Post analytical variation : impact of difference in reference intervals

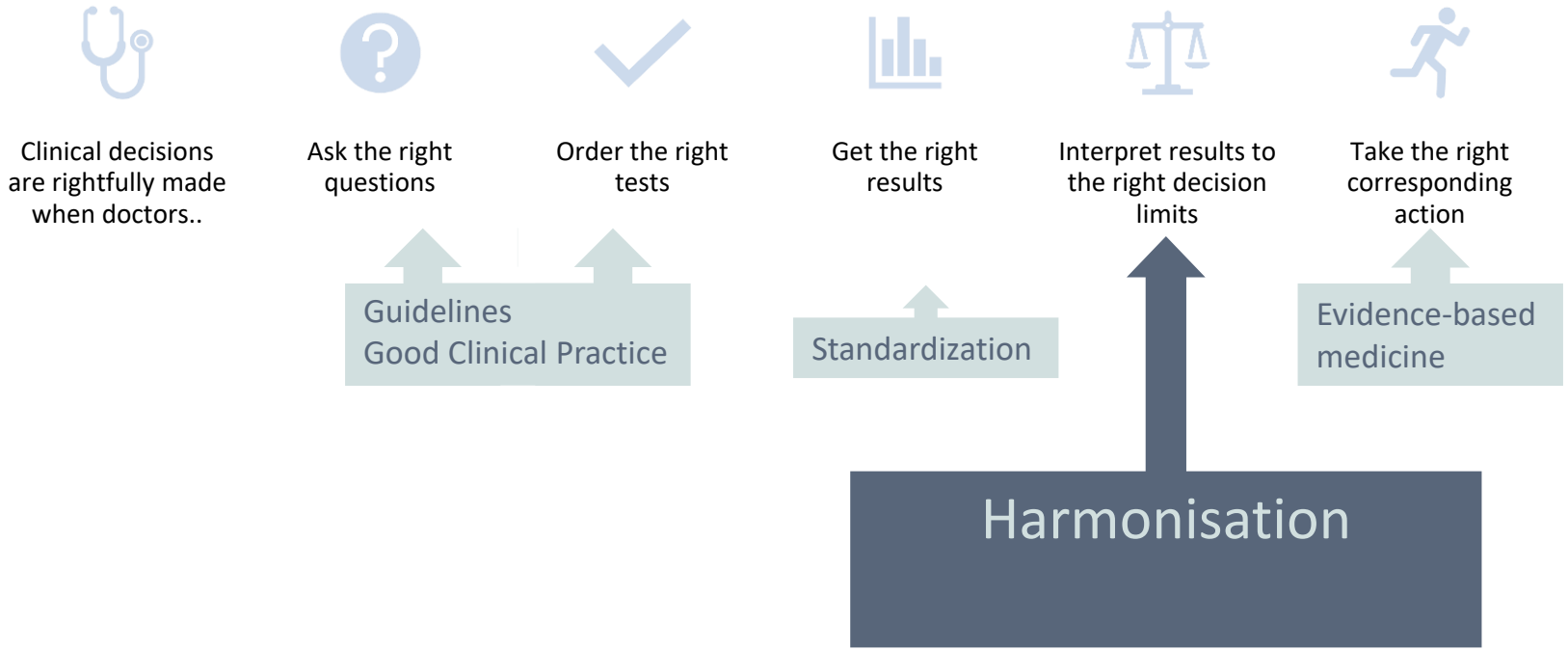
Dr. Miranda van Berkel, General Clinical Chemistry EQA
Radboudumc Nijmegen

Radboudumc

Disclosure

- The speaker has no financial relationship with any IVD industry

Clinical decision making



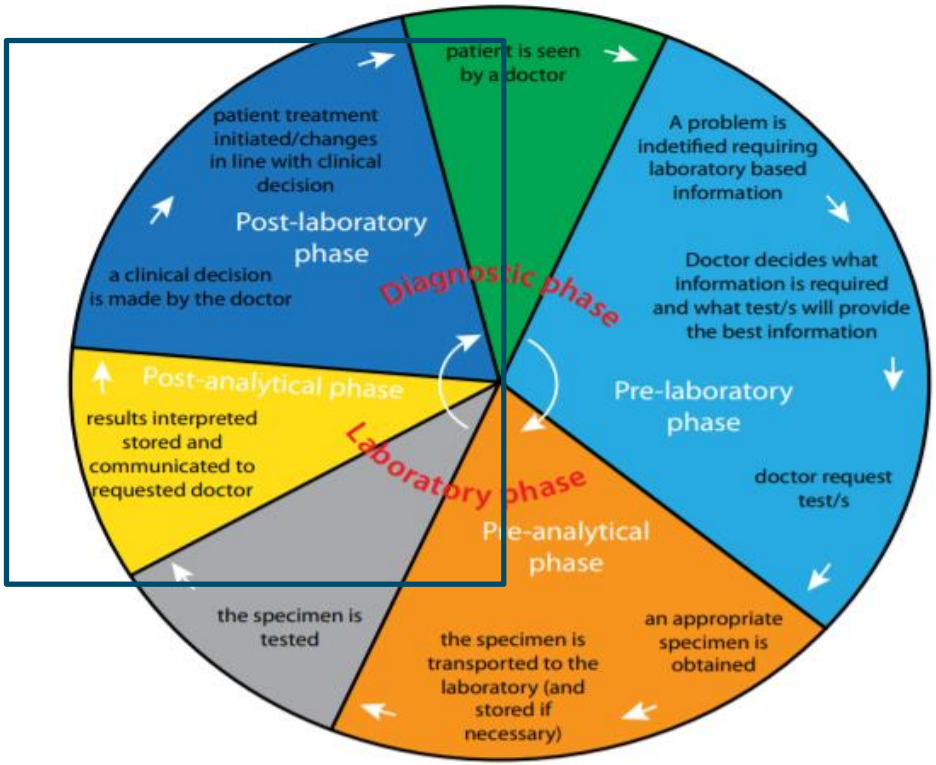


Figure 1. The phases of laboratory testing

Biochemia Medica 2017;27(1):73–80

Evaluation of test results:

- Interpretative comments
- Appropriate calculation
- Reference intervals & decision limits
- Reporting units
- Critical values
- Turnaround time

Radboudumc

ISO 15189

5.6.3 Interlaboratory comparisons

5.6.3.1 Participation

The laboratory shall participate in an interlaboratory comparison programme(s) (such as an external quality assessment programme or proficiency testing programme) appropriate to the examination and interpretations of examination results. The laboratory shall monitor the results of the interlaboratory comparison programme(s) and participate in the implementation of corrective actions when predetermined performance criteria are not fulfilled.

NOTE The laboratory should participate in interlaboratory comparison programmes that substantially fulfil the relevant requirements of ISO/IEC 17043.

The laboratory shall establish a documented procedure for interlaboratory comparison participation that includes defined responsibilities and instructions for participation, and any performance criteria that differ from the criteria used in the interlaboratory comparison programme.

Interlaboratory comparison programme(s) chosen by the laboratory shall, as far as possible, provide clinically relevant challenges that mimic patient samples and have the effect of checking the entire examination process, including pre-examination procedures, and post-examination procedures, where possible.

Radboudumc

My opinion of including post analytical phase in EQA program

A. It is of no added value for interpretation of patient results
B. It is suited for harmonisation of interpretation of patient results
C. Already in place, I use it regularly for interpretation of results
D. Only some elements (eg units and reference intervals) are useful

Radboudumc

vote at skmlcongres.participoll.com

What can be learned from other EQA organisers?

Due Date : 23/03/2015 **Case 16-01**

A Suggested Comment

Extremely high osmolal gap (>25 mmol/kg) with high anion gap metabolic acidosis. Ingestion of alcohol(s) (e.g. ethanol, methanol and/or ethylene glycol) must be assumed; particularly methanol as vision is affected. Blood alcohols should be measured but must not delay immediate specialist supportive management including investigations for other possible co-ingested toxins and blood gas analysis.

Rationale and References

The osmolal gap; difference between measured and calculated (2 x Na + Urea + glucose) osmolality, is usually < 10 mmol/kg. A large gap (here, 56 mmol/kg) with a high anion gap acidosis is typical of recent significant ingestion of an alcohol. In this case, methanol should be especially suspected as its metabolite (formic acid) is commonly associated with visual disturbances. Although the osmolal gap generally correlates with the amount consumed, most alcohols contribute more than their molar amount to the measured osmolality; particularly methanol and ethanol where the contribution is 3.09 and 2.12 times their serum concentration, respectively. In addition, only the parent alcohol and not the toxic metabolite contributes to osmolality; hence small or absent osmolal gaps are seen in late presentations and do not indicate a better prognosis. With time, as the ingested alcohol is metabolised, the osmolal gap falls and the acidosis worsens. Confirmatory testing of the parent alcohol should never delay immediate resuscitation and treatment as these poisonings may be fatal.

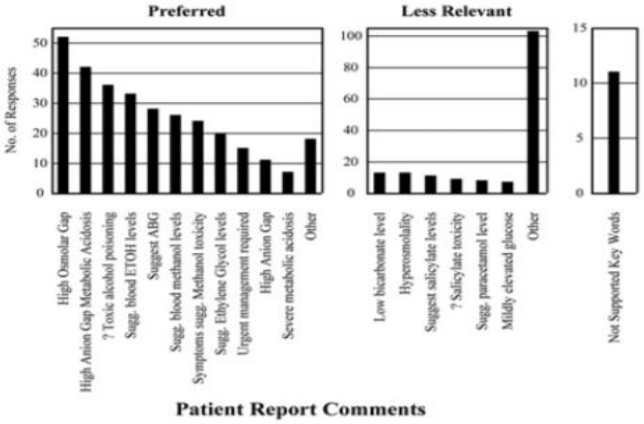
Reference: Kraut JA & Kurtz I, Toxic Alcohol Ingestions: clinical Features, Diagnosis, and Management. CJASN 2008 (3): 208-225.

Patient Report Comments

Patient ID 42 year old man
Patient Location ED
Clinical Notes on Request Form
SOB, vision disturbance

Case Details

Sodium	135		(136-145)	mmol/L
Potassium	3.7		(3.5-5.1)	mmol/L
Chloride	100		(98-107)	mmol/L
Bicarbonate	**8**	L	(22-29)	mmol/L
Urea	**2.7**	L	(3.2-7.3)	mmol/L
Creatinine	73		(62-106)	umol/L
Glucose	**6.4**	H	(3.5-5.4)	mmol/L
Lactate	1.6		(0.5-1.6)	mmol/L
eGFR	>90		(>90)	mL/min/1.73m2
Osmolality	**335**	H	(280-300)	mmol/kg



Participant No.

Your Comment

Severe metabolic acidosis with a high anion and osmolar gap.?Methanol toxicity. Suggest ethanol level and ABG. Requires urgent management.

Your Key Words

Severe metabolic acidosis	Pref
High Anion Gap Metabolic Acidosis	Pref
High Osmolar Gap	Pref
? Methanol poisoning	Pref
Sugg. blood ETOH levels	Pref
Suggest ABG	Pref
Urgent management required	Pref

Returned Comments

Total 61

Key Word Summary

Number of key words 65

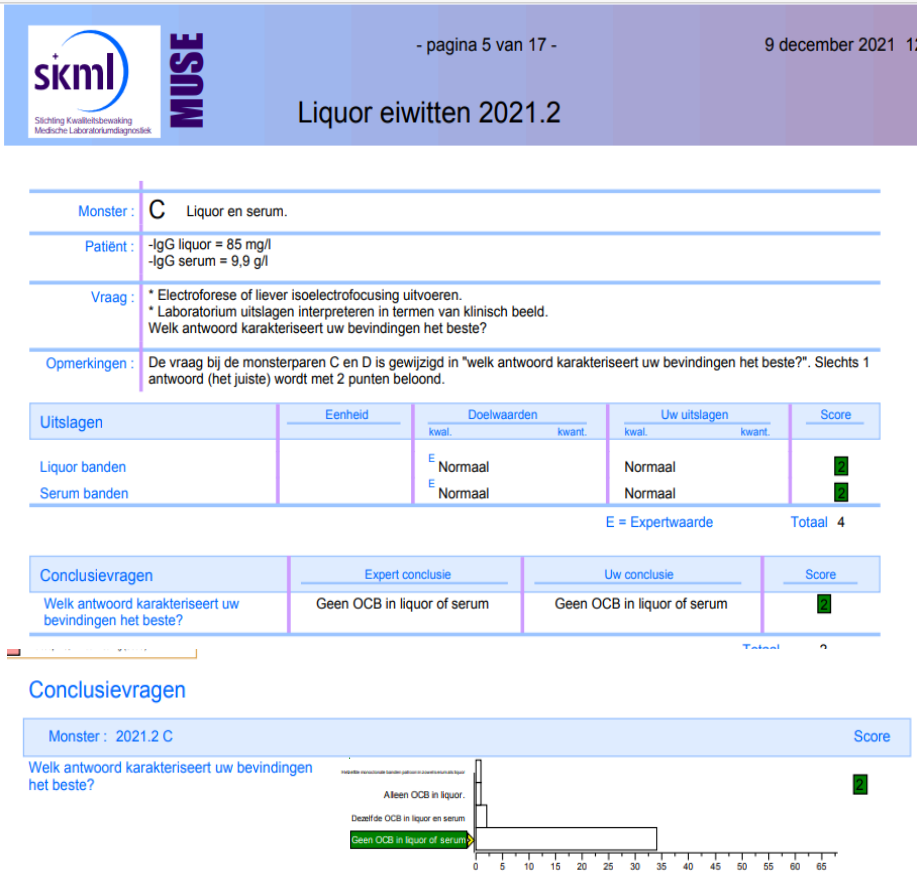
No. of Key Words Used Per Comment

	Pref	
Sugg Comment	6	1
Your Comment	7	

Post analysis in EQA

Evaluation of test results:

- Interpretative comments
- Appropriate calculation
- Reference intervals & decision limits
- Reporting units
- Critical values
- Turnaround time



skml
Stichting Kwaliteitsbewaking Medische Laboratoriumdiagnostiek
MUSE

- pagina 5 van 17 -

9 december 2021

Liquor eiwitten 2021.2

Monster :	C Liquor en serum.
Patiënt :	-IgG liquor = 85 mg/l -IgG serum = 9,9 g/l
Vraag :	* Electroforese of liever isoelectrofocusing uitvoeren. * Laboratorium uitslagen interpreteren in termen van klinisch beeld. Welk antwoord karakteriseert uw bevindingen het beste?
Opmerkingen :	De vraag bij de monsterparen C en D is gewijzigd in "welk antwoord karakteriseert uw bevindingen het beste?". Slechts 1 antwoord (het juiste) wordt met 2 punten beloond.

Uitslagen	Eenheid	Doelwaarden kwal.	Doelwaarden kwant.	Uw uitslagen kwal.	Uw uitslagen kwant.	Score
Liquor banden		E Normaal		Normaal		2
Serum banden		E Normaal		Normaal		2

E = Expertwaarde Totaal 4

Conclusievragen	Expert conclusie	Uw conclusie	Score
Welk antwoord karakteriseert uw bevindingen het beste?	Geen OCB in liquor of serum	Geen OCB in liquor of serum	2

Conclusievragen

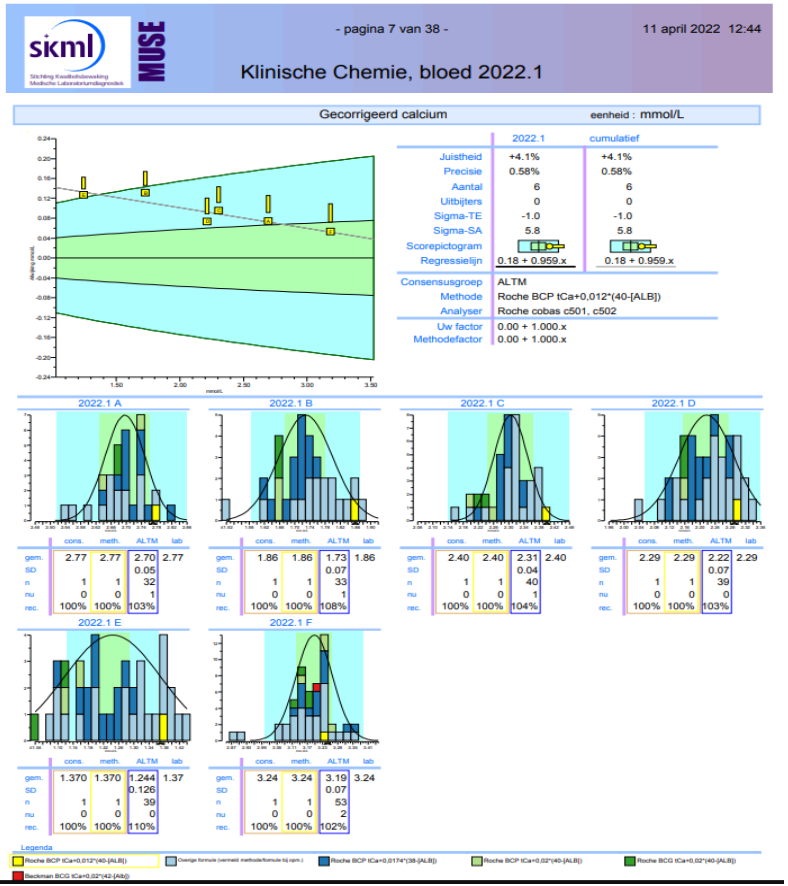
Monster : 2021.2 C — Score

Welk antwoord karakteriseert uw bevindingen het beste? 2

Post analysis in EQA

Evaluation of test results:

- Interpretative comments
- Appropriate calculation
- Reference intervals & decision limits
- Reporting units
- Critical values
- Turnaround time



Radboudumc

Post analysis in EQA

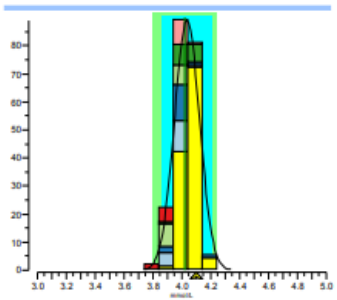
Evaluation of test results:

- Interpretative comments
- Appropriate calculation
- Reference intervals & decision limits
- Reporting units
- Critical values
- Turnaround time

Incongruence in reference-intervals

Analytes

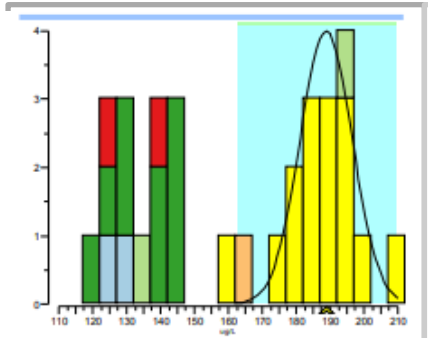
ALAT
ASAT
CK
GGT
LD
Amyl
AF
Ca
Cl
Gluc
K
Kreat
Mg
Na
TE

not Standardized	Standardized
A	B
C	

Harmonisation ref intervals:

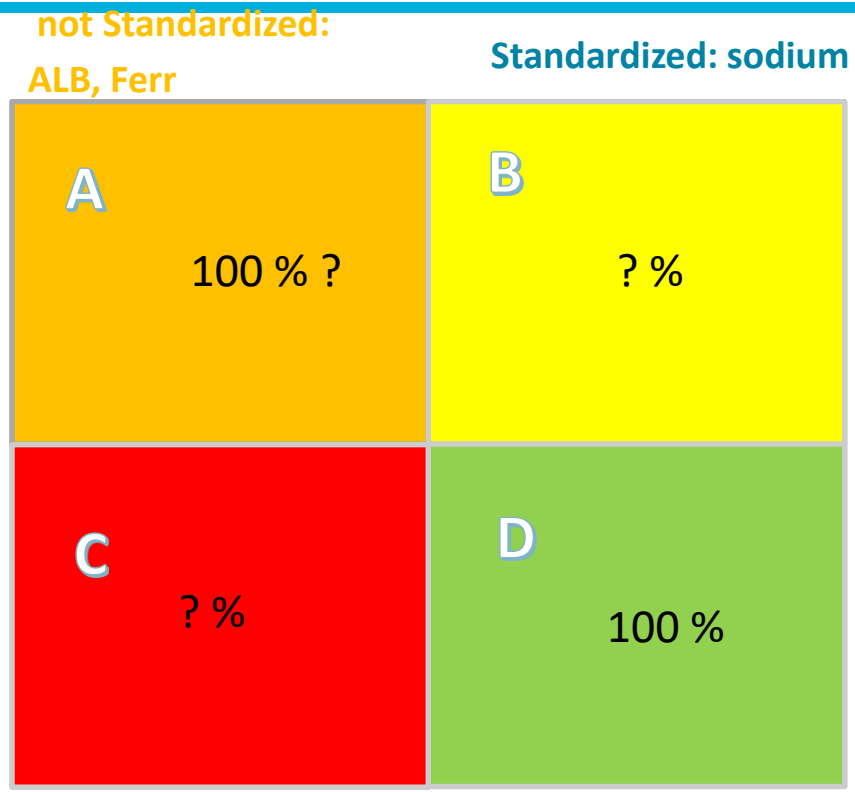
Analytes

- ferritine
- Albumin
- ACE
- Lp(a)
- Ammonia
- PCT
- Fosfaat
- Fe
- Urea
- lipase

not Standardized	Standardized
	B
C	D

Harmonisation ref intervals:

Analytes



Harmonisation ref intervals:

Estimated agreement in interpretation

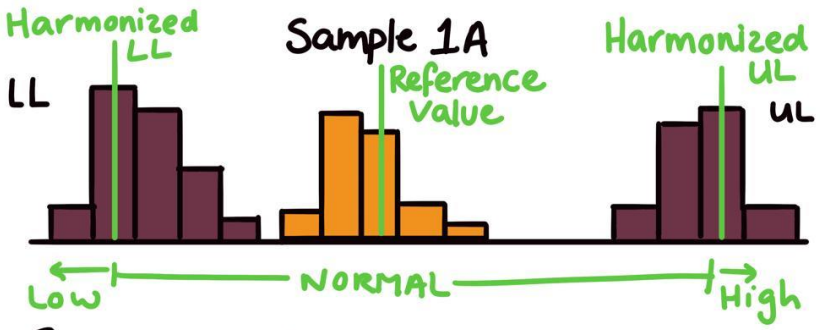
Goal post analysis EQA

- Create insight into differences in ref interval
- Impact on interpretation of result
- Compare individual laboratory interpretation with ‘harmonized’ interpretation

Radboudumc

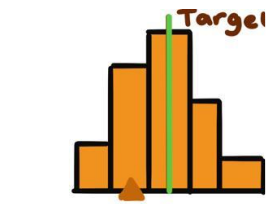
Methods

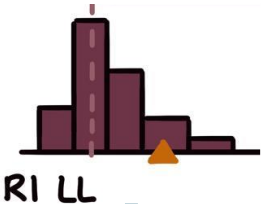
1. Questionnaire for reference intervals of 8 analytes (n=55 laboratories)
    1. 55yr old woman
2. Visualize LL and UL
3. Calculate interpretation ‘low’, ‘normal’, ‘hi’ with EQA results compared to ‘target decision’ with:
    a) Own reference intervals
    b) Harmonized reference intervals
4. Calculate disagreement of decision between a & b)



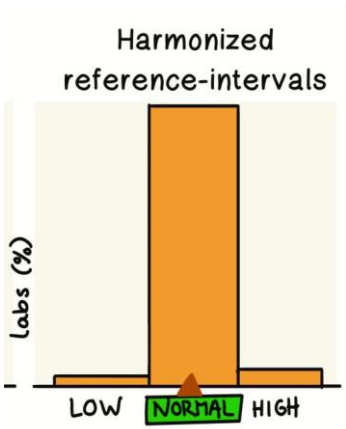
Sample 1a 'Target' decision

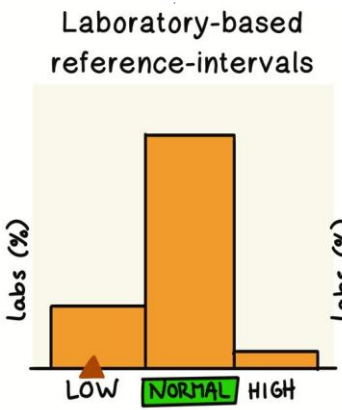
Ref value vs harmonized LL & UL

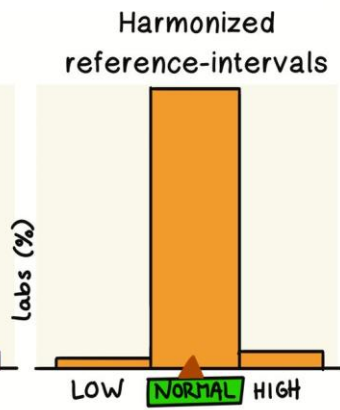




Target decision

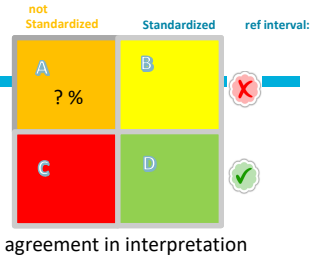


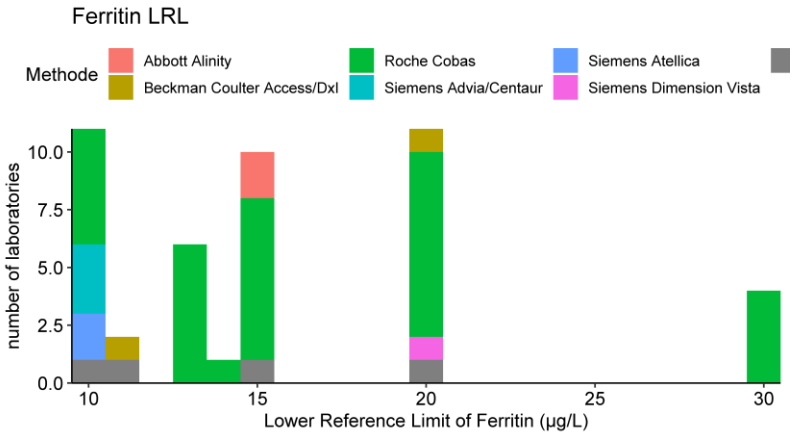


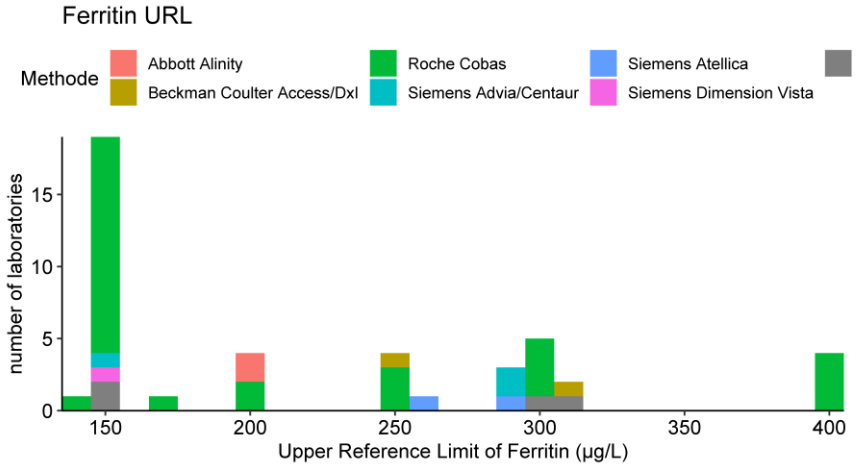


% agreement: 80 % 95%

Reference interval ferritin

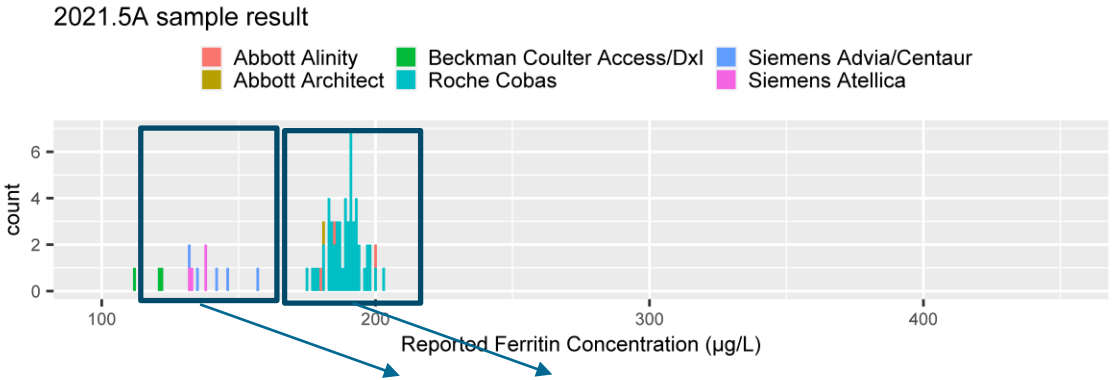




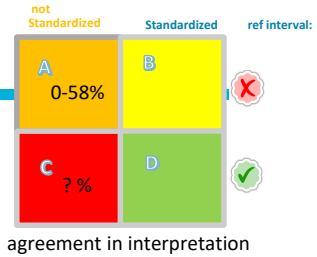


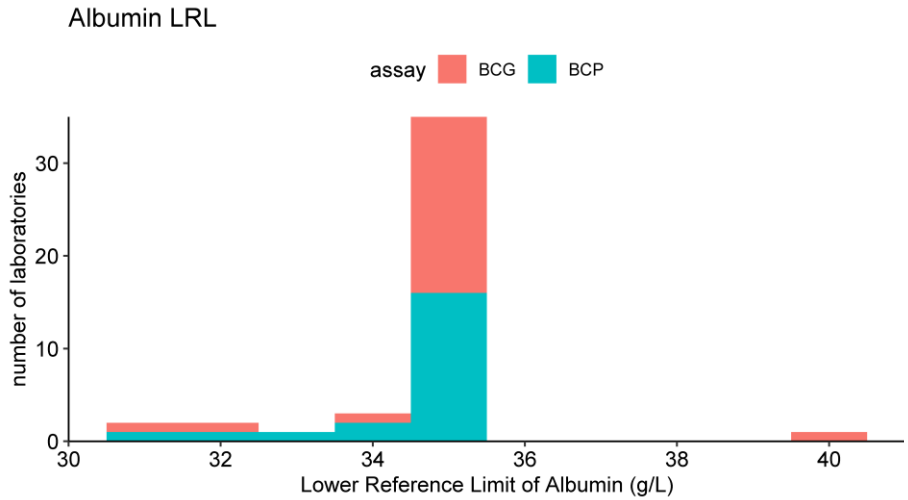
Radboudumc

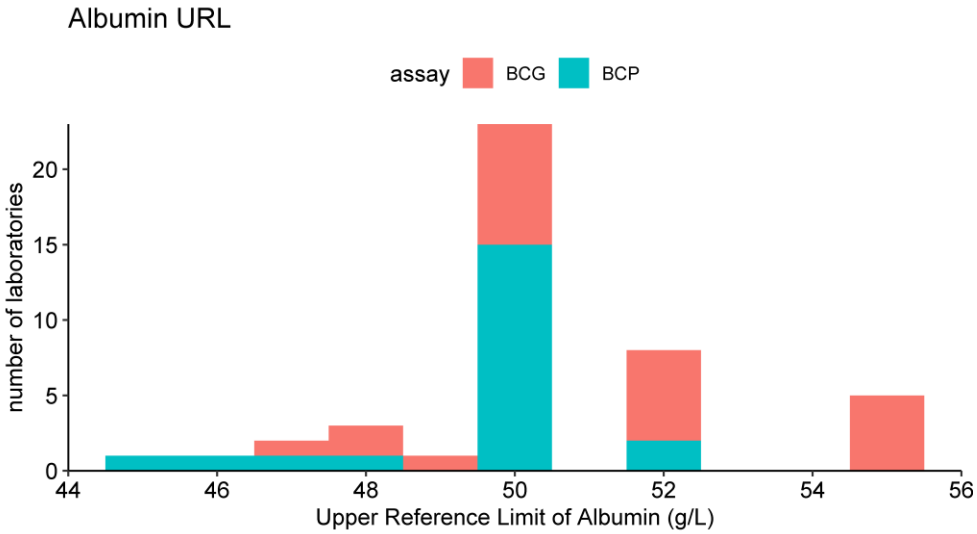
Agreement in interpretation?



Reference interval: Albumin



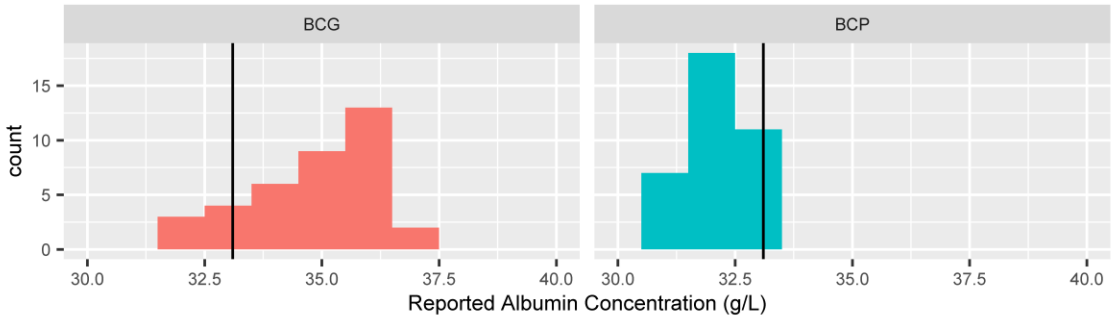




Radboudumc

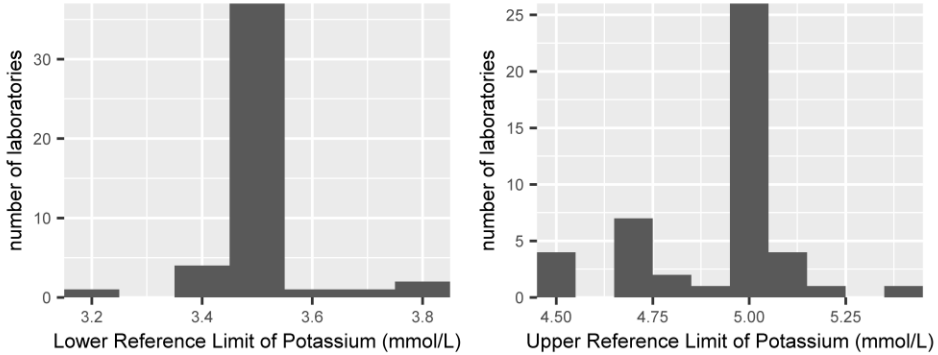
Agreement in interpretation : **Albumin**

Albumin 2021.1B sample result (g/L)



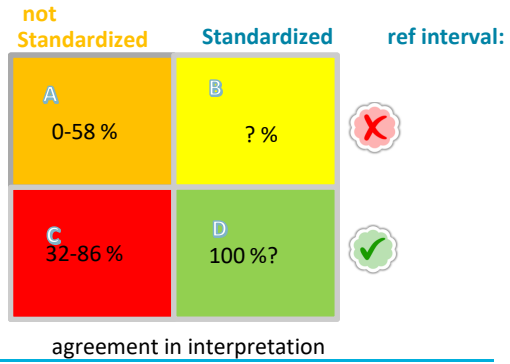
Albumin laboratory LRL

Visualise LL and UL: standardised tests



The agreement for interpretation of sodium 147 mmol/l is

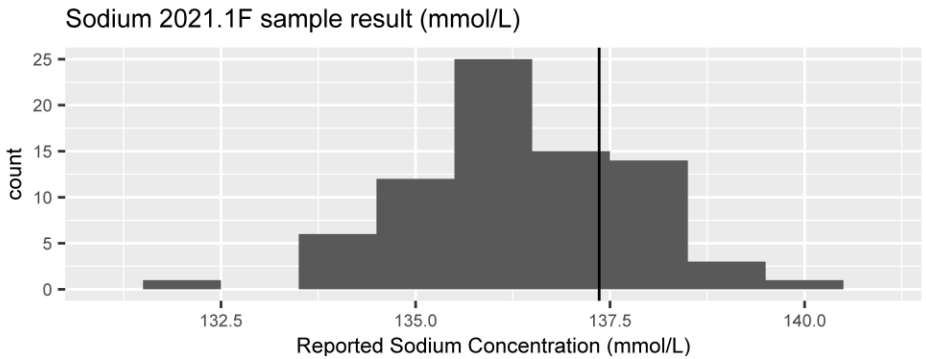
A. Less than 80%
B. Between 80-90%
C. Between 90-95%
D. Higher than 95%



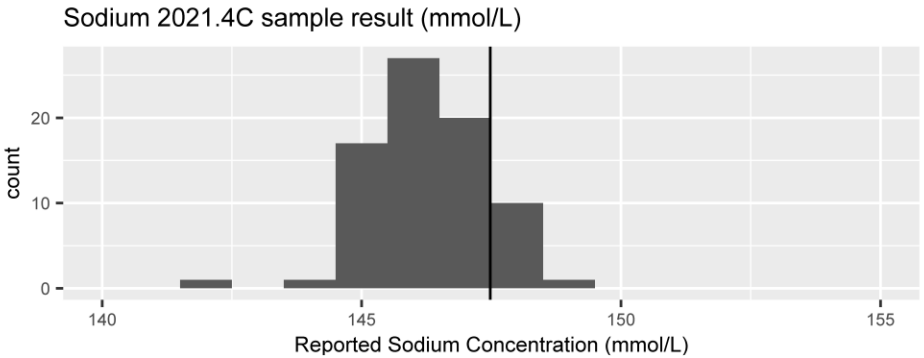
Radboudumc

vote at skmlcongres.participoll.com

LL and agreement in interpretation: Sodium

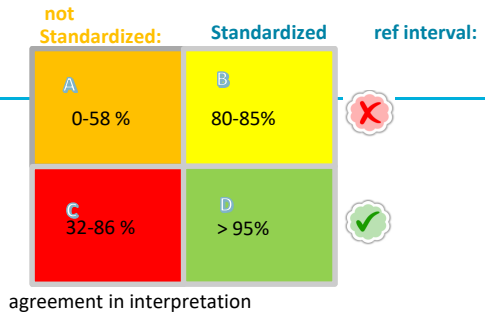


UL and agreement in interpretation : Sodium



Take home

- Discrepancies in ref intervals still exists for standardized analytes
- Use of ‘harmonized’ ref intervals lead to ‘harmonized interpretation’
- EQA program for harmonization of ref intervals can aid
- Pilot: **SKML rondzending ‘interpretation harmonization’**



Radboudumc

Special thanks to

Marith van Schrojenstein-Lantman
Marc Thelen
EQA general clinical chemistry members

Radboudumc