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# Analytical performance specifications (APS) - are we providing clinically appropriate APS for External Quality Assessment?

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## Introduction

In terms of EQA, 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.

## Aims

The aim of the study was to review the strengths and weaknesses of the various models and compare with what was achievable in a real-world environment to establish clinically appropriate APS for routine chemistry measurands. Models based on the biological variation of the measurand (Model 2), and the highest level of analytical quality achievable (Model 3) were reviewed respectively.

## Method

Laboratory and Point of Care method performance data from Weqas in the UK was collected over the last five years across a wide clinical concentration for the common measurands in Clinical Biochemistry. The data covered 60 distributions using 240 samples, assayed by 200 laboratories for a range of measurands. Precision profiles were calculated for each measurand and for each of the major methods used for that measurand. These were represented as Standard Deviation (SD) and Coefficient of Variation (CV%) against measurand concentration. The overall and method profiles were compared with the optimal, desirable, and minimum APS based on Model 2 and the methods with the best analytical quality established.

## Results

The strengths and weaknesses of the various models were reviewed and compared with what was achievable in a real-world environment. For Potassium, Urate and Cholesterol an universal APS based on the desirable EFLM Total allowable error, (TEa) from Model 2 was achievable for all methods, although in the case of Cholesterol, the performance was influenced by the triglyceride concentration in the sample. For Sodium and HbA1c, the APS based on Model 2 minimum TEa was not achievable and alternative models are proposed. For Creatinine and glucose an universal APS based on desirable Model 2 TEa was achievable at concentrations > 100 µmol/L and > 3.0mmol/l respectively. For Calcium the minimum TEa was achieved at a concentration > 1.8 mmol/L for the majority of methods and 2 methods achieved performance between desirable and optimum. For HDL an universal APS based on the Minimum TEa was achieved at concentration > 1.0 mmol/L.

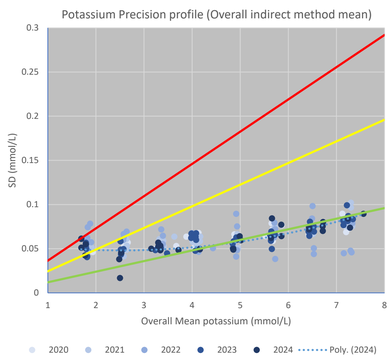
### Table 1 -Proposed APS for 9 routine measurands

| | Intervention target | TEa ( %) | | | Proposed APS |
|---|---|---|---|---|---|
| Analyte | Conc. | Min | Des | Opt | TEa (%) |
| Na | 135 mmol/L | 0.9 | 0.6 | 0.3 | 1.0 hybrid (best method) |
| K | 3.5 mmol/L | 7.3 | 4.9 | 2.4 | Hybrid (2.4 opt + 4.9 des) |
| Ca | 2.2 mmol/L | 3.4 | 2.3 | 1.1 | 3.4 min |
| Creat | 90 µmol/L | 11.7 | 7.8 | 3.9 | 7.8 des |
| Glucose | 2.0 / 6.5 mmol/L | 9.2 | 6.1 | 3.1 | 6.1 des |
| Urate | 360 µmol/L | 19 | 12.6 | 6.3 | Hybrid (6.3 opt +12.6 des) |
| Cholesterol | 5.0 mmol/L | 12.5 | 8.3 | 4.2 | 8.3 des |
| HDL | 1.0 mmol/L | 14.9 | 9.9 | 5.0 | 9.9 des |
| HbA1c | 48 mmol/mol | 4.7 | 3.1 | 1.6 | 5.0 hybrid (min + best method) |

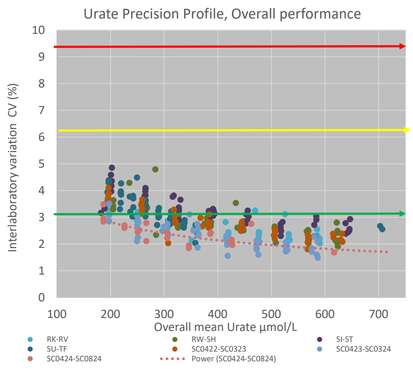
Key
Minimum
Desirable
Optimum

- Can we use universal APS based on biological variation? – **YES**
- **Desirable** APS achieved for most methods for K, urate & Chol.

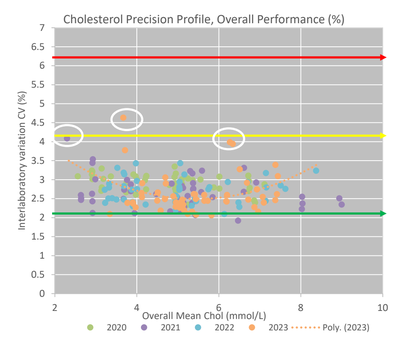
### Potassium Precision Profile




### Urate Precision Profile

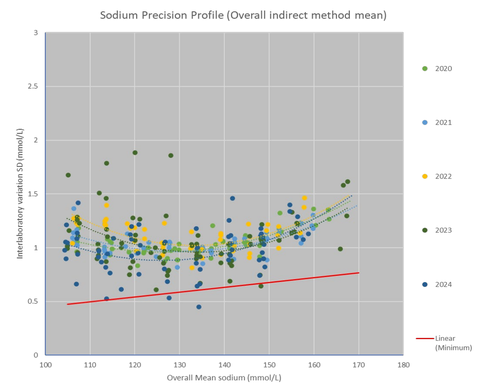


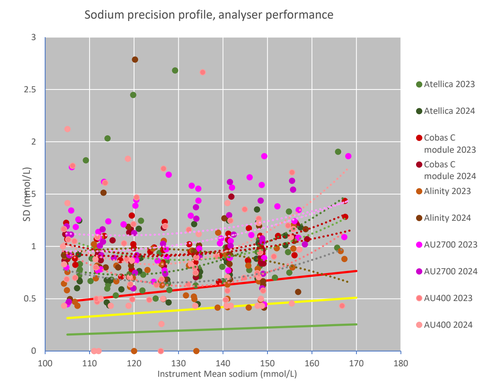

### Cholesterol Precision Profile




### Sodium Precision Profile

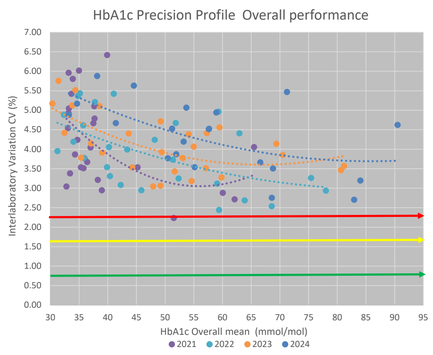
- Can we use universal APS based on biological variation? – **NO**
- Minimum APS based on biological variation rarely achieved – some improvement in 2024 but not consistent
- Can we determine the APS based on best analytical method available? Best fit of the current "best method" TEa = 1.4mmol/L now close to **Minimum** TEa of 0.9% @135-160 mmol/L
- Relationship of performance against concentration polynomial not linear

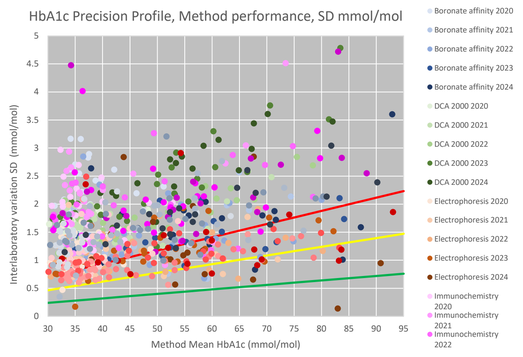



### HbA1c Precision Profile

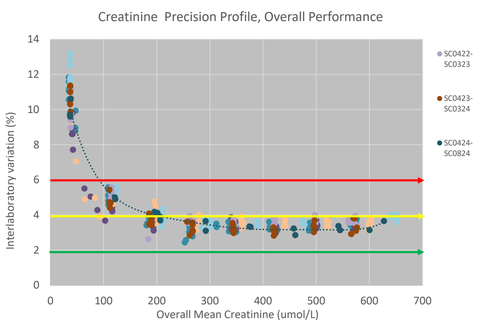
- Can we use universal APS based on biological variation? – **NO**
- Can we determine the APS based on best analytical method available? –**YES**
- Most laboratory electrophoresis and Ion exchange methods can achieve **Minimum**
- Should we use different APS for laboratory and POCT methods? – **YES (if only used for monitoring)**
- Overall data also includes effects of bias. Data includes laboratory and POCT methods

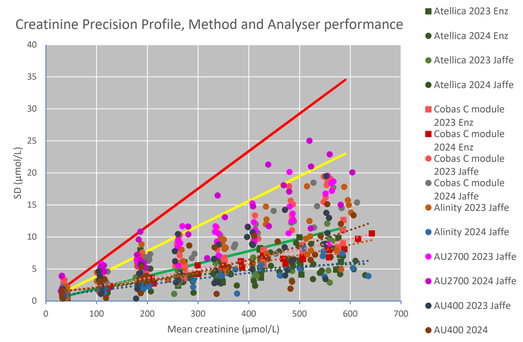



### Creatinine Precision Profile

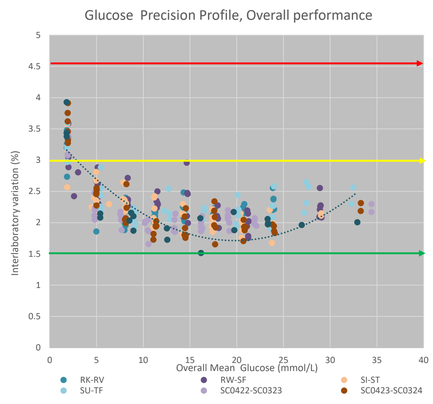
- Can we use universal APS based on biological variation? – **YES**
- **Minimum** APS achieved >70 µmol/L
- **Desirable** APS achieved > 200 µmol/L
- Variation includes method bias
- Are there methods that can achieve better? – **YES**
- **Desirable** APS achieved to 100 µmol/L for all methods.
- **Optimal** APS achieved for all other enzymatic methods as well as 2 Jaffe methods at a concentration > 100 µmol/L

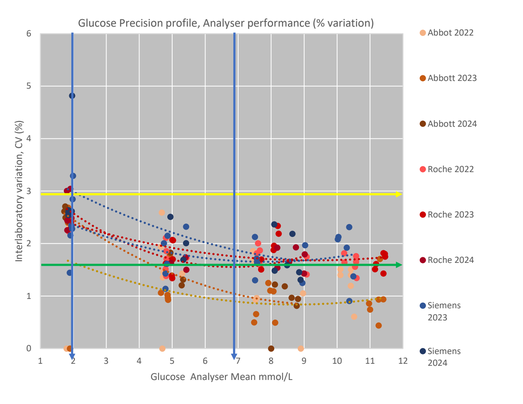



### Glucose Precision Profile

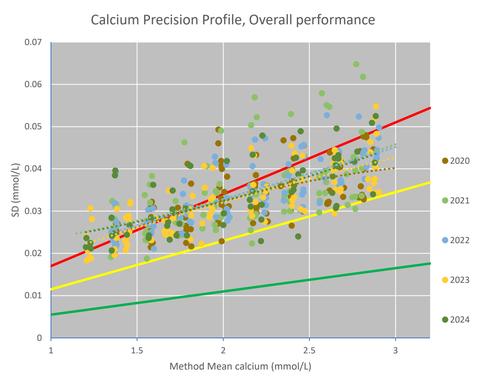
- Can we use universal APS based on biological variation? – **YES**
- **Desirable** APS achieved >3.0 mmol/L for most methods.
- Can we do better at critical decision points for individual analysers?
- **Desirable** APS based on biological variation achieved < 2 mmol/L for Abbott, Roche and Siemens methods.
- **Optimum** APS achieved for Abbott method at 2.5, 4.0 and 7.0 mmol/L and close to optimum at 2 mmol/L.

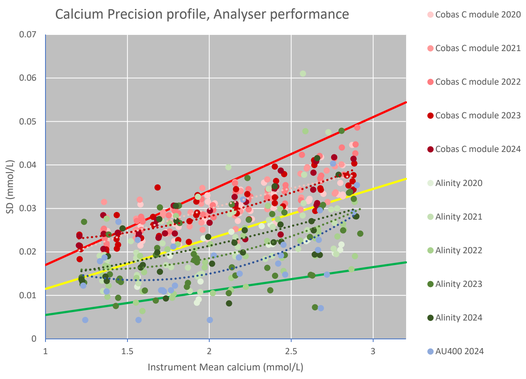



### Calcium Precision Profile

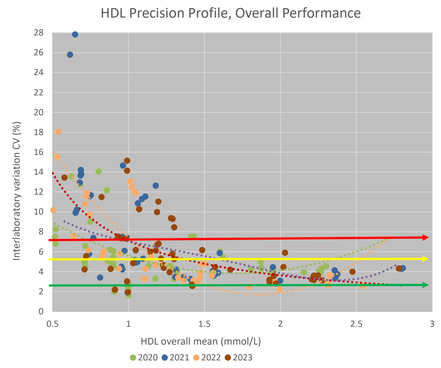
- Can we use universal APS based on biological variation? – **YES (partly)**
- **Minimum** APS achieved > 1.8 mmol/L for most methods.
- Relationship of performance against concentration close to linear
- Use minimum to 1.8 mmol/L and then best fit.
- Are then any methods that can achieve **desirable**? – **YES**
- Cobas C at concentration > 1.7mmol/L achieves performance between minimum and desirable
- Alinity > 1.4 mmol/L achieves performance between desirable and optimum
- AU400 mostly achieves performance between desirable and optimum

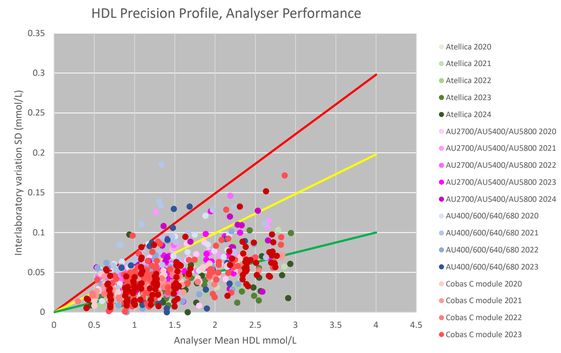



### HDL Cholesterol Precision Profile

- Can we use universal APS based on biological variation? – **MAYBE**
- **Minimum** APS achieved at > 1.0 mmol/L concentration.
- Data also includes effect of bias.
- Can we determine APS based on best technology?
- Most can achieve **Desirable**
- Some methods can achieve **optimum**




## Conclusion

Although Model 2 was achievable for a number of measurands, it was rarely achievable across the full pathological range. The relationship between performance in terms of SD or CV and measurand concentration was rarely linear, and a hybrid (mixed) model was proposed in this situation. APS should be designed to provide performance assessment that best meets the needs of the service, whether used for screening, monitoring or diagnosis. Where clinical utility of the test includes 2 or more then the more stringent model is selected.