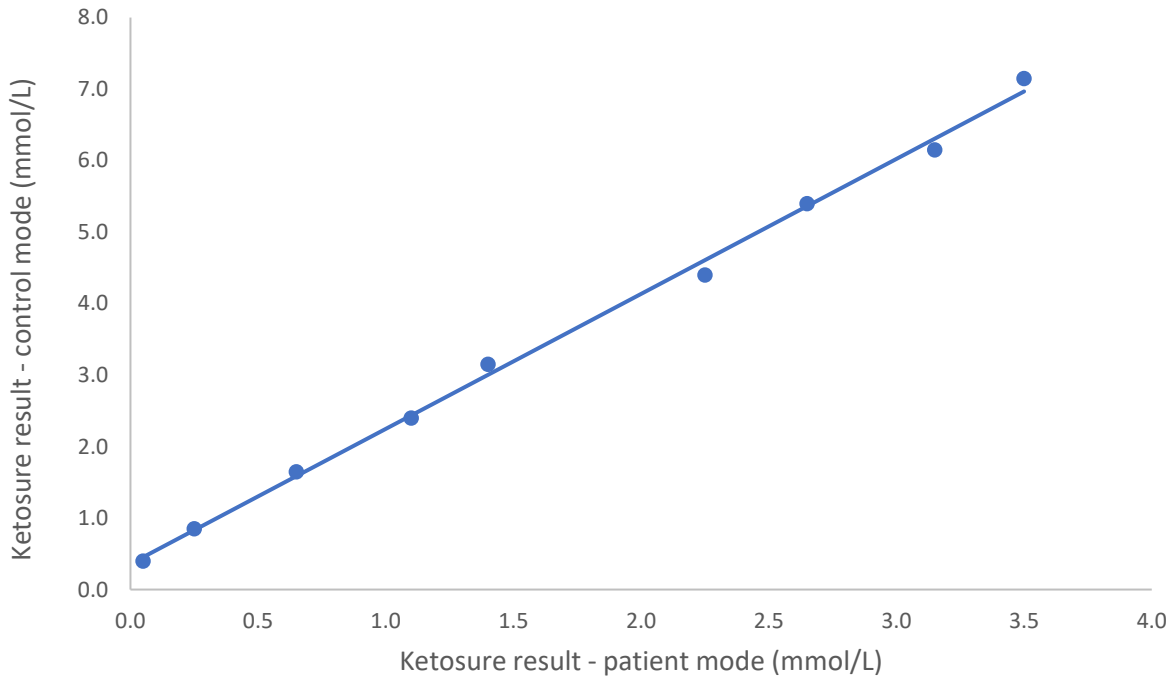
Eric S Kilpatrick, Alexandra E Butler, Stephen L Atkin, David B Sacks

Clinical Chemistry, Volume 69, Issue 5, May 2023, Pages 519–524,

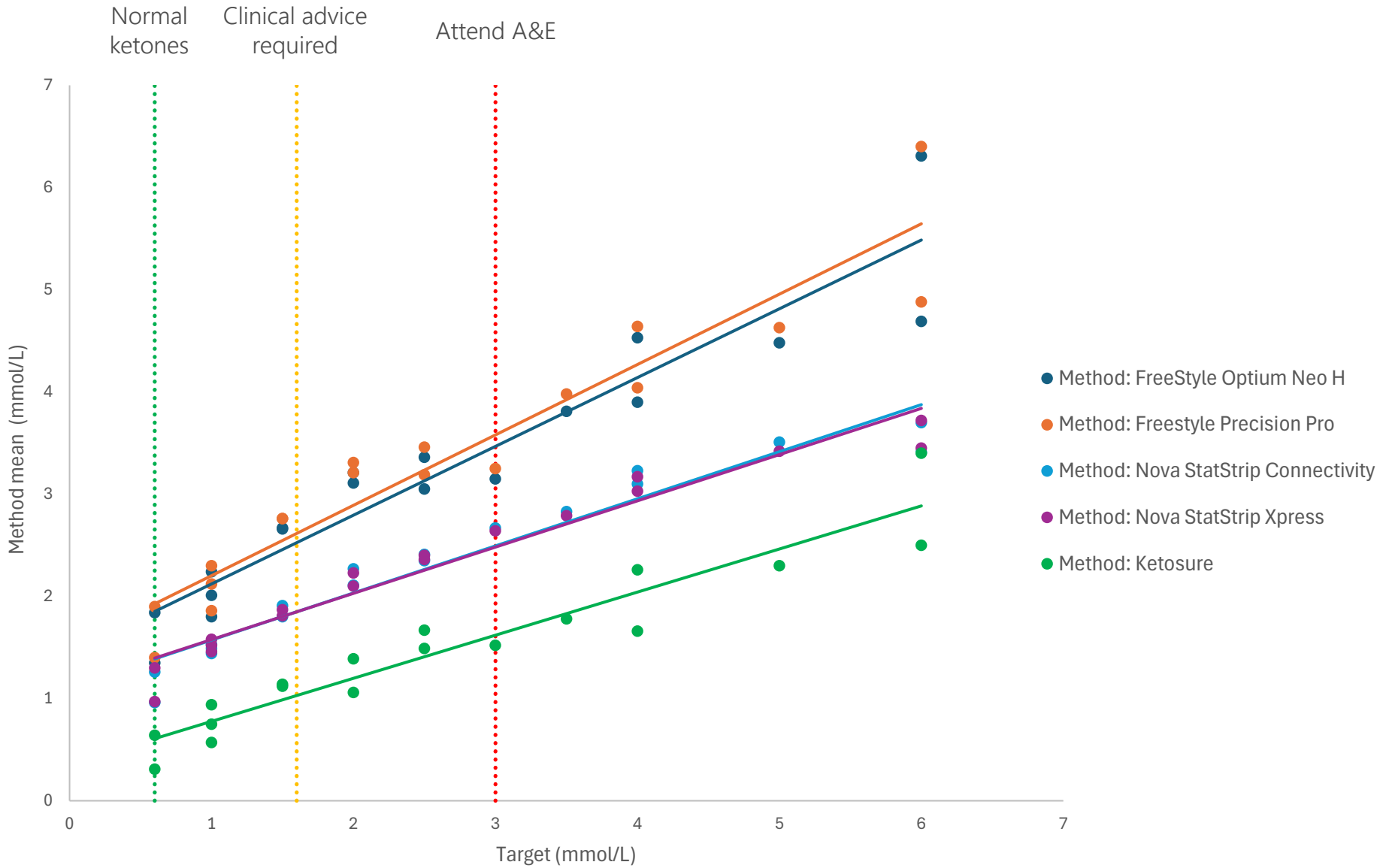
An analytical coefficient of variation (CV) of <21.5% could reliably distinguish all non-adjacent diagnostic categories with >99% certainty, assuming zero bias. In contrast, within-day CVs of 4.9%, 7.0%, and 9.1% at 3 mmol/L BOHB were required to assure truly falling ketone concentrations with 99% (optimal), 95% (desirable), and 90% (minimal) probability, respectively. These CVs are larger at lower BOHB concentrations and smaller at higher concentrations.

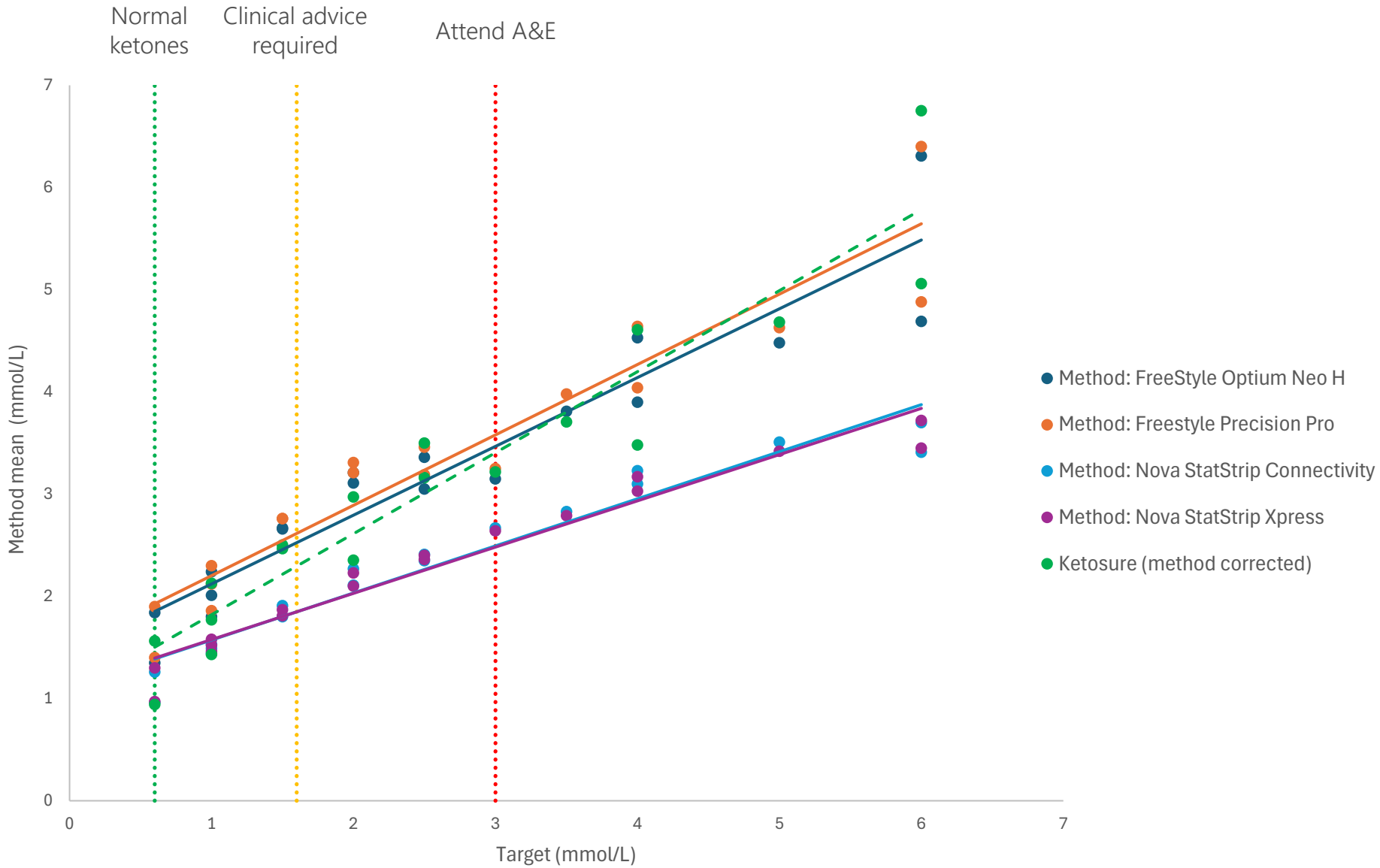

Normal ketones
Clinical advice required
Attend A&E
Method mean (mmol/L)
Target (mmol/L)
0
1
2
3
4
5
6
7
Method: FreeStyle Optium Neo H
Method: Freestyle Precision Pro
Method: Ketosure
Method: Nova StatStrip Connectivity
Method: Nova StatStrip Xpress

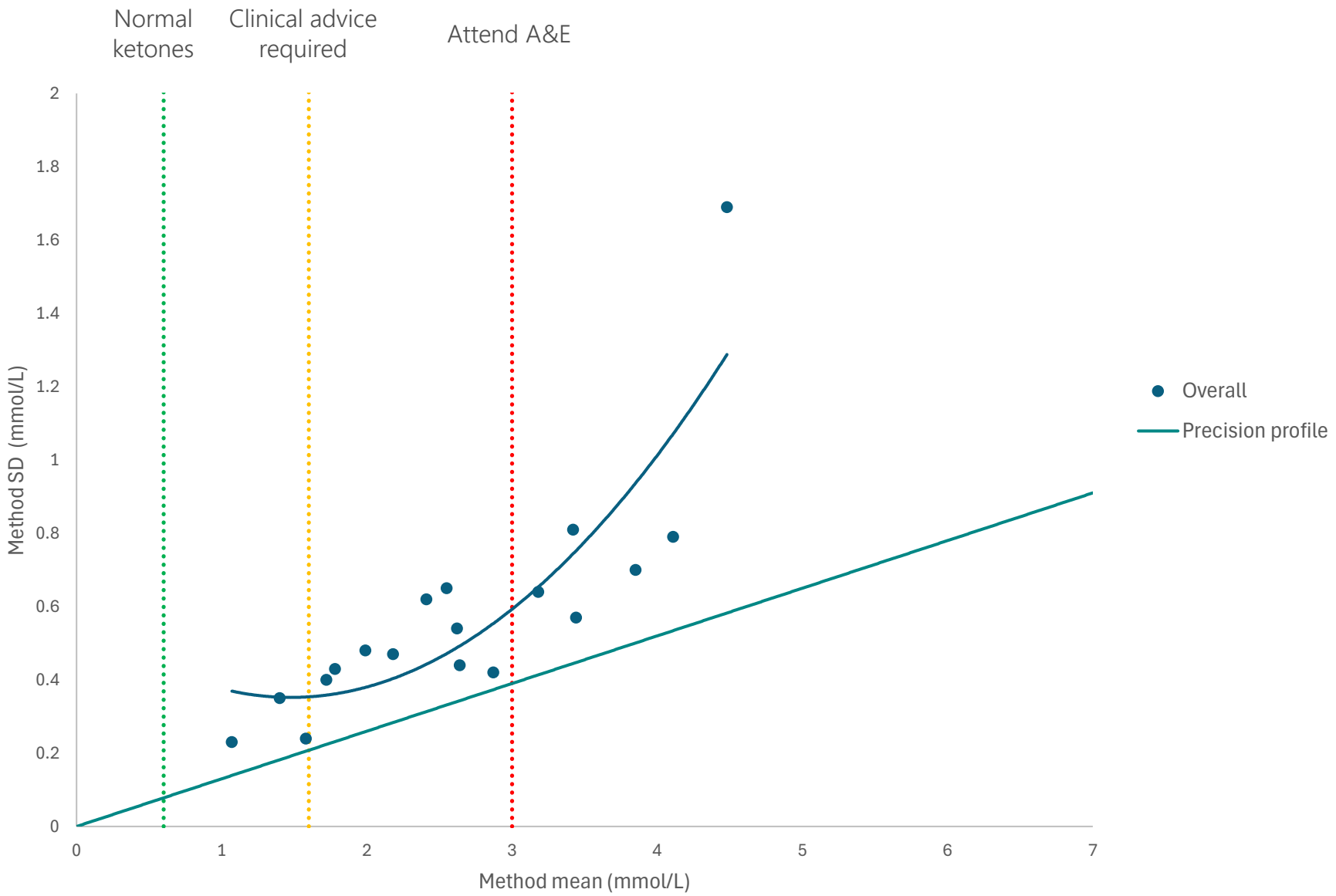
KetoSure result correction – preliminary results

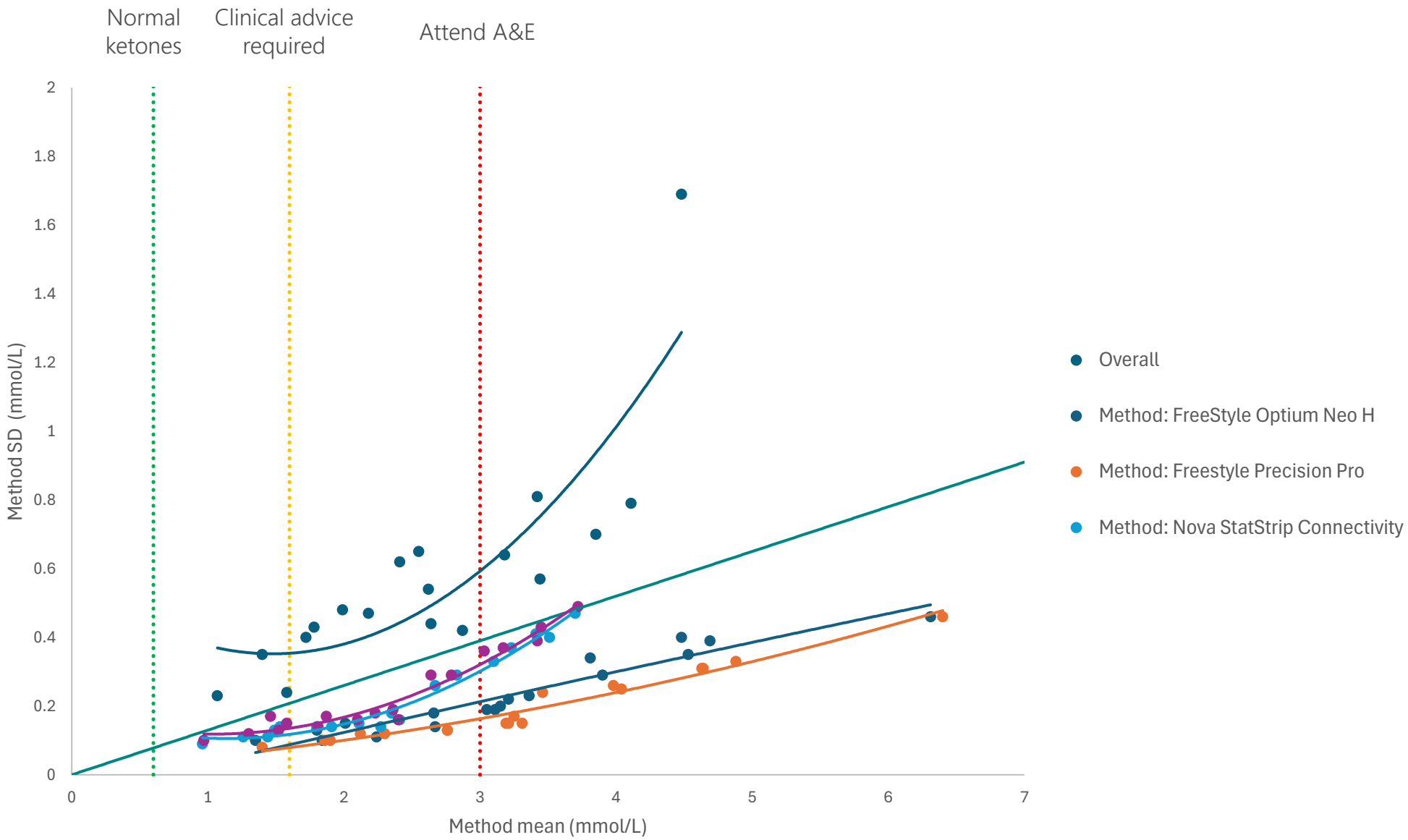


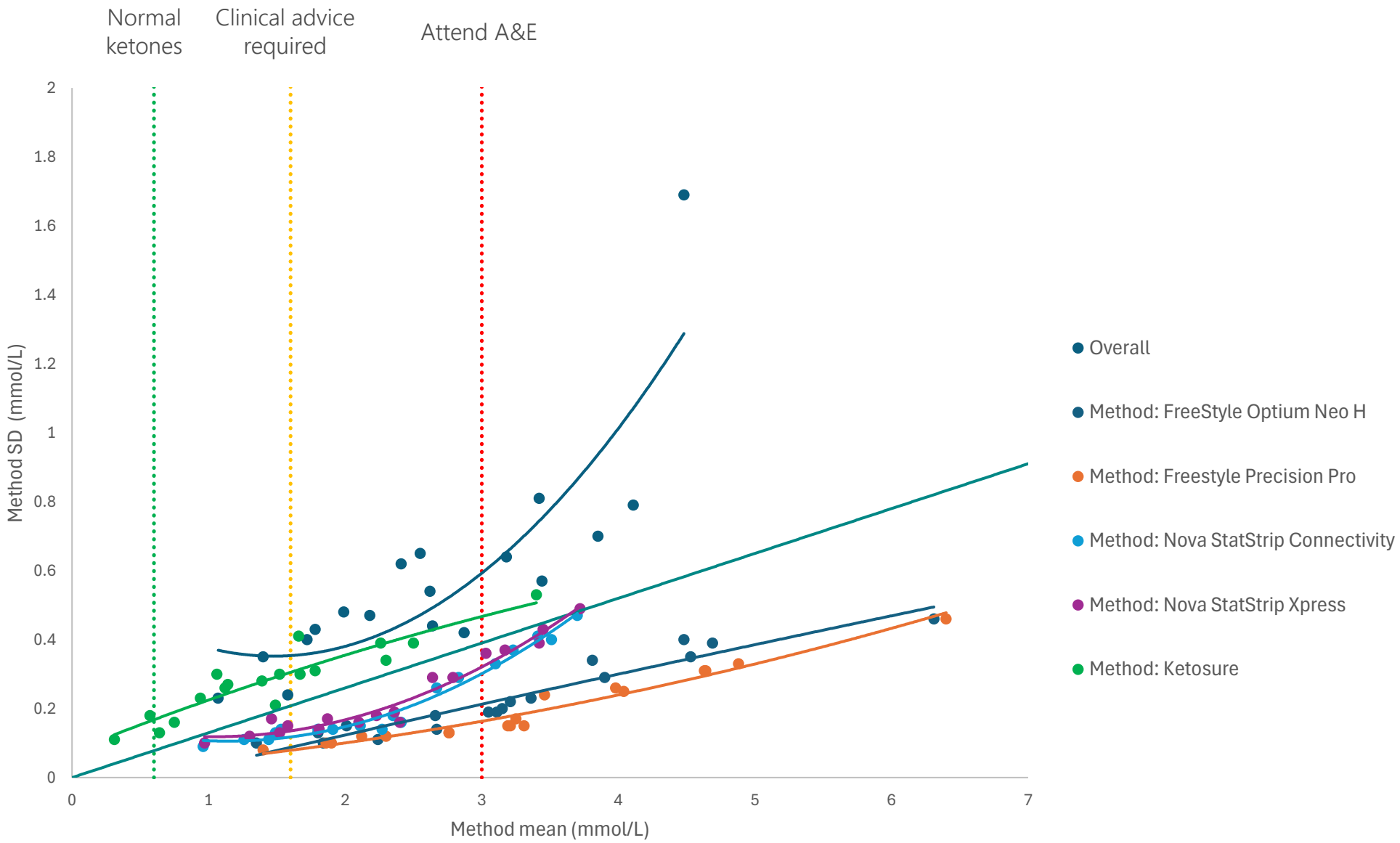
- EQA samples run in ‘patient mode’ and ‘QC mode’ across analytical range
- Linear relationship between modes established
- Enables adjustment of EQA results obtained in patient mode
- Currently not possible for participants to use QC mode for running EQA samples

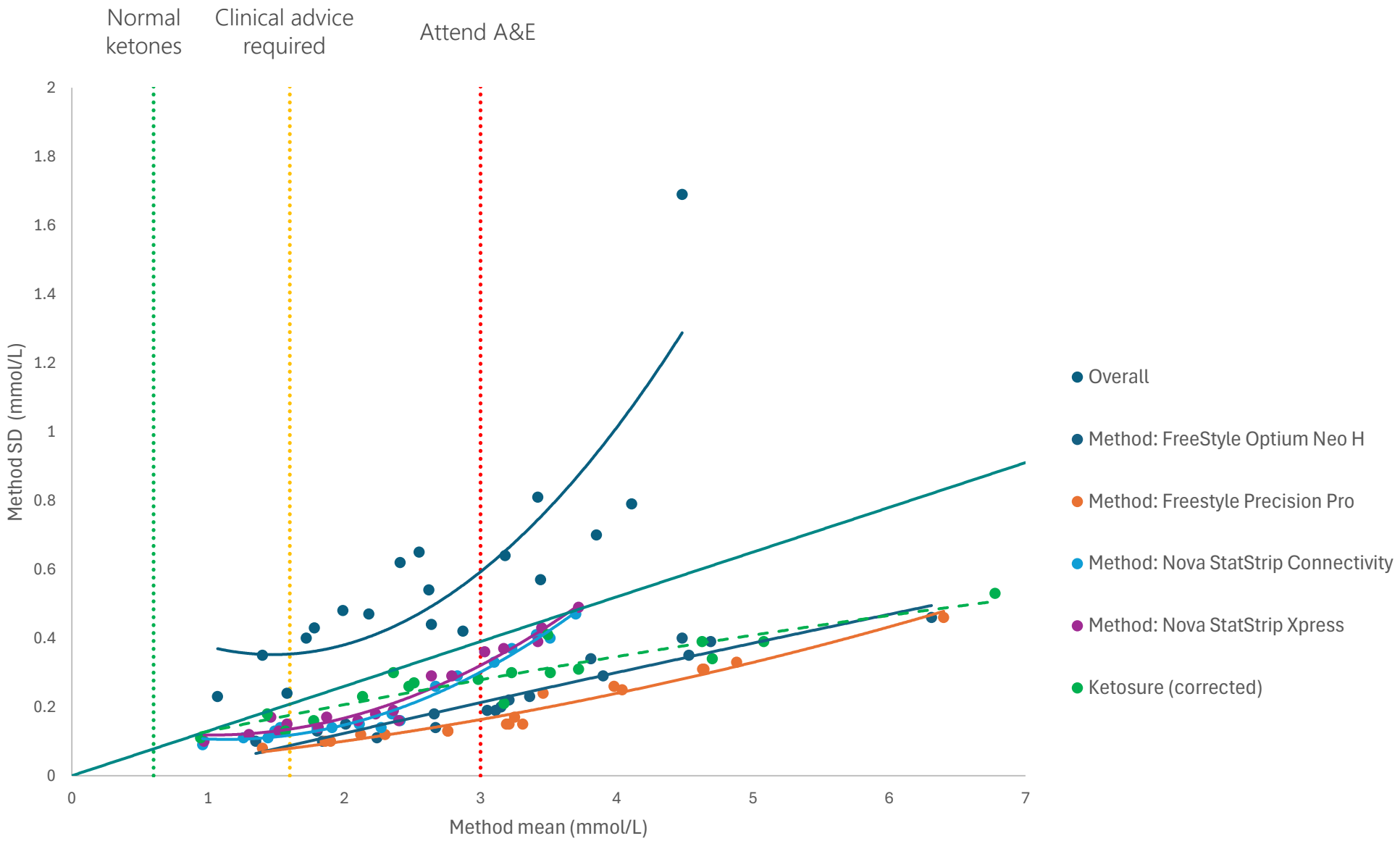

Normal ketones
Clinical advice required
Attend A&E
Method mean (mmol/L)
Target (mmol/L)
0
1
2
3
4
5
6
7
Method: FreeStyle Optium Neo H
Method: Freestyle Precision Pro
Method: Nova StatStrip Connectivity
Method: Nova StatStrip Xpress
Method: Ketosure


Normal ketones
Clinical advice required
Attend A&E
Method mean (mmol/L)
Target (mmol/L)
0
1
2
3
4
5
6
7
Method: FreeStyle Optium Neo H
Method: Freestyle Precision Pro
Method: Nova StatStrip Connectivity
Method: Nova StatStrip Xpress
Ketosure (method corrected)


Normal ketones
Clinical advice required
Attend A&E
Method SD (mmol/L)
Method mean (mmol/L)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
0
1
2
3
4
5
6
7
Overall
Precision profile


Normal ketones
Clinical advice required
Attend A&E
Method SD (mmol/L)
Method mean (mmol/L)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
0
1
2
3
4
5
6
7
Overall
Method: FreeStyle Optium Neo H
Method: Freestyle Precision Pro
Method: Nova StatStrip Connectivity


Normal ketones
Clinical advice required
Attend A&E
Method SD (mmol/L)
Method mean (mmol/L)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
0
1
2
3
4
5
6
7
Overall
Method: FreeStyle Optium Neo H
Method: Freestyle Precision Pro
Method: Nova StatStrip Connectivity
Method: Nova StatStrip Xpress
Method: Ketosure


Normal ketones
Clinical advice required
Attend A&E
Method SD (mmol/L)
Method mean (mmol/L)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
0
1
2
3
4
5
6
7
Overall
Method: FreeStyle Optium Neo H
Method: Freestyle Precision Pro
Method: Nova StatStrip Connectivity
Method: Nova StatStrip Xpress
Ketosure (corrected)

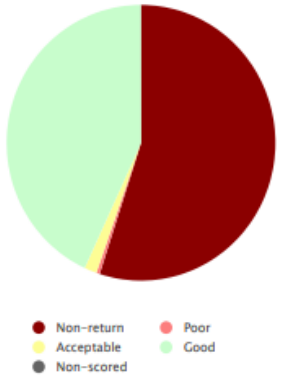
POCT Ketones

- KetoSure results are out of sync with other instruments – known issue
- Likely due to haematocrit correction when running EQA samples in patient mode
- Experiments to optimise ketone material are ongoing

Participation rates

Programme: **POCT Glucose and Ketones** • Distribution Code: **GK0925** • Analyte: **Glucose** • Units: **mmol/L**
Distribution Start: 02-Sep-2025 • Distribution End: 24-Sep-2025 • Report Issued: 01-Oct-2025 • Report Status: Final

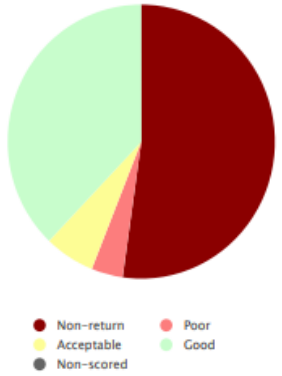
Overall



	Overall		Sample 1	
	n	%	n	%
Good	307	43.1	307	43.1
Acceptable	11	1.5	11	1.5
Poor	3	0.4	3	0.4
Non-Return	392	55	392	55
Non-scored	0	0	0	0
Total	713		713	

Programme: **POCT Glucose and Ketones** • Distribution Code: **GK0925** • Analyte: **Ketones** • Units: **mmol/L**
Distribution Start: 02-Sep-2025 • Distribution End: 24-Sep-2025 • Report Issued: 01-Oct-2025 • Report Status: Final

Overall



	Overall		Sample 1	
	n	%	n	%
Good	50	37.9	50	37.9
Acceptable	8	6.1	8	6.1
Poor	5	3.8	5	3.8
Non-Return	69	52.3	69	52.3
Non-scored	0	0	0	0
Total	132		132	

Conclusions

- POCT INR
  - Well-established clinical use outside of the laboratory
  - Known variation between POCT instruments – patients should be monitored on one instrument only
  - Performance is generally good – but non-returns are an issue

- POCT Glucose
  - Extensive use outside of laboratory – both on wards, clinics and at home
  - Defined performance standards
  - Majority of instruments meeting standards

- POCT Ketones
  - Extensive use outside of laboratory – both on wards, clinics and at home
  - Performance standards under review
  - Known issues affecting KetoSure – work underway to optimise EQA material for use on all devices

Thank you for listening!