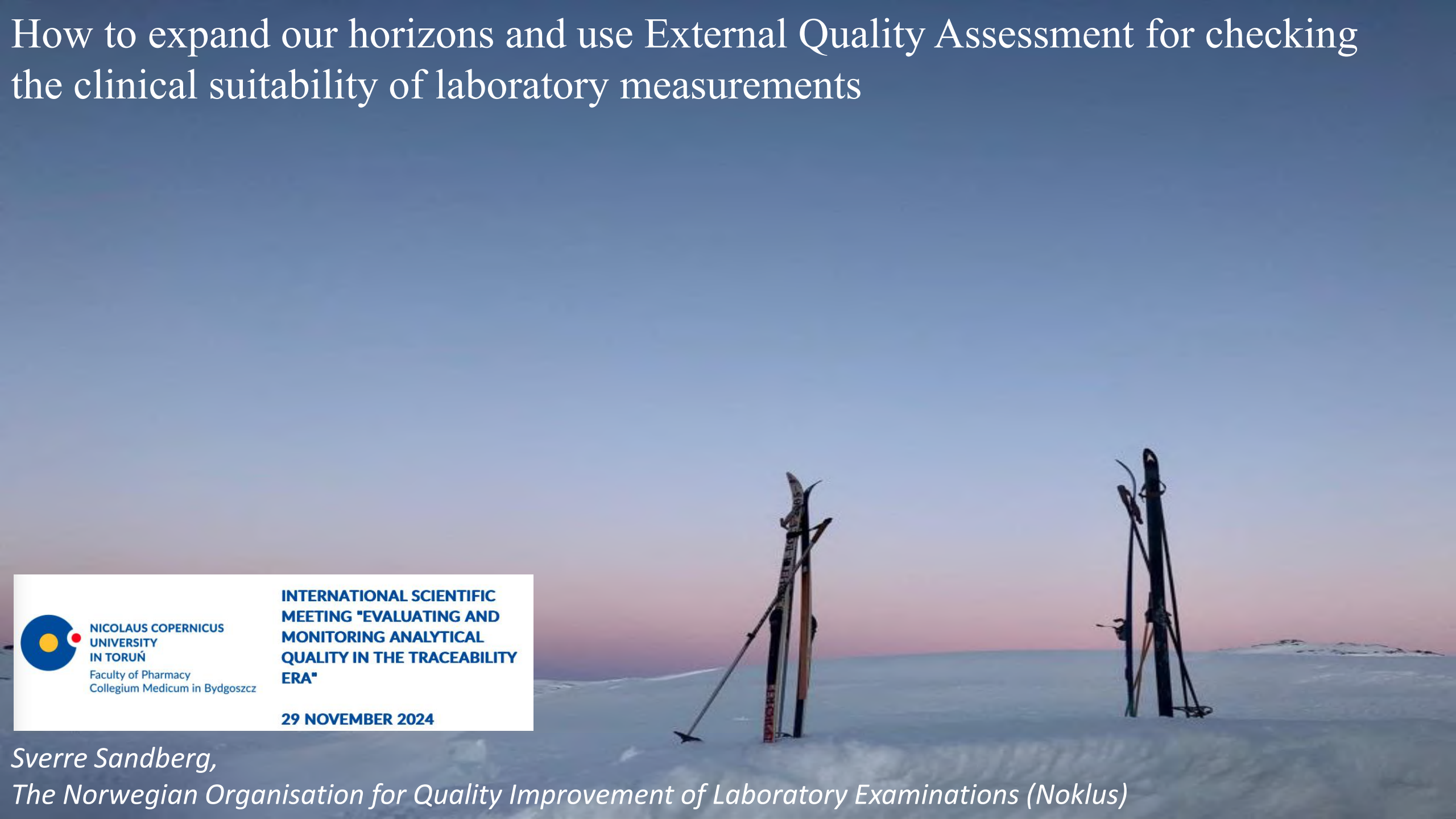
How to expand our horizons and use External Quality Assessment for checking the clinical suitability of laboratory measurements



NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ
Faculty of Pharmacy
Collegium Medicum in Bydgoszcz

INTERNATIONAL SCIENTIFIC MEETING "EVALUATING AND MONITORING ANALYTICAL QUALITY IN THE TRACEABILITY ERA"

29 NOVEMBER 2024

Sverre Sandberg,
The Norwegian Organisation for Quality Improvement of Laboratory Examinations (Noklus)

- *Expand our horizon* and use
- *External Quality Assessment* to check
- *clinical suitability of laboratory measurands*

Clinical suitability of laboratory measurands

- - to request the right measurand in a clinical situation
- - to deliver the clinician a trustworthy result

  that the result is a) correct and b) similar to what you would have obtained from other laboratories

Evaluating and monitoring analytical quality in the traceability era

Laboratories should prioritize the perspectives and needs of their customers (the patients and healthcare personnel).

Among them, comparability of results from the same patient sample when measured by different laboratories using different IVD medical devices is a logical priority to avoid result misinterpretation and potential patient harm.

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Clinical suitability of laboratory measurands

- - to request the right measurand in a clinical situation
- - to deliver the clinician a trustworthy result
  - that it is a) correct and b) similar to what you would have obtained from other laboratories
  - We will expand our horizon - that is – to do EQA in a better way

We have to expand our thinking about EQA to be able to monitor harmonisation and standardization efforts of measurands

This will change the way we run EQA

Analytical EQA

The value of the information you get from the analytical EQA is dependent on:

- What EQA control materials that are used
- How the target values are established
- How many replicates that are analysed
- What information that is registered in the EQA scheme from labs
- What analytical performance specifications that are used
- (How peer groups are composed)
- (Frequency)

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Control material

The control material is extremely important in EQA.

Is the control material commutable between measurement procedures (behaves similar to patient material) – and how is that verified?

Is the control material commutable between measurement procedures and between lots of a measurement procedure?

Is it non-commutable?

Commutable control material is necessary to assess metrological traceability

A commutable control material is usually liquid and less stable than non-commutable material and must therefore often be produced fresh locally.

It is therefore more difficult for the «big» EQA providers to produce such control material.

- EQA providers usually do not examine EQA control material for commutability

- EQA providers have to “expand” and do this – even if it is cumbersome

Clinical Chemistry 69:11
1227–1237 (2023)

Special Report

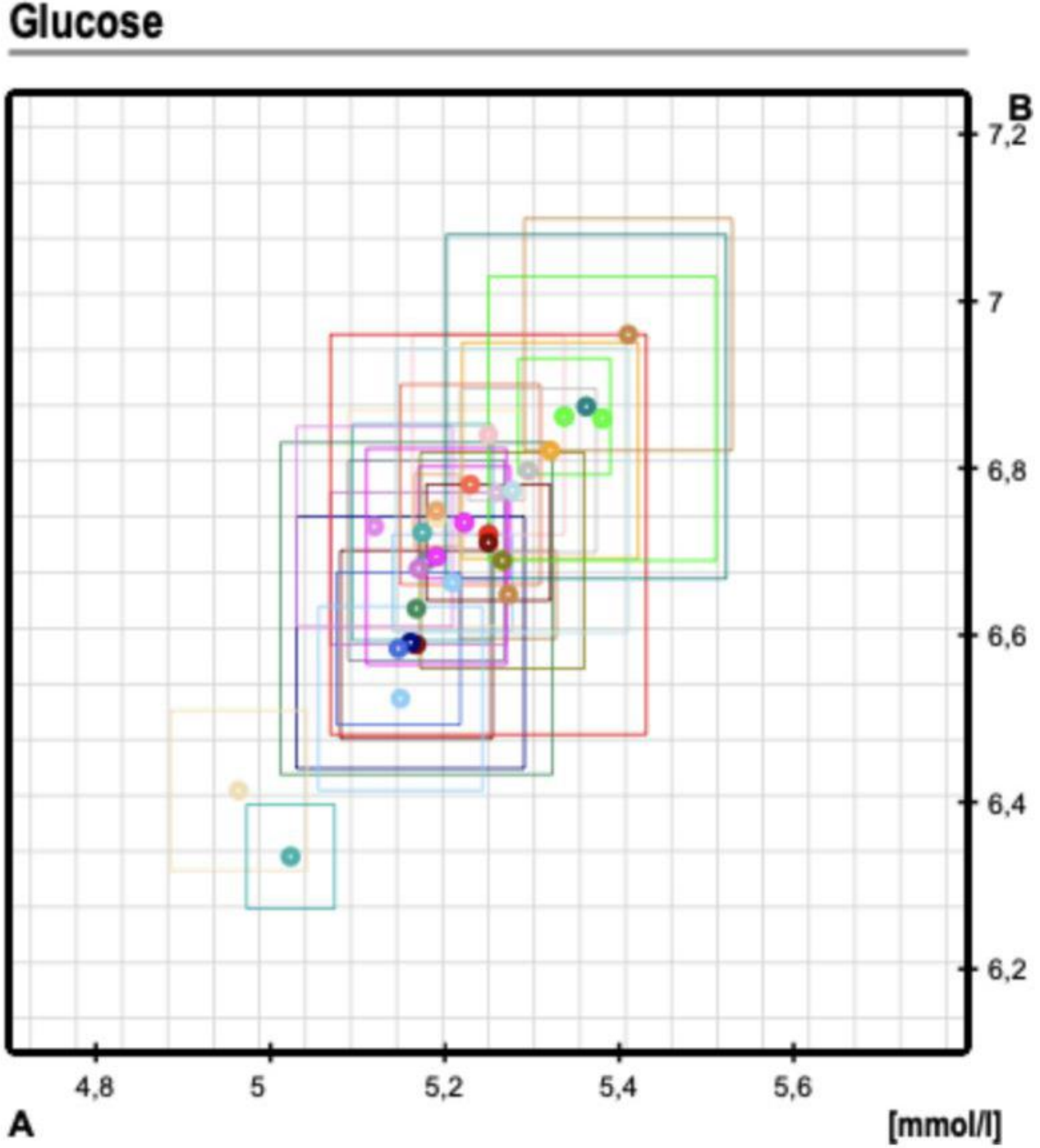
Recommendations for Setting a Criterion and Assessing Commutability of Sample Materials Used in External Quality Assessment/Proficiency Testing Schemes

Sverre Sandberg,[a,b,c,*] Pernille Fauskanger,[a] Jesper V. Johansen,[d] Thomas Keller,[e] Jeffrey Budd,[f] Neil Greenberg,[g] Robert Rej,[h] Mauro Panteghini,[i] Vincent Delatour,[j] Ferruccio Ceriotti,[k] Liesbet Deprez,[l] Johanna E. Camara,[m] Finlay MacKenzie,[n] Alicia N. Lyle,[o] Eline van der Hagen,[p] Chris Burns,[q] and W. Greg Miller[r]; for the IFCC Working Group on Commutability in Metrological Traceability

Target values

Use a target value from a reference measurement procedure (RMP) or by using a certified reference material?

Only useful if you have commutable control material



RELA 2022 Differences between RMPs

Differences between RMPS should be reduced

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Replicates

If control material is analysed once – only information about accuracy can be given

If control material is analysed several times, information about bias and imprecision can be given.

For EQA trueness schemes, the samples should be analysed in replicates

Reagent lot registration

Differences between lots for the same measurement procedure(MP) can contribute to the

- between laboratory variation for that MP procedure in one EQA scheme
- and to biases between the same MP in different EQA schemes .

It can also explain why one laboratory have a deviant result.

In most cases it is therefore useful to register which reagents lots are used

Reagent lots, example urine-albumin - a “commutability light” experiment

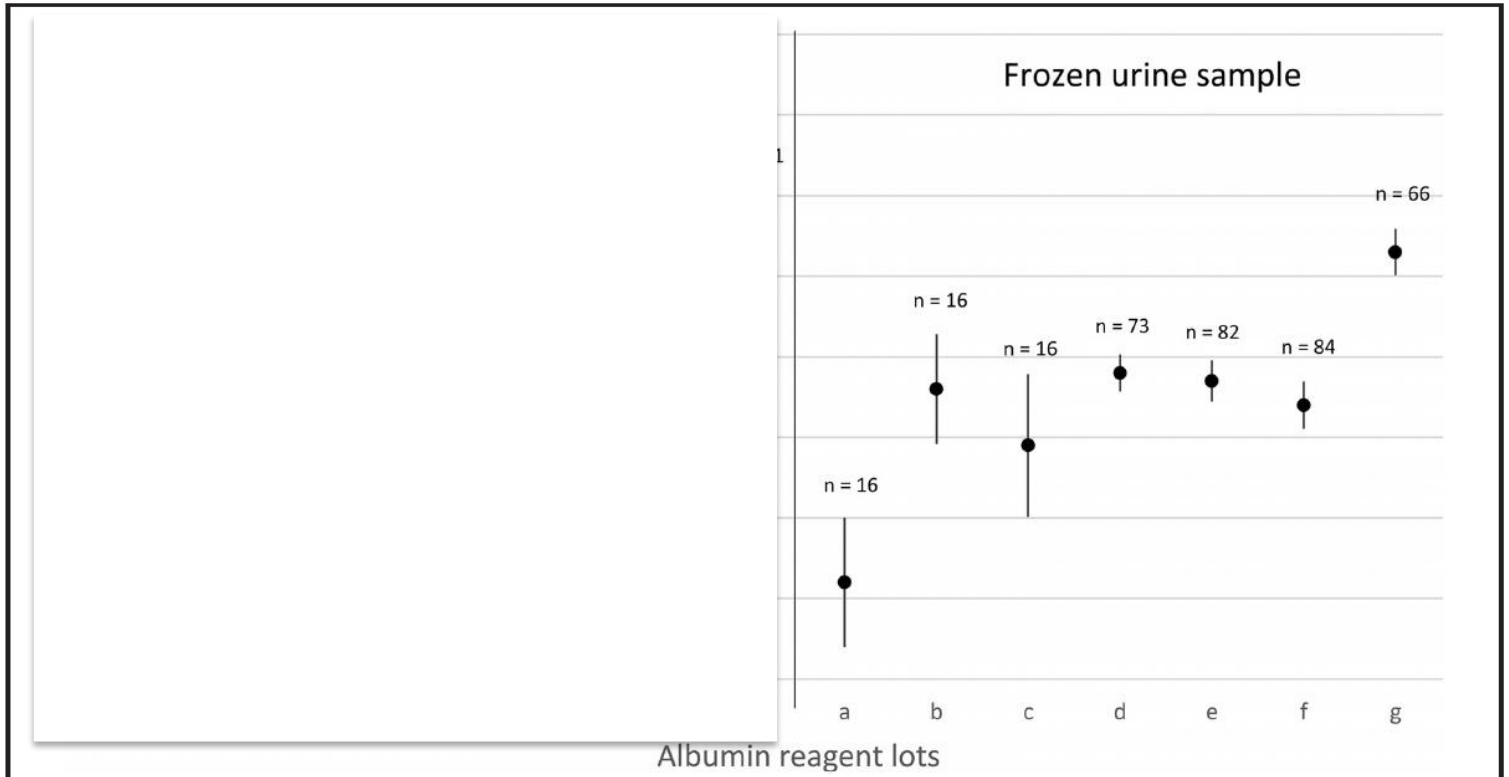


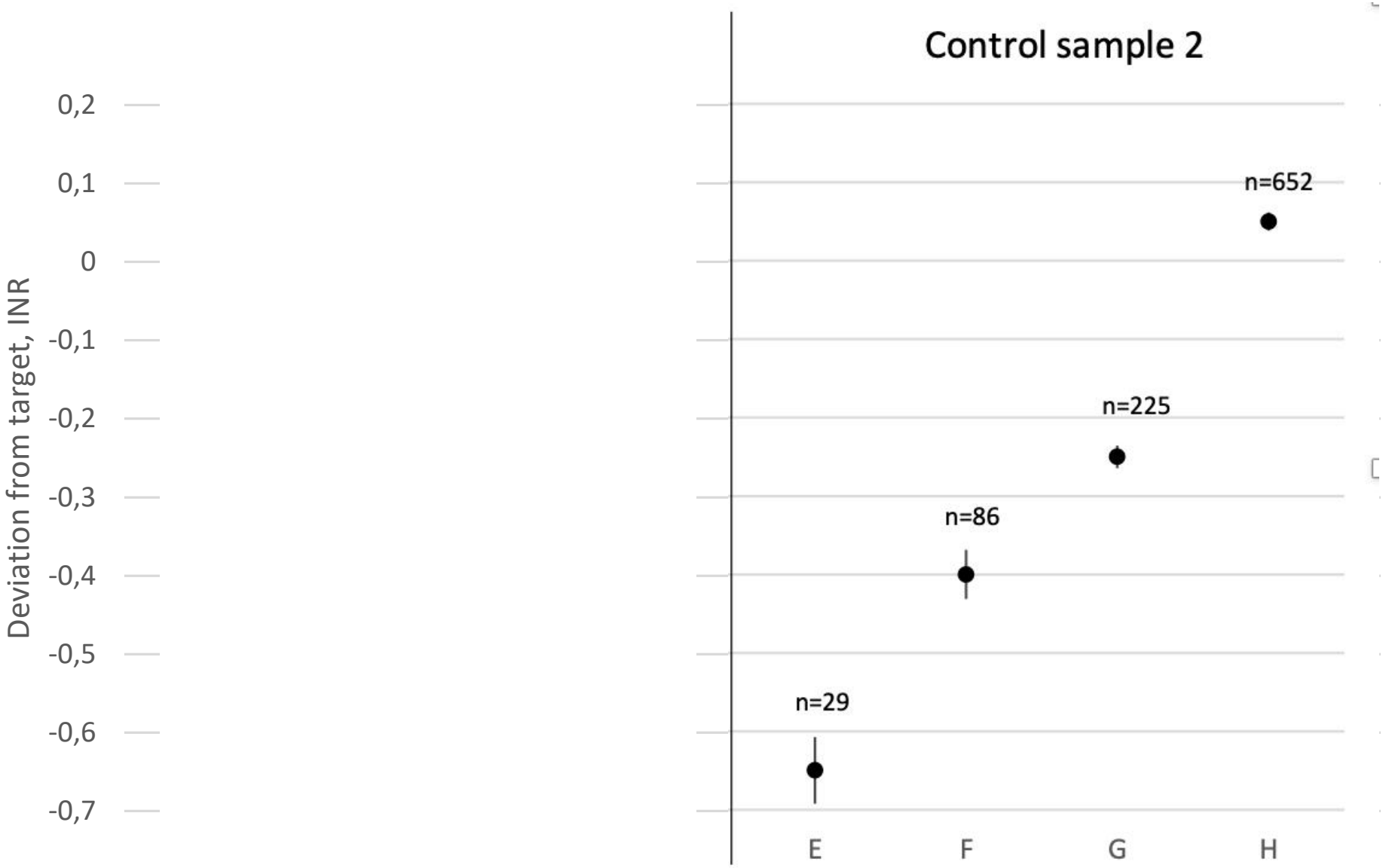
Fig. 3. Median deviations (95% CI) from the target values in 1 survey (1/2014) for 7 Afinion albumin lots (a to g) using both fresh and frozen urine samples, with target values of 76 mg/L and 69 mg/L, respectively.

Conclusion: The reagent lot used can explain a deviant EQA result and should be communicated to the participants

Stavelin et al. The importance of reagent lot registration in EQA. Clin Chem 2016; 62(5): 708-715

INR survey to 2000 GPs using Coagucheck

Split sample *EQA control material*



Conclusion: The reagent lot used can explain a deviant EQA result and should be communicated to the participants

BUT the control material is not commutable between lots and do not reflect patient samples

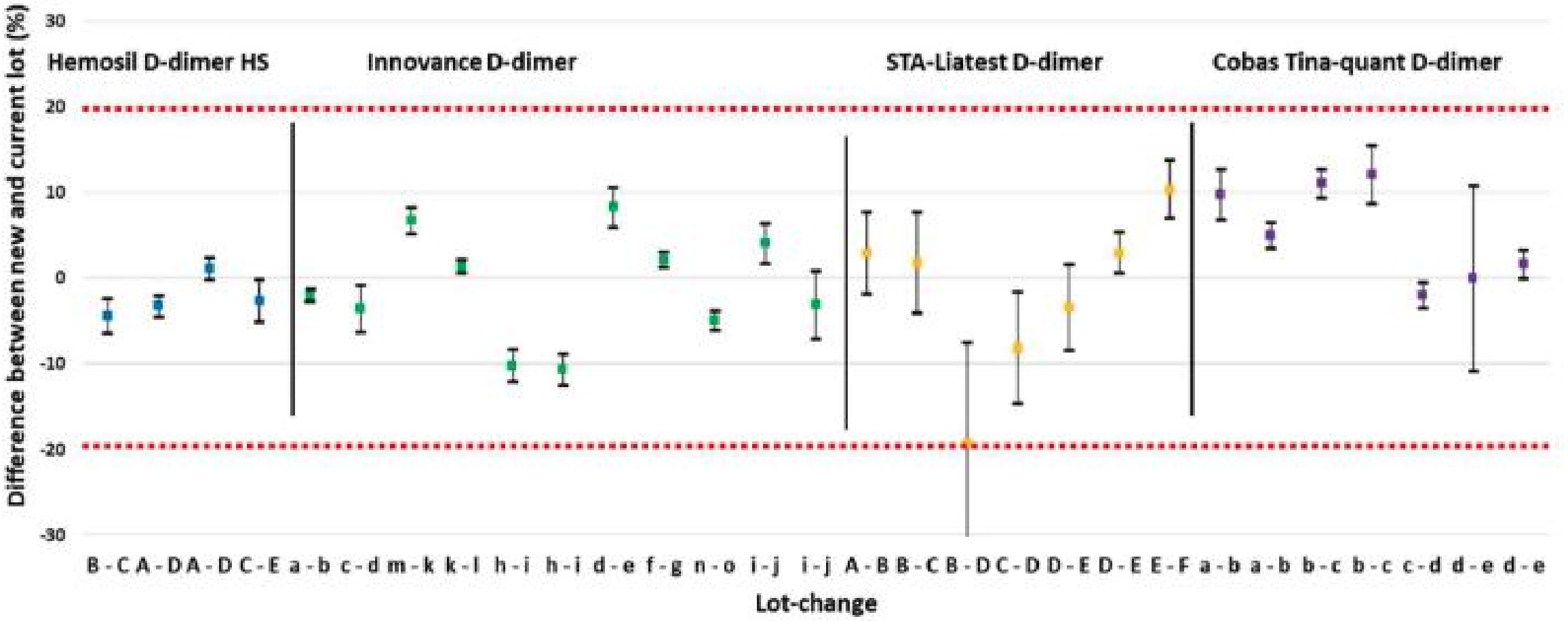
DE GRUYTER Clin Chem Lab Med 2022; 60(3): 351–360

Anne Elisabeth Solsvik*, Ann Helen Kristoffersen, Sverre Sandberg, Gro Gidske,
Anne Vegard Stavelin, Joakim Eikeland and Erik Amundsen

A national surveillance program for evaluating new reagent lots in medical laboratories

Laboratories in Norway examined differences between reagent lots when changing from one lot to another. These changes were reported to Noklus.

D-dimer - difference between new and old lot



- EQA providers usually do not register reagent and calibrator lots

- EQA providers have to “expand” and do it – even if it is cumbersome

Analytical performance specifications

Based on

- Clinical outcome
- Biological variation
- State of the art
  - How are the performance specifications calculated, many different models exist

For biological varation – see:

https://biologicalvariation.eu

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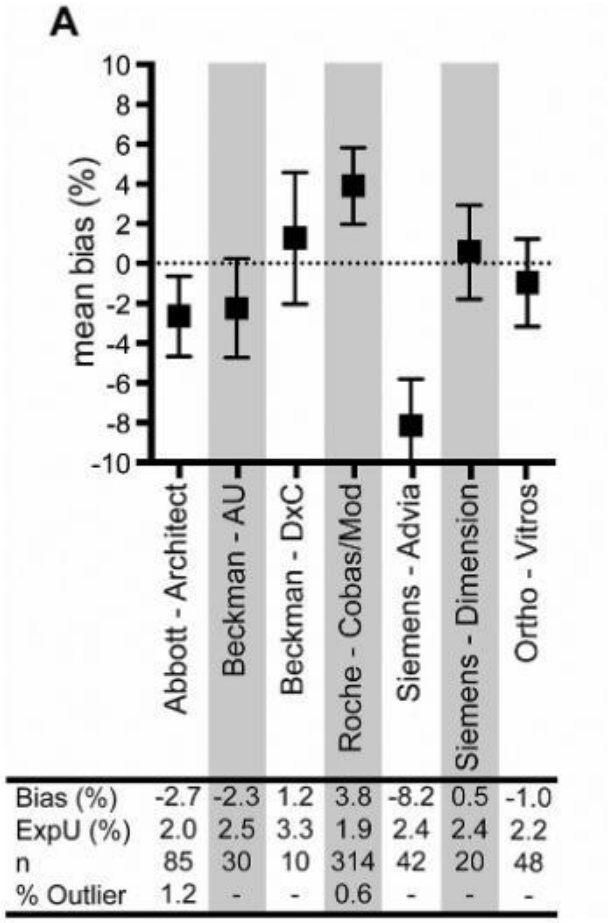
Can we aggregate results to be able to examine harmonisation and standardisation efforts.

1. Aggregated results from different EQA providers
2. Aggregated results from patient medians from different laboratories

Creatinine



Bias (%)	-2.7	-2.3	1.2	3.8	-8.2	0.5	-1.0
ExpU (%)	2.0	2.5	3.3	1.9	2.4	2.4	2.2
n	85	30	10	314	42	20	48
% Outlier	1.2	-	-	0.6	-	-	-

Mean % bias for the aggregated results from 4 EQA providers

But we dont know if the control material is commutable – although they were claimed to be commutable

- or all the control materials can have similar non-commutability issues and therefore not reflect patient samples

Van der Hagen E. et al. Clin chem Lab Med 2021; 59:117-25

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The HALMA project

Harmonization of Measurands in Laboratory Medicine

through Data Aggregation from EQA providers

Cooperation between ICHCLR and EQALM

EQA provider[1]	Number of samples	Number of results, Albumin	Number of results, Creatinine	Number of results, Calcium
CAP	14	161	1254	357
Croqalm	1	85	199	125
Equalis	1	104	114	103
KEQAS	3	0	5118	0
Labquality	7	922	1116	964
NCCL	4	0	924	776
Oequasta	4	210	626	428
RCPAQAP	2	492	492	482
SEQC	6	875	996	995
SKML	6	1122	1176	1128
WEQAS	4	600	624	528

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Preliminary Conclusions

Lack of agreement between different EQA providers concerning results of differences between measurement procedures for albumin, calcium and creatine (less) using their own EQA quality control materials.

Possible explanations

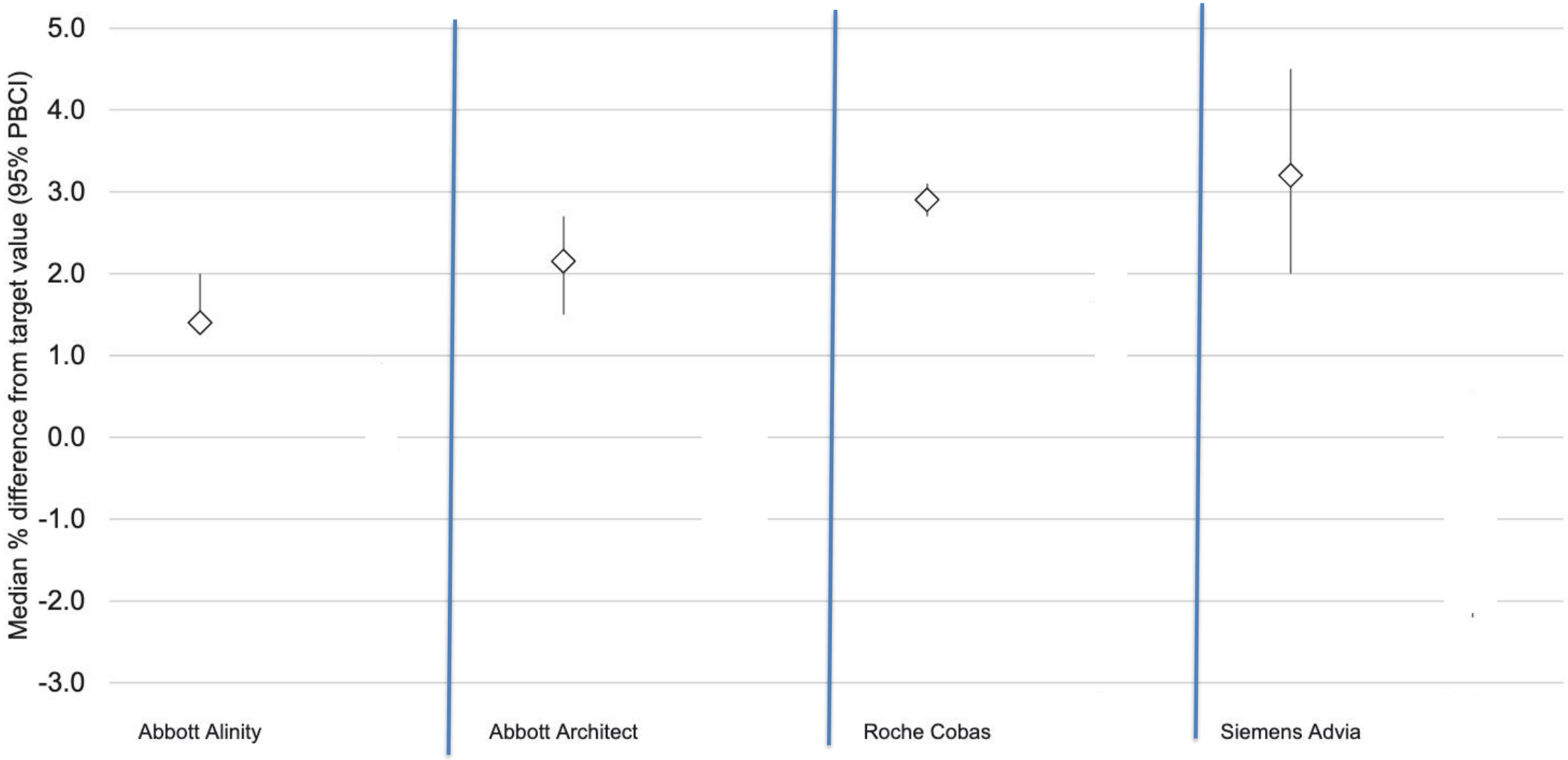
1. Quality control material not commutable
2. Different reagent/calibrator lots in different countries
3. Other

Do EQA results from different schemes for the same measurand give the same results when analysed by the same laboratories?

- Noklus established a scheme for only glucose and used verified commutable material and target values from a RMP.

- EQA results from one year from the same 58 Norwegian hospital laboratories using both EQA schemes from Labquality (Finland) and from Noklus (Norway).

Gidske G. et al. Clin Chem Lab Med 2023 62:77-84



Results from Labquality EQA using assumed commutable material and Noklus using verified commutable material

Conclusions:

The same laboratories participating in EQA schemes from two EQA providers at the same time, with different EQA materials from two different EQA providers, obtain different glucose results.

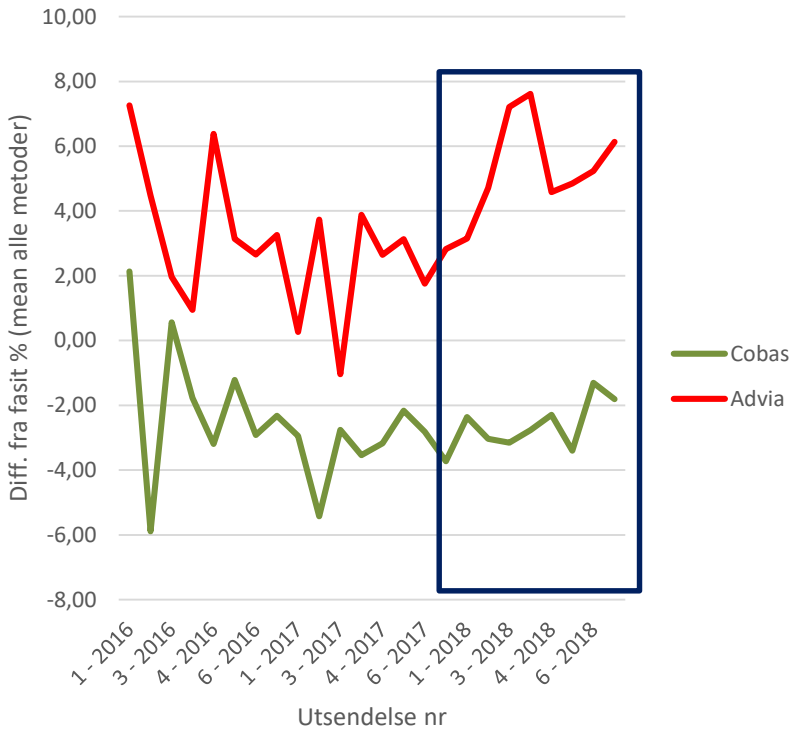
This underlines the importance of EQA providers using verified commutable EQAMs

Patient medians

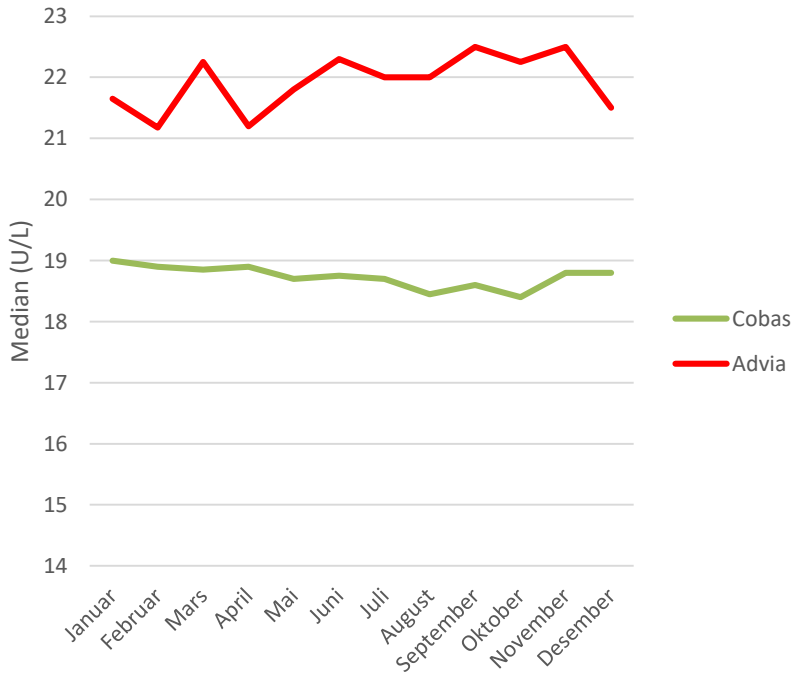
- Daily patient medians are submitted to a database from 120 laboratories throughout the world
- Patient medians tend to be stable

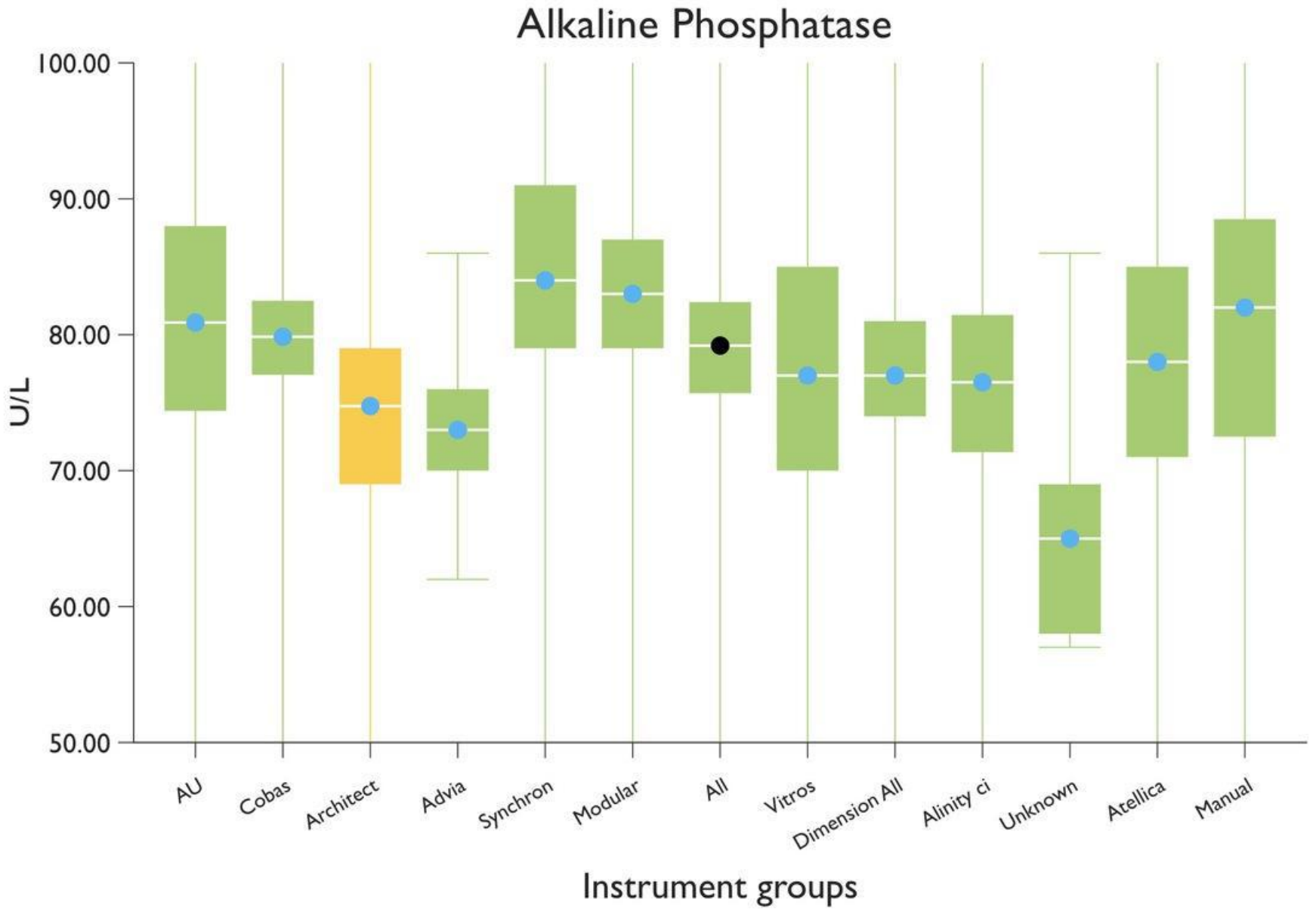
Patient medians ALT compared to EQA

EQA program



Patient medians




Alkaline Phosphatase
100.00
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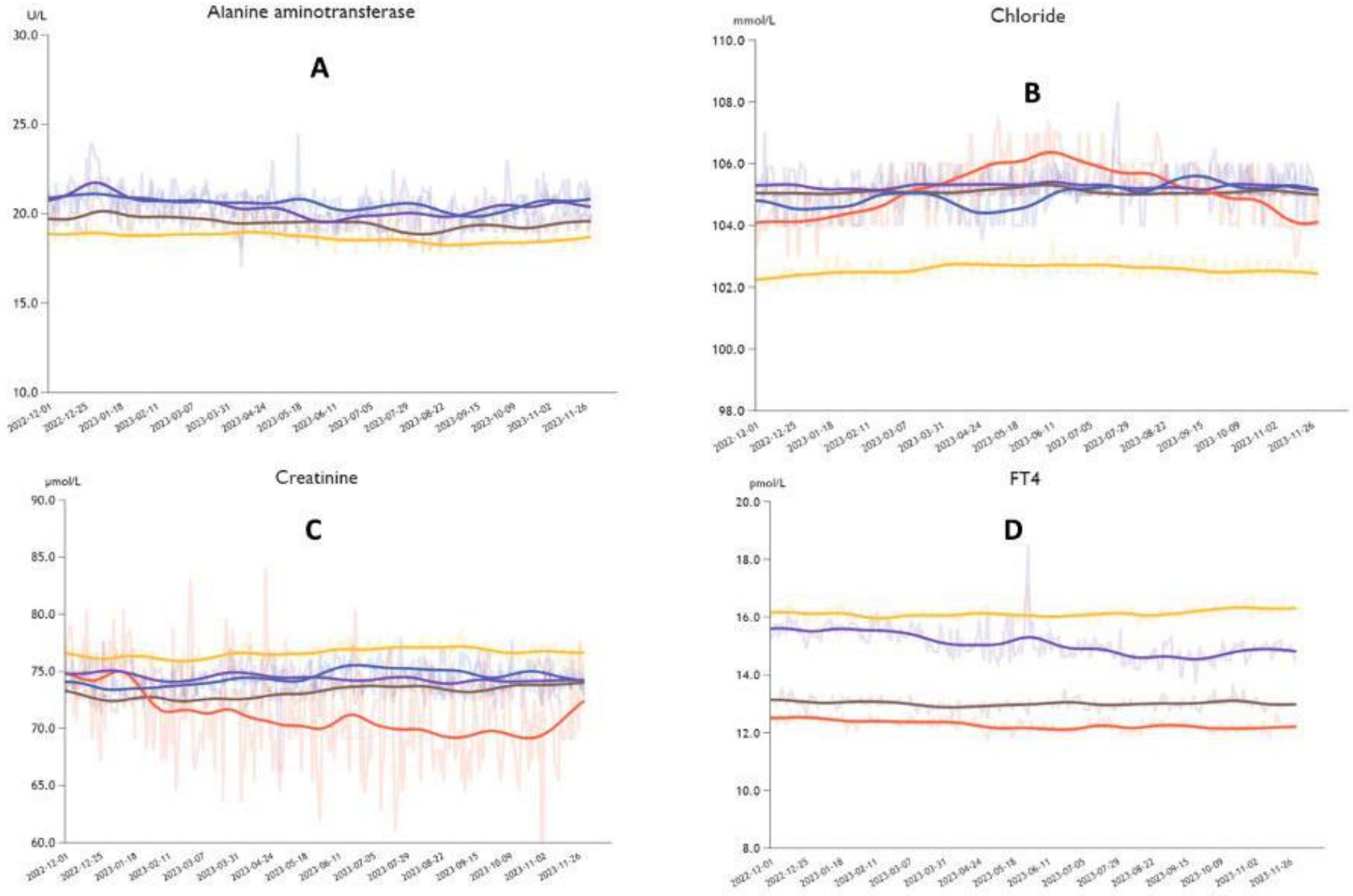
Instrument groups



A) ALT, B) chloride, C) creatinine and D) FT4 for instrument groups with five or more laboratories for the period 2023
The yellow line represents the kernel-smoothed curve for the Roche Cobas group, brown line the Abbott Architect group, purple line the Abbott Alinity group, and the blue line the Siemens Atellica group..

Analytes included:

ALP	ALT	AST	Bilirubin	BUN
Ca	Cholesterol	Cl	Creatinine	CRP
Ferritin	Folate (B9)	FT4	GGT	Glucose
Hb	HbA1c	HDL-cholesterol	IgA	IgG
IgM	K	LDH	MCV	Mg
Na	Phosphate	PLT	Protein	PSA
PTH	RBC	Triglycerides	TSH	Urea
Uric acid	Vitamin B12	Vitamin D	WBC	Albumin

+LDL-cholesterol + cortisol + active vitamin B12 + coagulation analytes?

Participation is free

Single laboratories can be enrolled

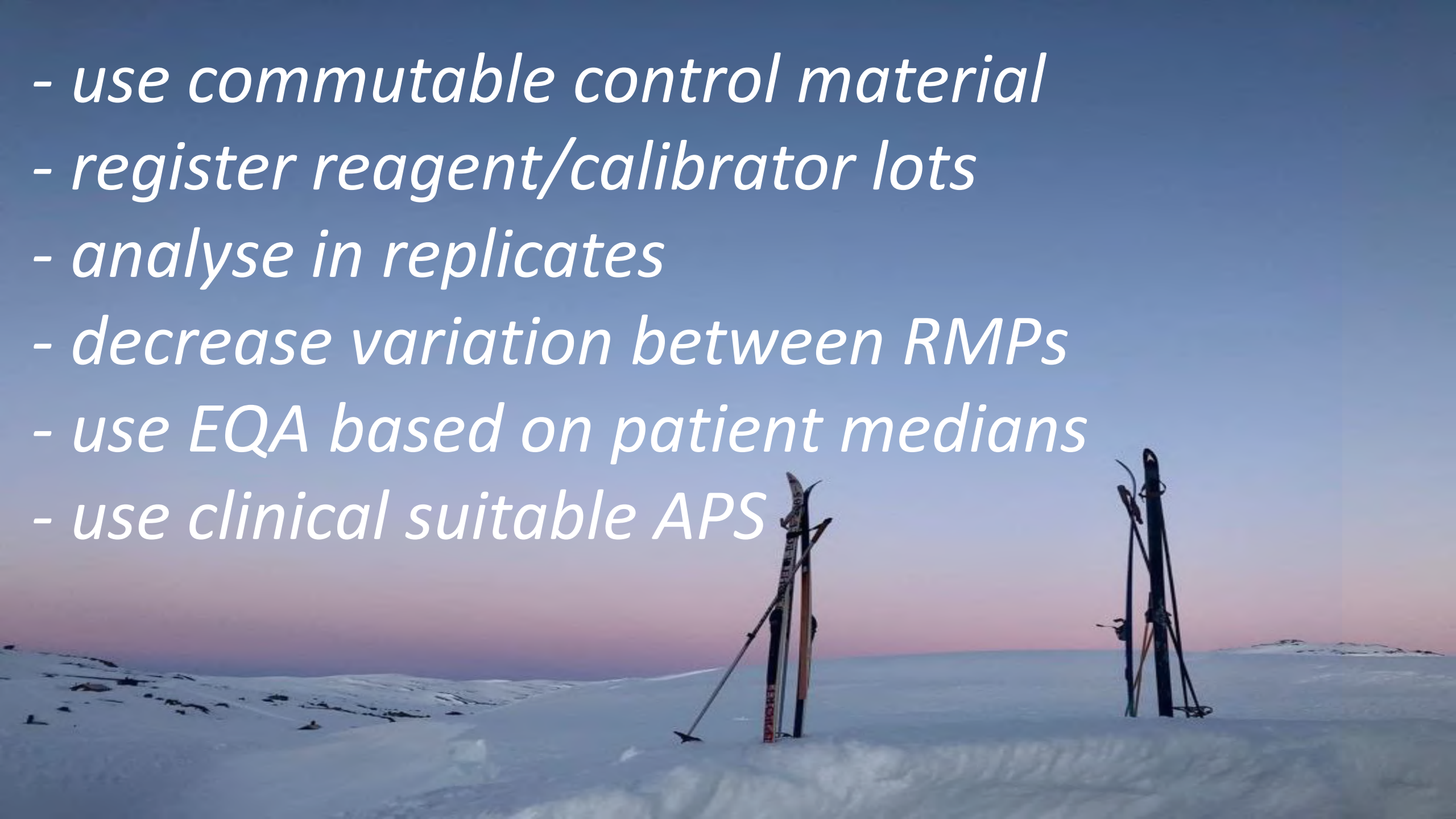
EQA providers can enroll laboratories

https://www.noklus.no/en/the-percentiler-and-flagger-programs/

CONCLUSIONS

We must **expand our horizons** and use External Quality Assessment in a way that we can check the clinical suitability of laboratory measurements

This means that we must improve our EQA programs


- use commutable control material
- register reagent/calibrator lots
- analyse in replicates
- decrease variation between RMPs
- use EQA based on patient medians
- use clinical suitable APS


Thank you