Andreas Bietenbeck
lab@bietenbeck.net

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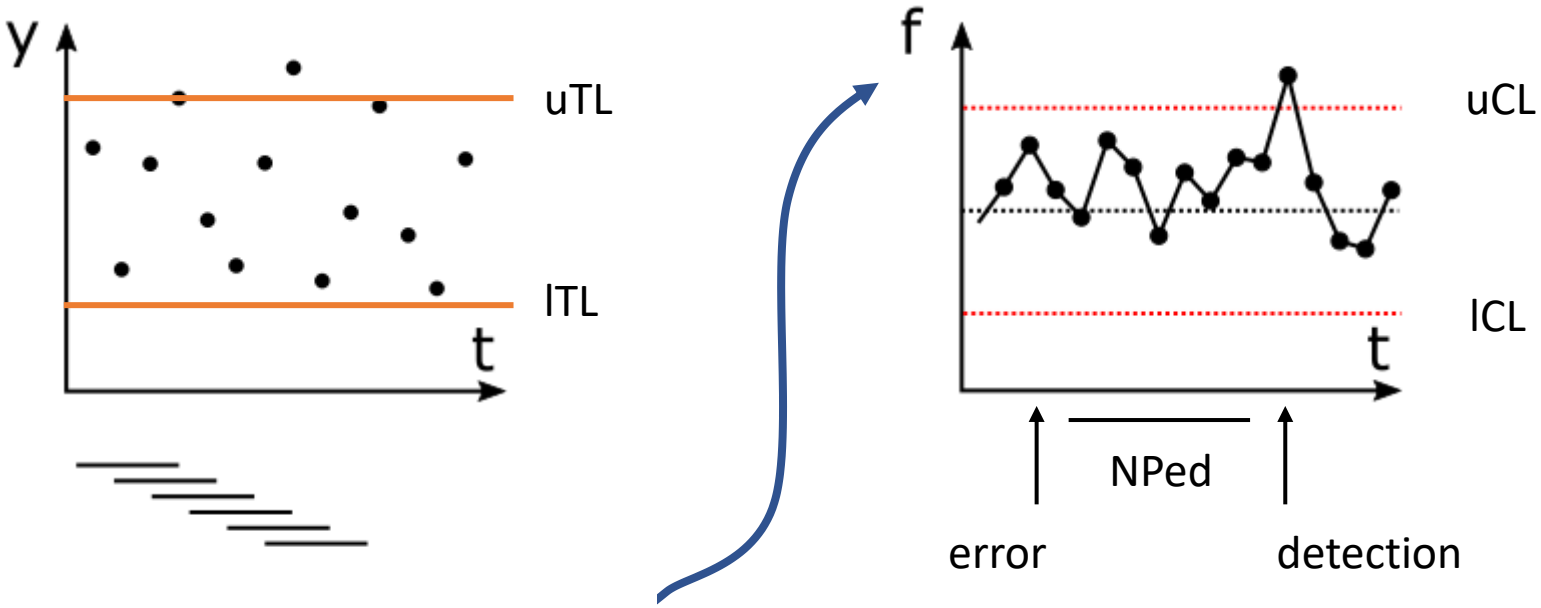
PBRTQC – IMPLEMENTING INTO ROUTINE PRACTICE – VALIDATION AND SIMULATION

Recap – PBRTQC process and terminology



- Upper and lower truncation limits
- Block size
- Algorithm (with or without transformation)
- Upper and lower control limits

PBRTQC for what analytes?

PBRTQC is suitable for

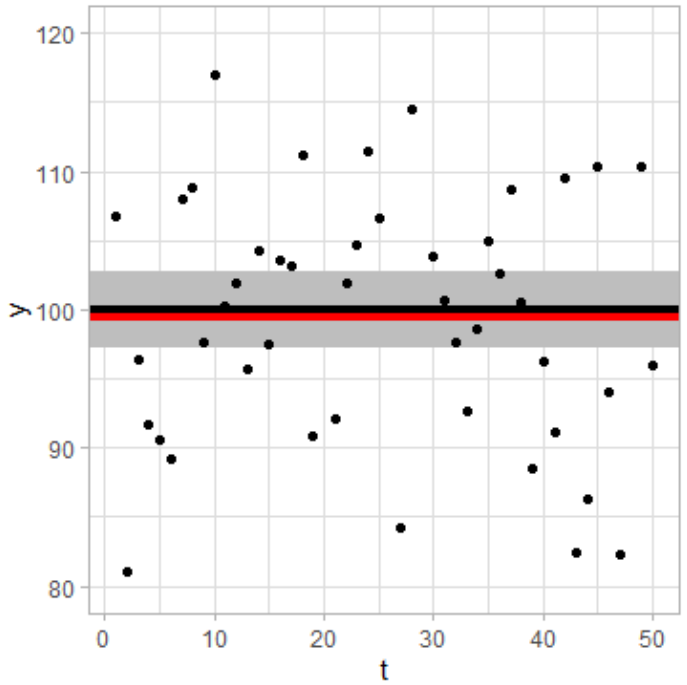
- Laboratories with data processing capabilities
- High-volume tests (e.g. > 200/day)
- Detecting a bias

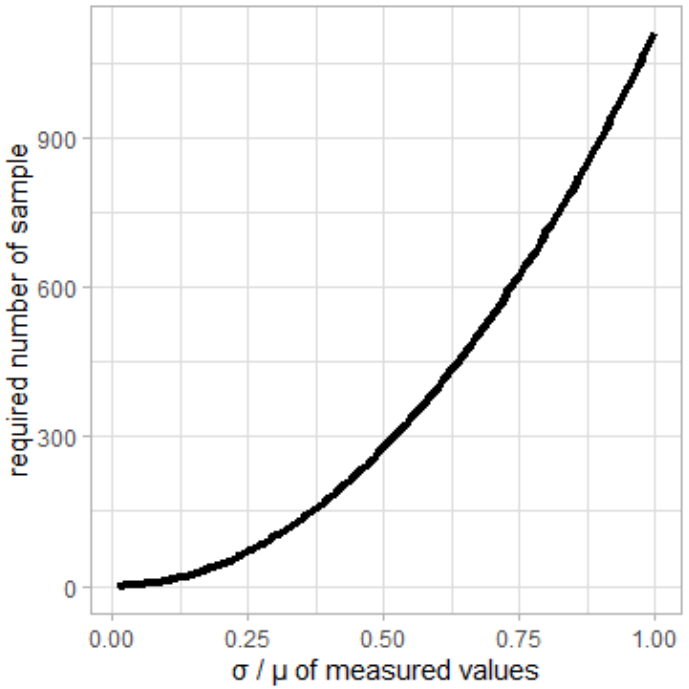
PBRTQC works best with low variation of measured values

$$Standard\ error\ of\ the\ mean$$

$$SEM = \frac{\sigma}{\sqrt{n}}$$

$$required\ SEM = 3\%$$





PBRTQC works best with…

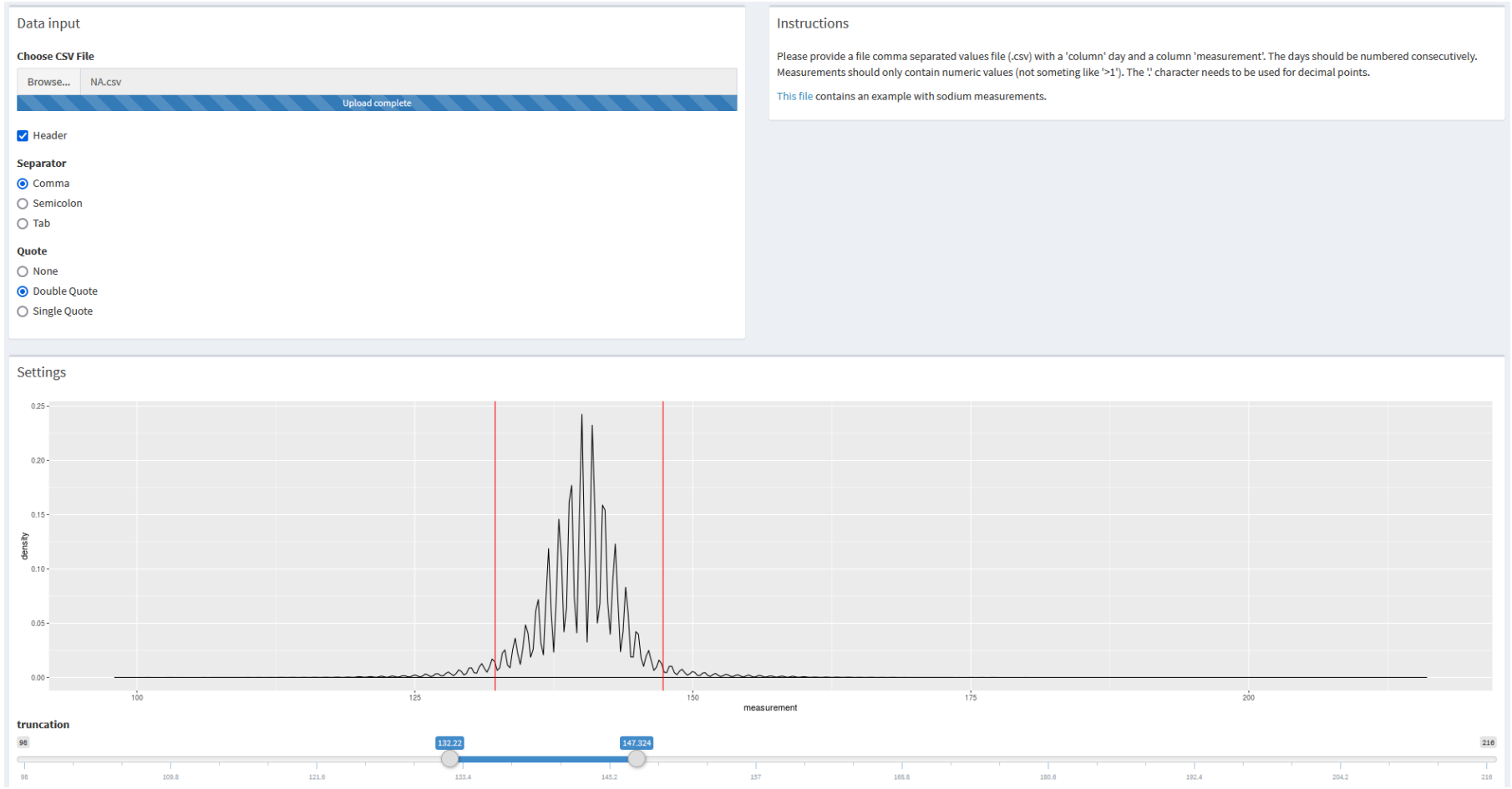
- Analytes with a “small” measuring range and a small *robust normalized spread*: IQR(measurements) /median(measurements) < 1
- Analytes with little temporal variation (e.g. no seasonal differences)
- Analytes with a homogenous distribution of extreme values (e.g. not all ICU samples at the same time)

- Biological variation, reference range, etc. do not matter !

Preliminary simulation

- PBRTQC has to be adjusted to the individual laboratory
- https://pbrtqc.bietenbeck.net

Preliminary simulation



Preliminary simulation

Acceptable number of days with false alarm (%)

10

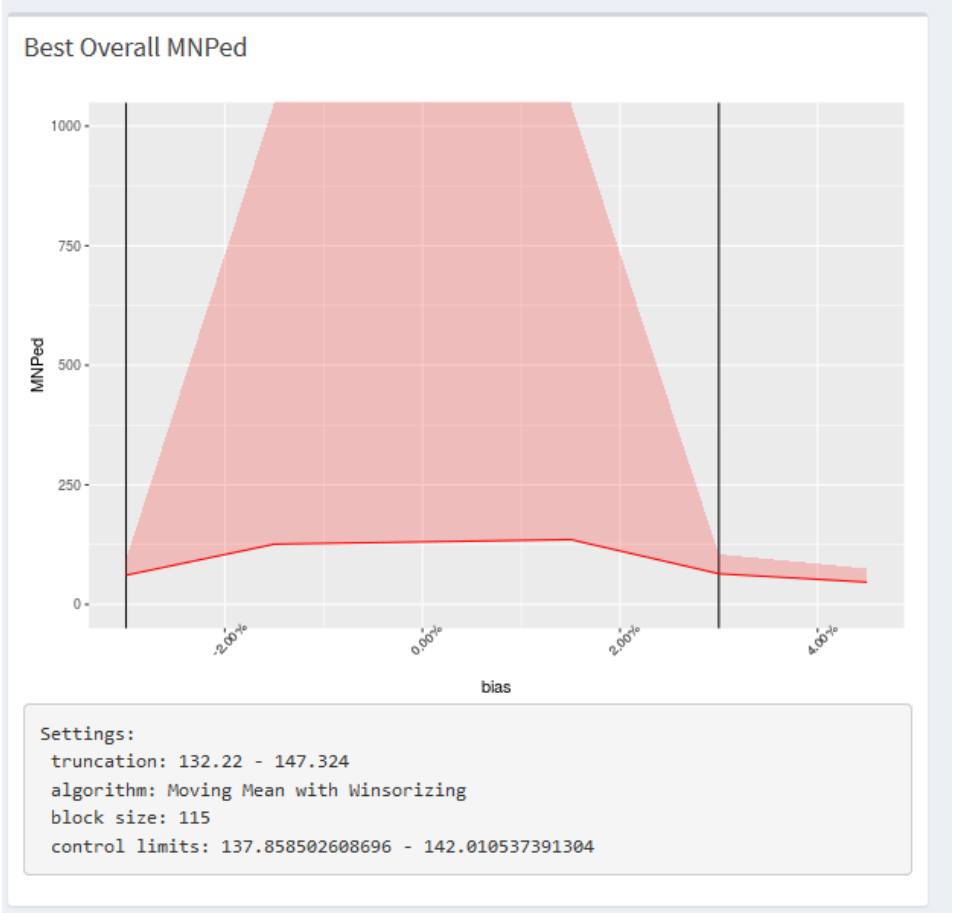
Allowable bias (%)

3

Algorithm

Moving Mean with Winsorizing

Simulate



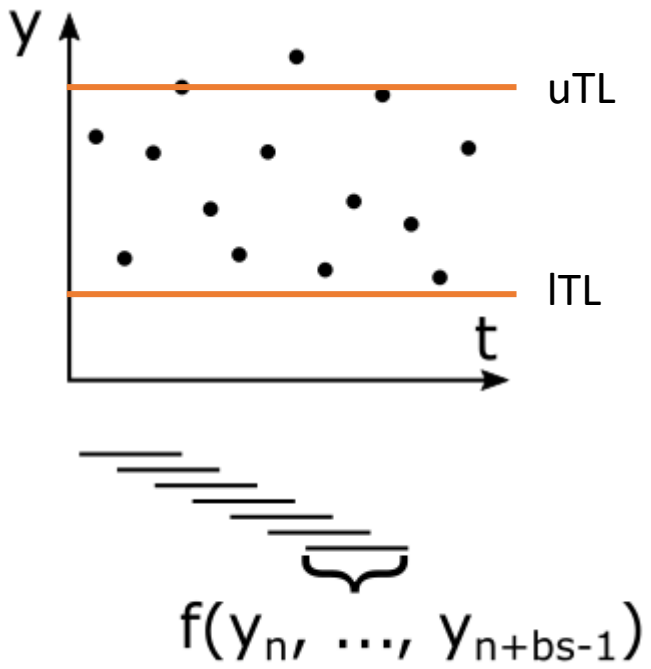
Please provide feedback!

Finetuning parameters

based on a simulation with 10 analytes and 460 000 historical patient measurements each

Bietenbeck et al., ClinChem 2020

Truncation limits

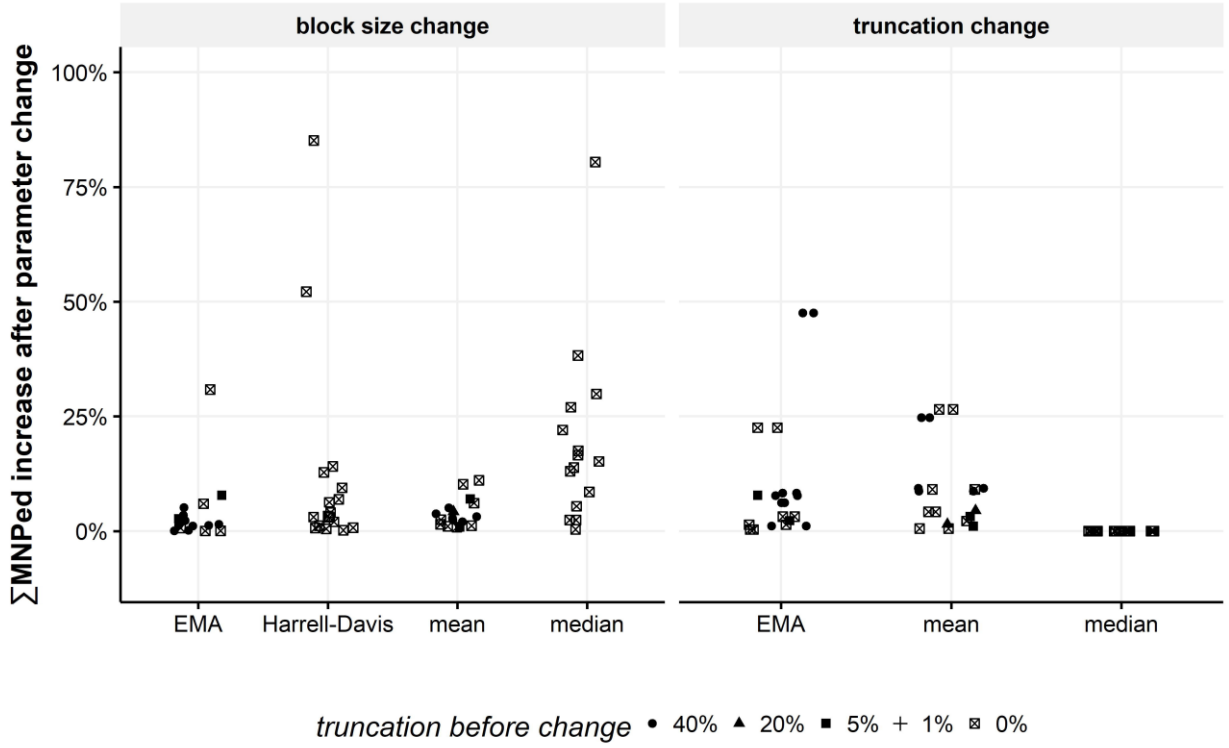


- Winsorizing (“moving” an outlier to the truncation limit) is almost always better than simple removal of outliers.
- Reference limits are poor truncation limits.
- Manually selected truncation limits perform well

Bietenbeck et al., ClinChem 2020

Block size

- Use simulation to find the best parameter, the block size is important



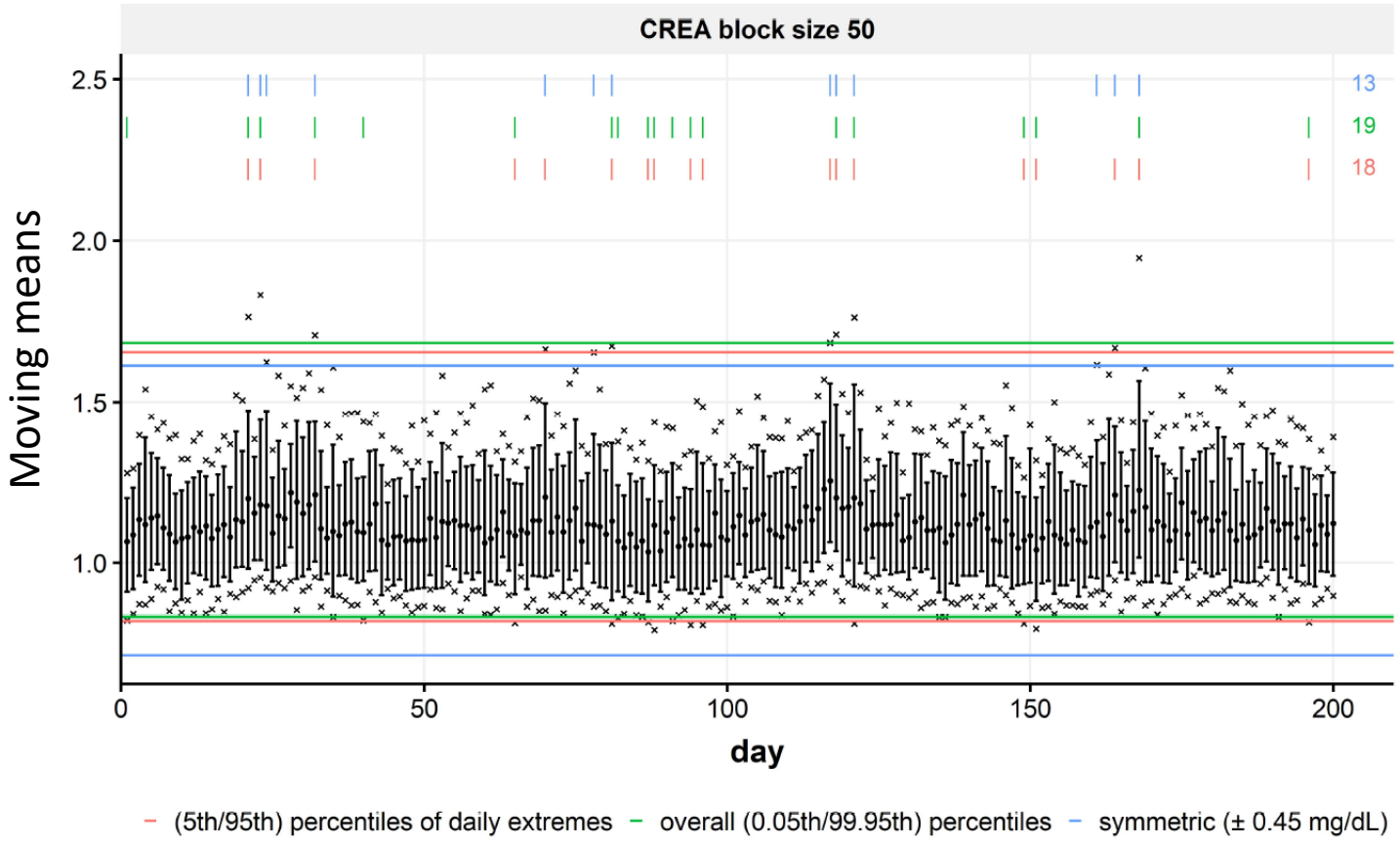
Algorithm

- exponentially (weighted) moving average, moving Harrell–Davis 50 percentile estimator (HD50), moving average, and moving median
- Use Box-Cox and not logarithmic transformation
- Medians need no truncation and no transformation.

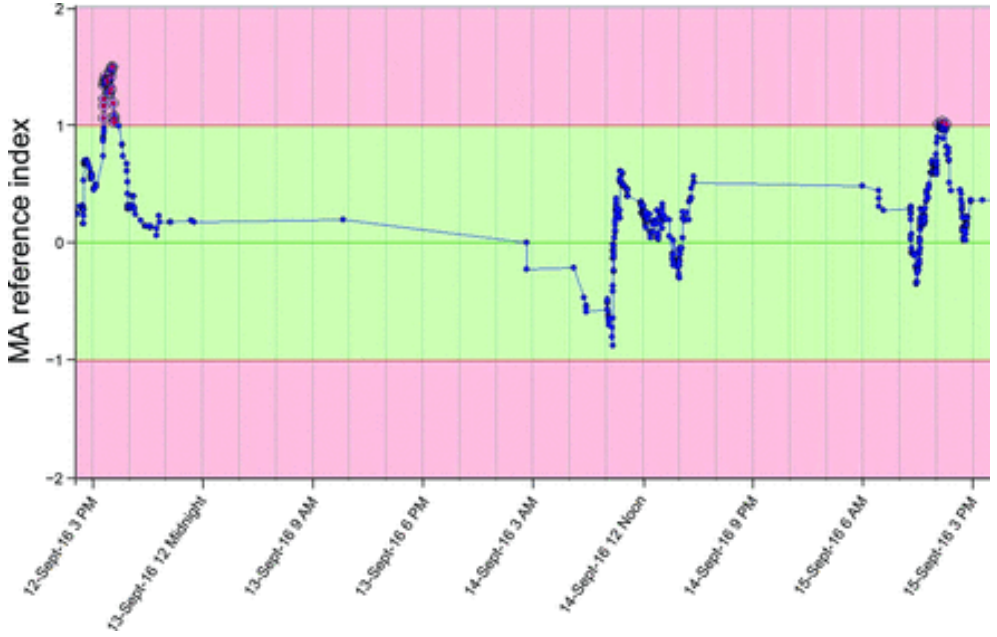
=> No algorithm is superior for all analytes.

Control limits

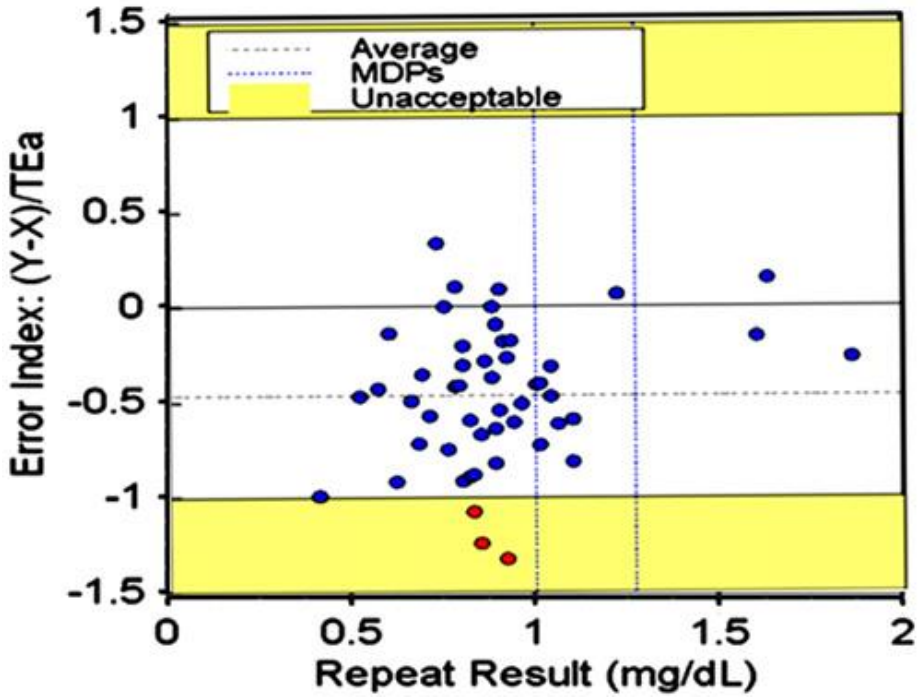
- How many false alarms can you tolerate?
- Use percentiles of daily extremes to set control limits as tight as possible.



Think ahead –
PBRTQC alarms can happen at any time



van Rossum et al., ClinChem 2017



Fleming et al., Clin Biochem 2015

The way ahead

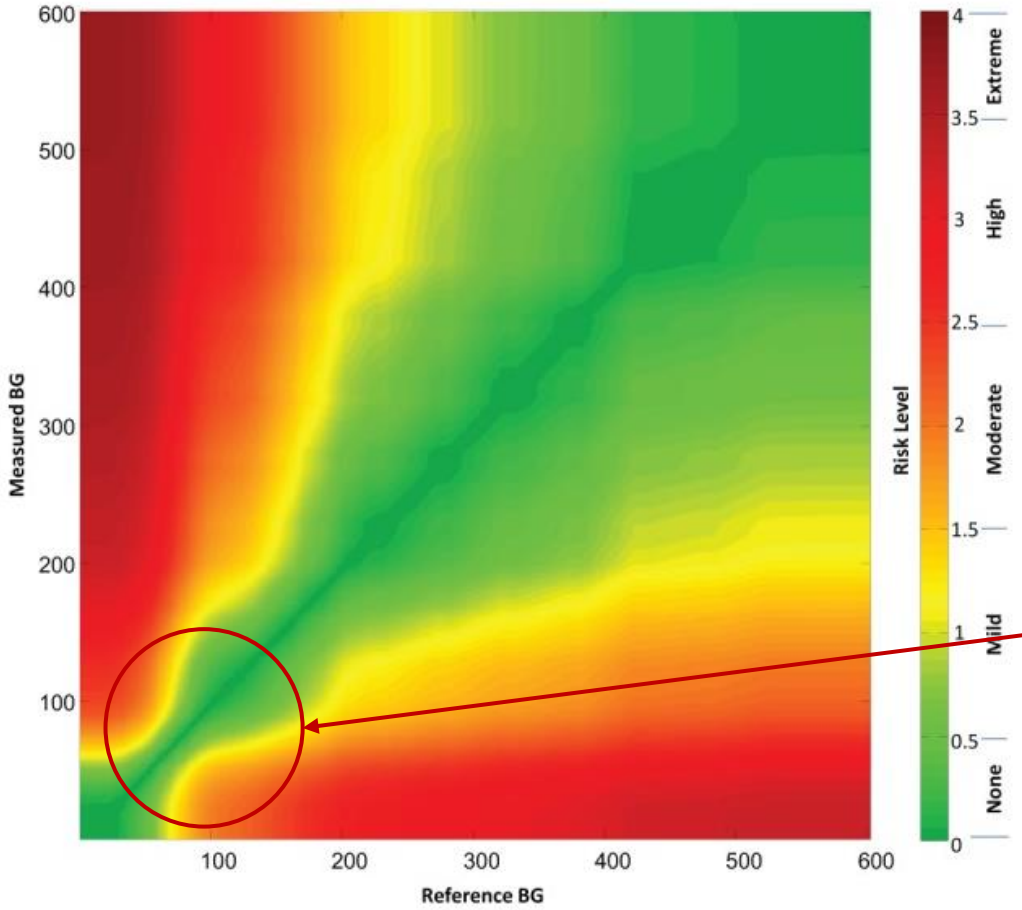
Detecting imprecision

Table 2
Average number of patient results affected before error detection (ANPed) for an increased analytical imprecision (CV_a) for 14 common biochemistry measurands under different block sizes (N) using the average of normals (AoN), moving standard deviation (movSD) and moving sum of outliers (movSO) approaches. The relative size of (within-individual, CV_i and between-individual, CV_g) biological variation to analytical imprecision is expressed as the ratio $\frac{CV_i^2 + CV_g^2}{CV_a^2}$.

Measurand		N = 100, CVa ↑50%			N = 100, CVa ↑100%			N = 100, CVa ↑200%			N = 200, CVa ↑200%		
	$\frac{CV_i^2 + CV_g^2}{CV_a^2}$	AoN	MovSD	Moving outliers	AoN	MovSD	Moving outliers	AoN	MovSD	Moving outliers	AoN	MovSD	Moving outliers
Alanine transaminase, IU/L	234	3215	3468	1885	3005	3531	1991	3067	2918	1594	3565	3335	1502
Albumin, g/L	5	2017	446	482	1174	129	153	458	36	62	849	49	33
Alkaline phosphatase, IU/L	20	2819	1896	2182	2369	864	1286	1459	173	259	2475	160	341
Bicarbonate, mmol/L	1	814	83	100	340	37	28	142	13	15	266	21	24
Calcium, mmol/L	3	1586	227	256	725	65	87	259	24	19	507	24	29
Cholesterol, mmol/L	67	3017	2514	2689	2875	2218	2593	2511	1301	2307	3475	1737	3244
Chloride, mmol/L	850	3155	2957	4070	3008	3411	3929	3147	3518	3552	3603	3224	3754
Creatinine, μmol/L	57	3015	2331	2794	2879	2057	1596	2366	918	1206	3316	1577	1893
Phosphate, mmol/L	18	2743	1945	1094	2256	728	607	1299	142	227	2308	128	263
Potassium, mmol/L	36	2953	2489	1435	2807	1854	1322	1904	610	822	2915	1376	1255
Protein, g/L	6	2266	264	565	1361	141	468	528	46	46	1012	52	69
Sodium, mmol/L	1	1070	92	135	444	43	39	166	13	12	313	21	10
Thyroxine, pmol/L	7	2176	854	588	1415	174	211	542	49	23	1076	54	71
Urea, mmol/L	55	2931	2154	2034	2954	1908	1286	2302	887	1125	3192	1501	1737

Liu et al., Clin Biochem. 2018

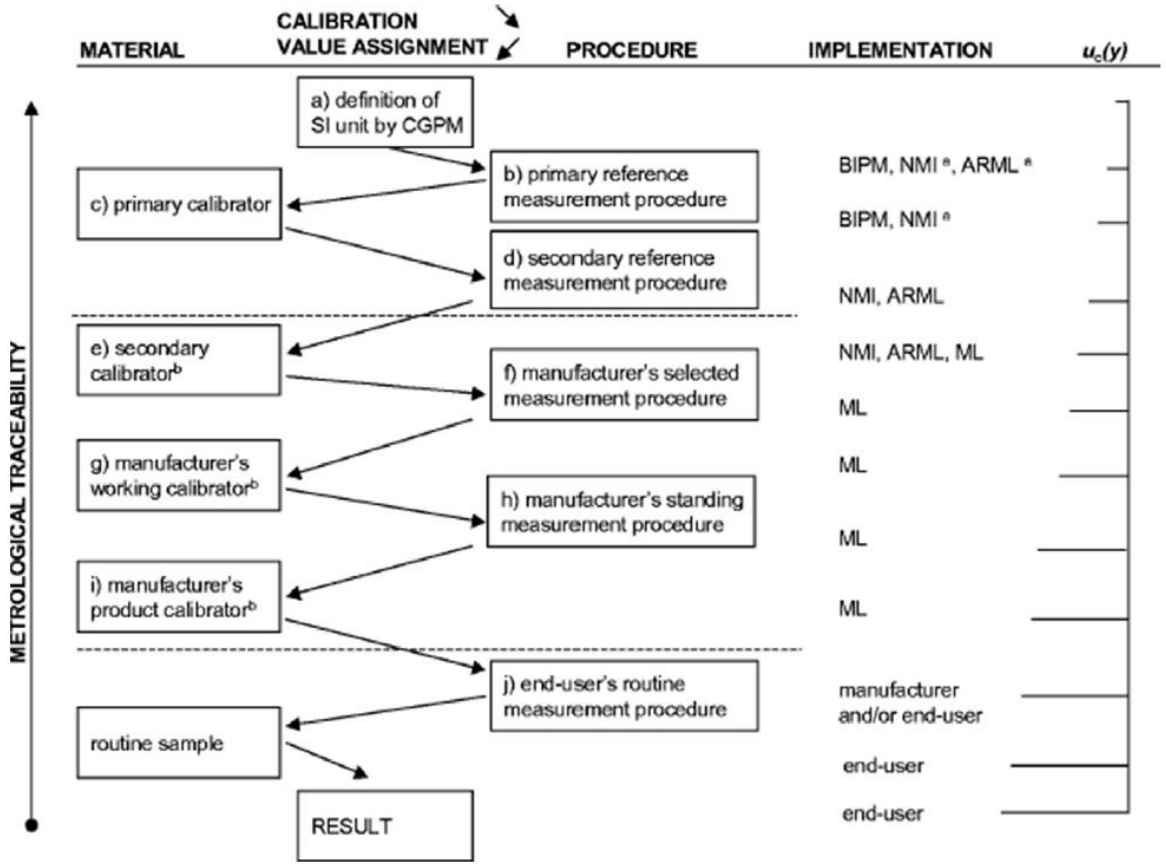
Risk-based PBRTQC ?

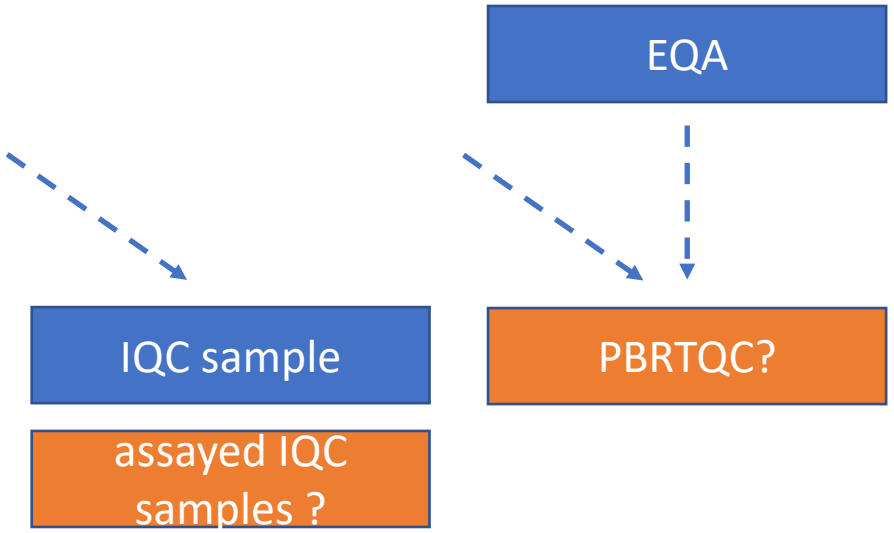


Critical range !

Klonoff et al.,
J Diabetes Sci Technol. 2014

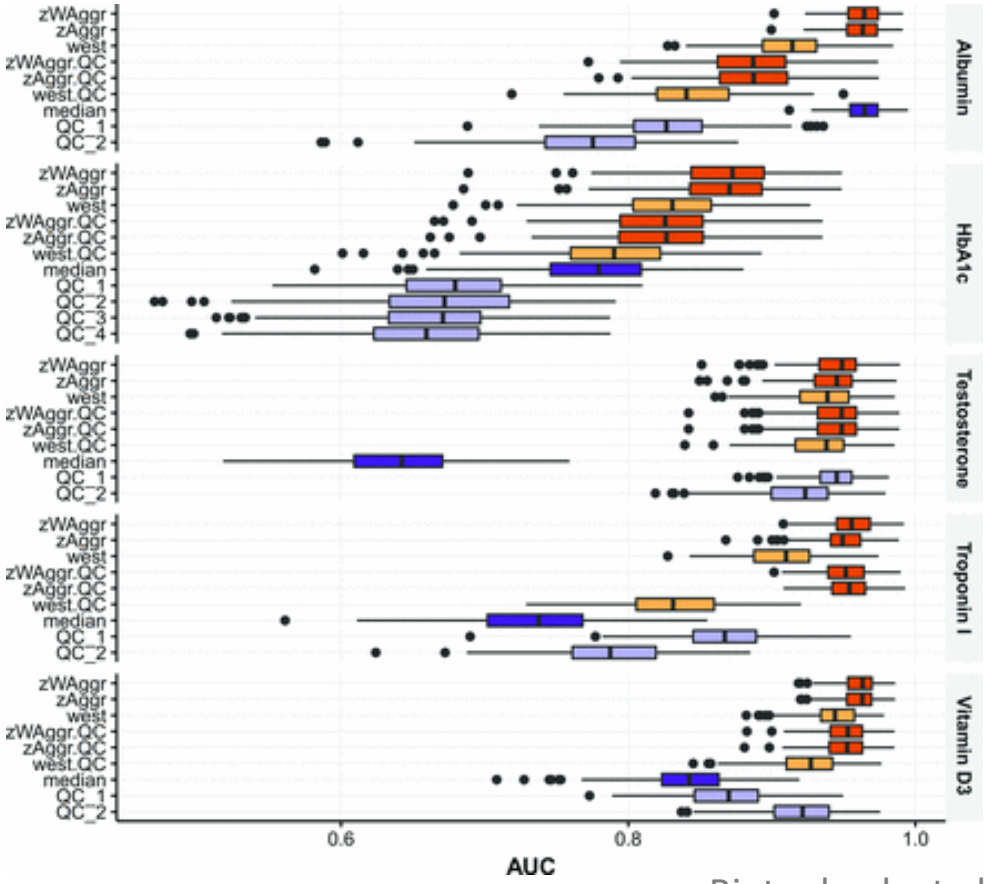
PBRTQC and meterological traceability?





Armbruster;
Clin Lab Med 2017

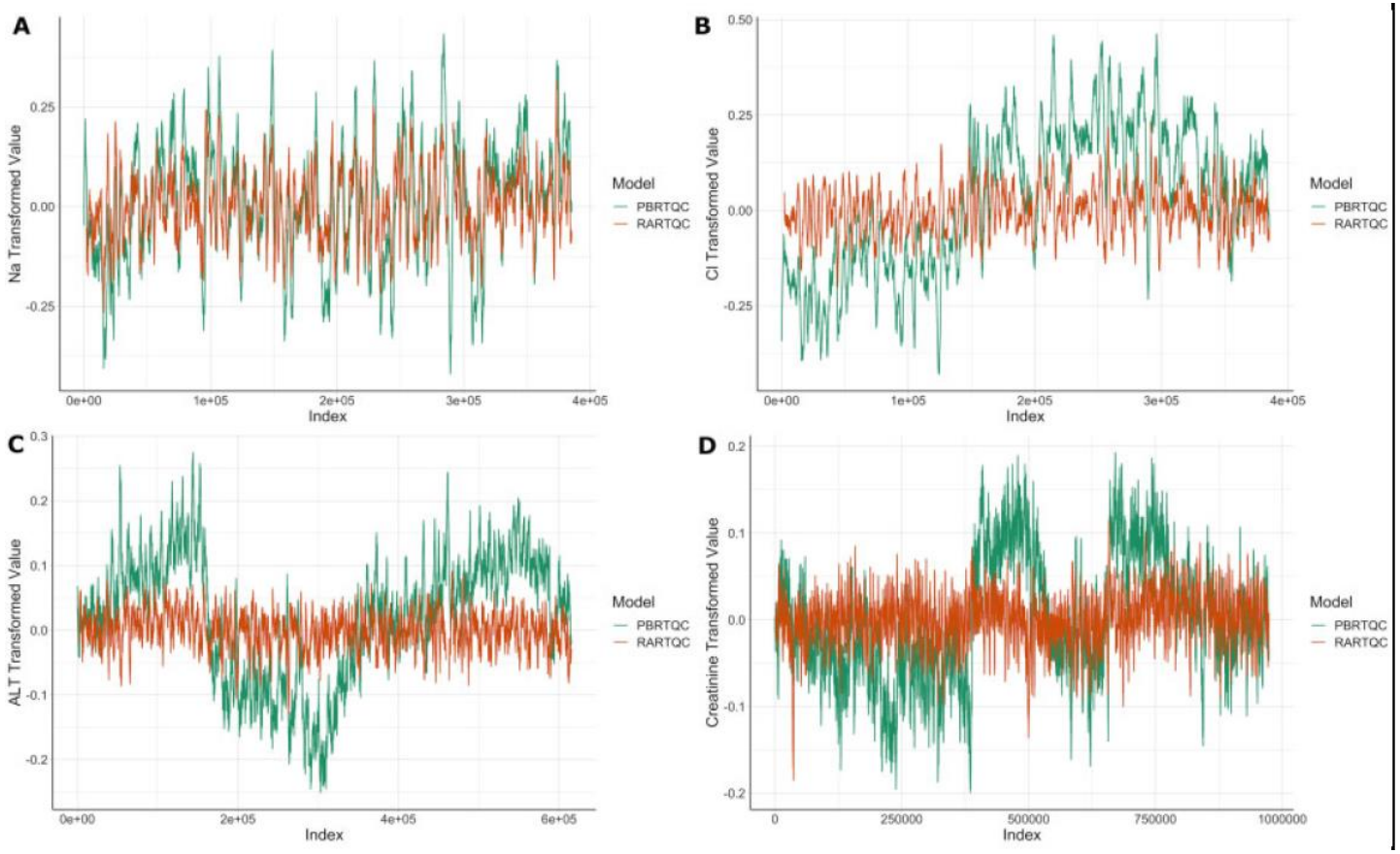
How to combine IQC and PBRTQC



Bietenbeck et al.
ClinChem. 2017

- IQC and PBRTQC complement each other

Regression-Adjusted Real-Time Quality Control

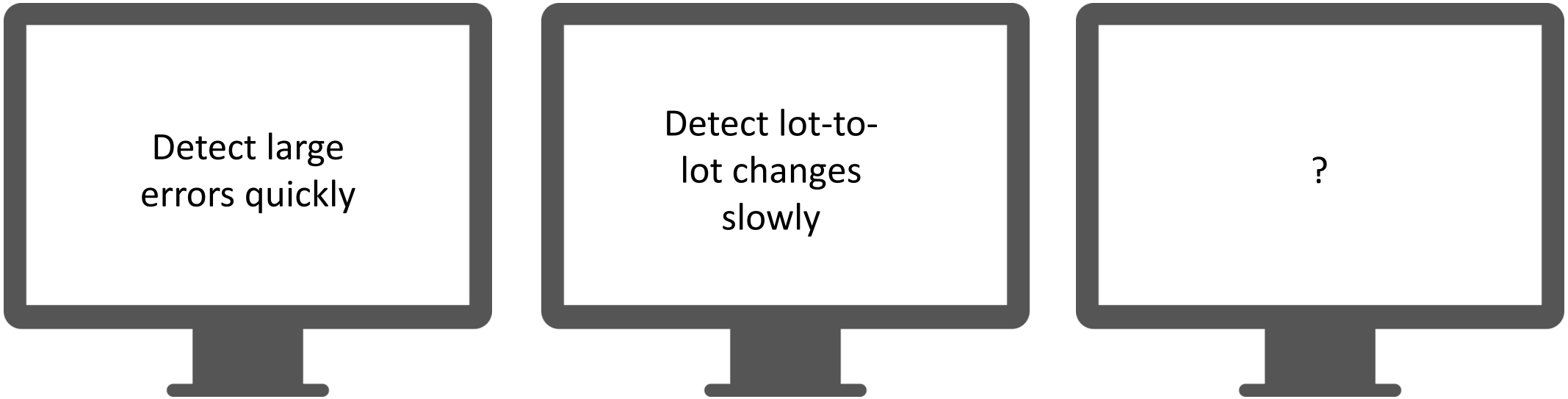


- PBRTQC on residuals of regression
- Regression adjusted
  - Department
  - Diagnosis
  - Age
  - Sex

Duan et al., ClinChem 2021

Multilevel PBRTQC?

"… the baseline regressor removes daily average autocorrelation, seasonality, small shifts caused by reagent lot change, calibration, and other subtle changes in the analytical process that do not have a significant clinical impact." (Duan et al., ClinChem 2021)

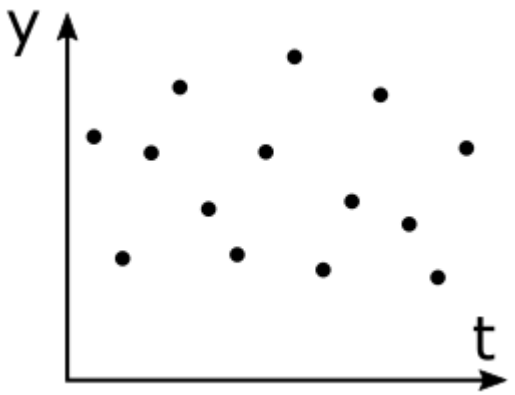


Conclusion

- PBRTQC is suitable analytes with a “small” measuring range
- Use simulations to determine the best parameters for your laboratory
- Learn how to use the powerful new QC tool PBRTQC in your QC strategy

Thank you for your attention

How to start PBRTQC?



- The first PBRTQC result is calculated after one “block size” of measurements is complete.
- Start with value from last day?