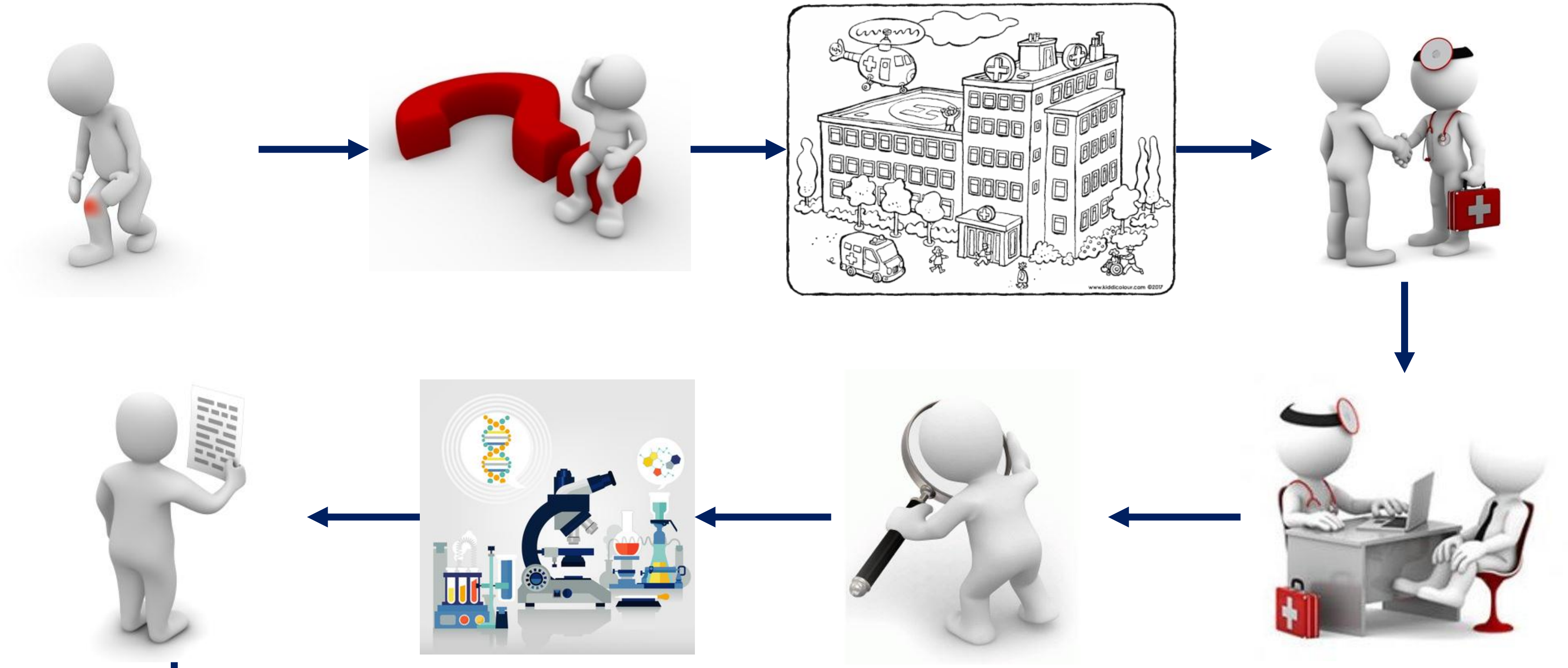
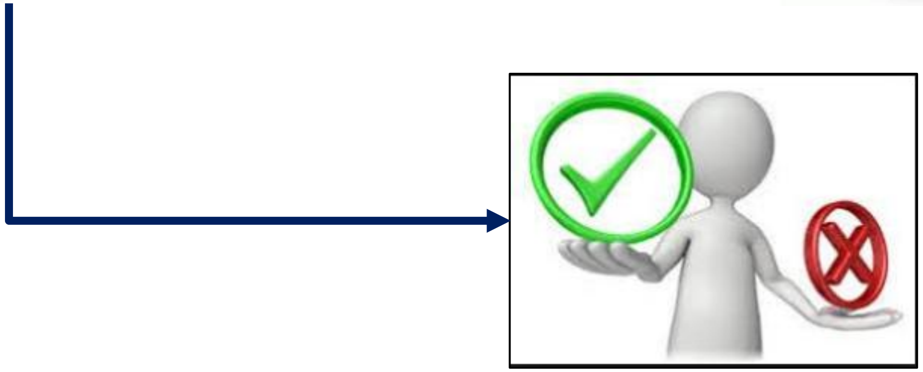
La logique bayésienne peut également optimiser l’analyse longitudinale des résultats d’EEQ.

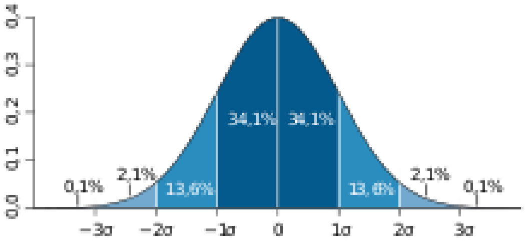
Piet Meijer
ECAT Foundation
The Netherlands

The story of the patient





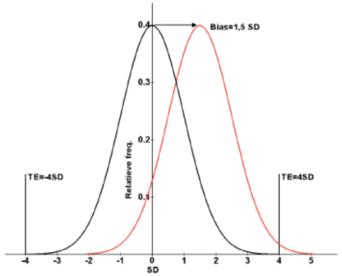
The laboratory should deliver reliable results to the physician to make proper decision-making possible.

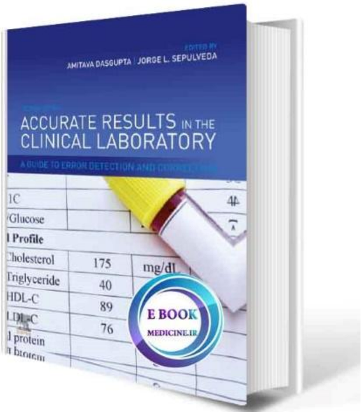


IMPRECISION

Laboratory Result

INACCURACY

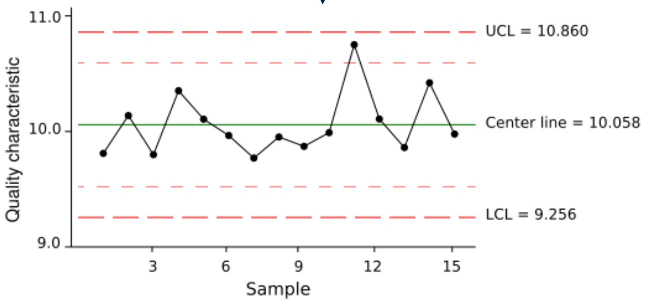




Control of Analytical Process

IQC

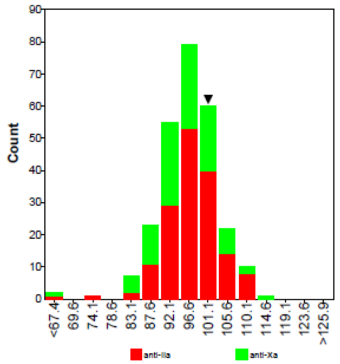
Imprecision
(Bias)



Does the analytical test system provides reliable result?

EQC

Bias
(Imprecision)



Does the analytical test system provides accurate result?

Control of Analytical Process

	EXTERNAL	INTERNAL
PERMANENT	Variables of the analytic process that have a permanent character and defined by a third party	Variables of the analytic process that have a permanent character and defined by the laboratory
VARIABLE	Variables of the analytic process that have a variable character and defined by a third party	Variables of the analytic process that have a variable character and defined by the laboratory

Control of Analytical Process

	EXTERNAL	INTERNAL
PERMANENT	EQA	EQA
VARIABLE	IQC EQA	IQC EQA

IQC	Primary focus: Random errors (transient deviations), trends in deviation from the internal expected value, shifts
EQA	Primary focus: Systematic deviation from the “true” value = bias, trends and shifts, Random errors.

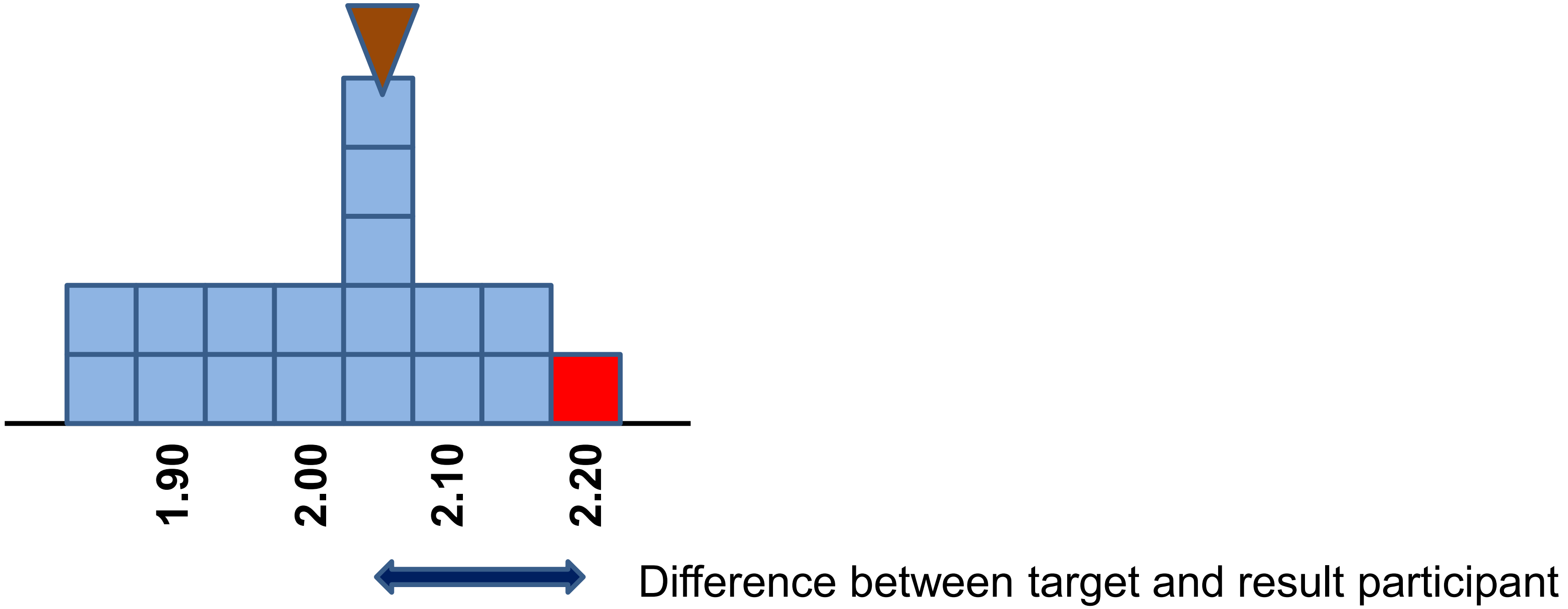
EXTERNAL QUALITY CONTROL TOOLBOX

How can Bayesian statistics advance the longitudinal evaluation of laboratory performance?

The primary aim of EQA is to focus on the laboratory's analytical performance in comparison to its peers or to an accuracy-based reference system.

Miller, W.G. Clin Biochem, 2009; 42: 232-5.

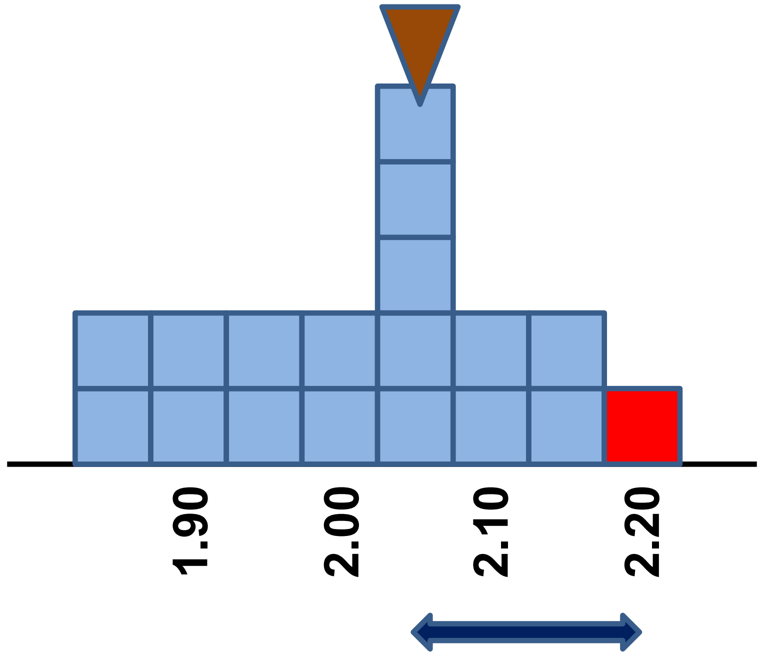
Example:



Performance evaluation

Individual performance indicator:

A numerical indicator representing the position of the individual lab result with respect to the consensus value – measure for accuracy



Examples:

Absolute difference

Relative difference

Z-score

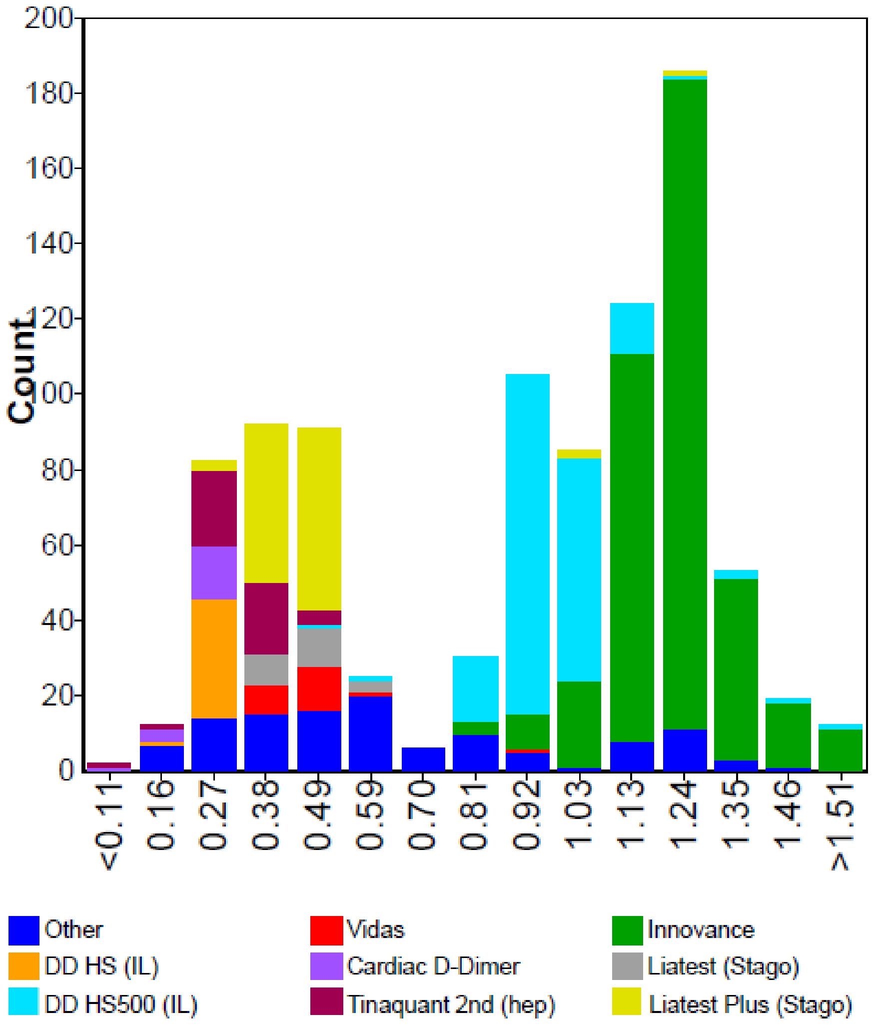
Performance evaluation

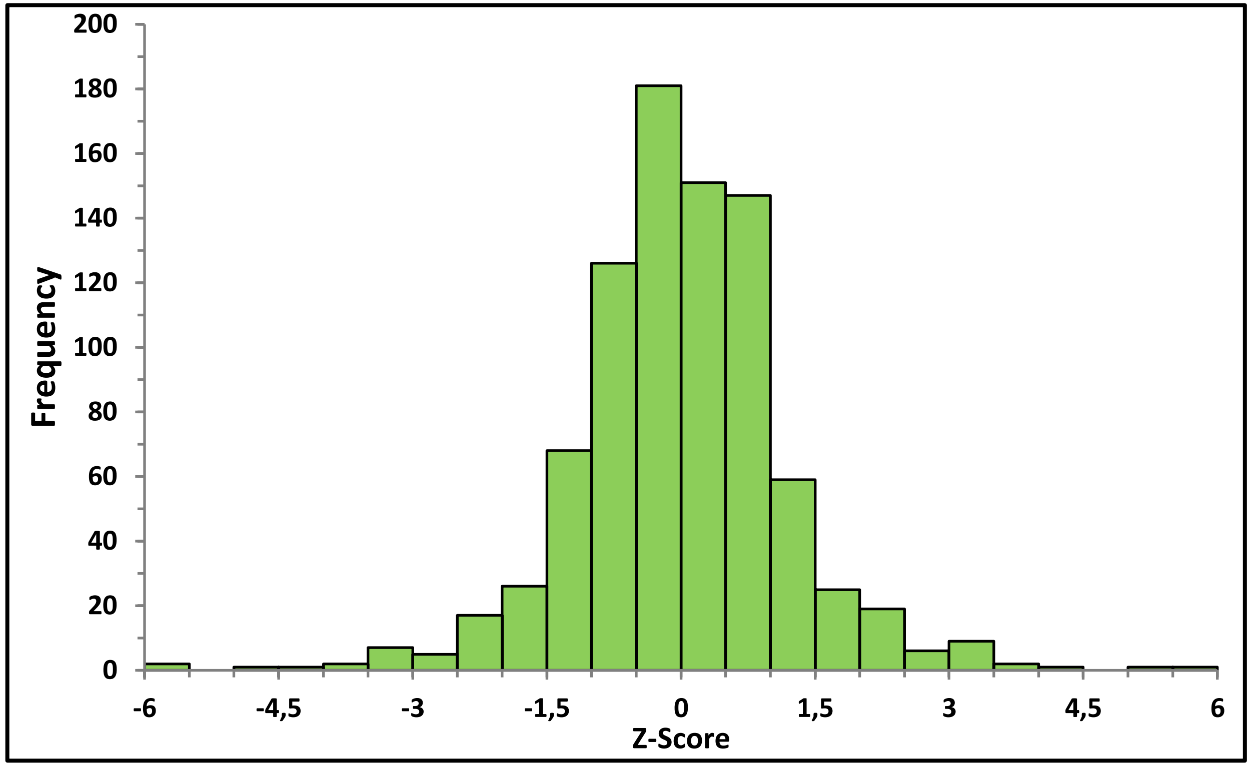
Z-score = Standard Deviation Index

It describes the systematic error or bias of the individual result from the consensus value as a multiplier of the standard deviation.

The z-score is especially helpful for comparing participants' performance of peer groups with consensus values which are not standardised nor harmonised.

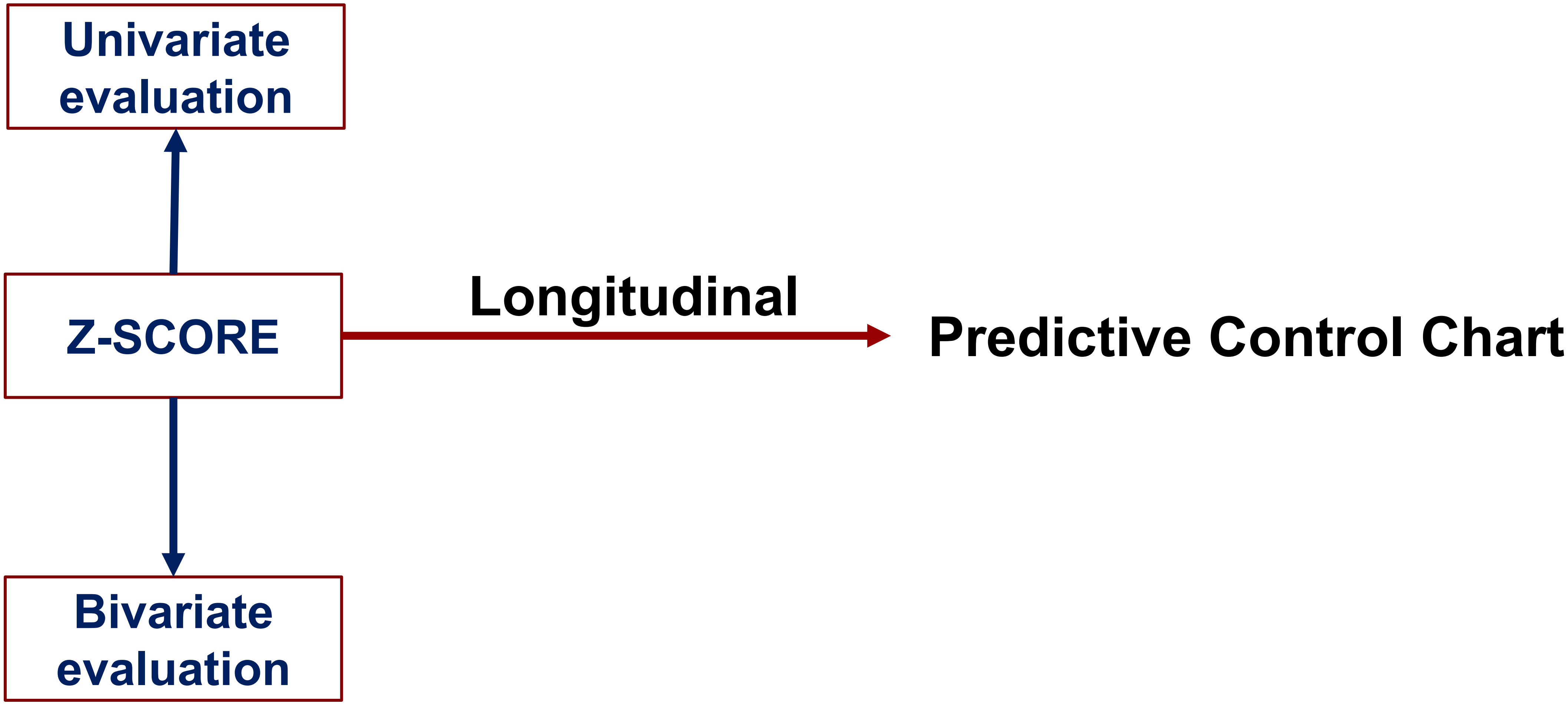
Distribution of results and Z-score



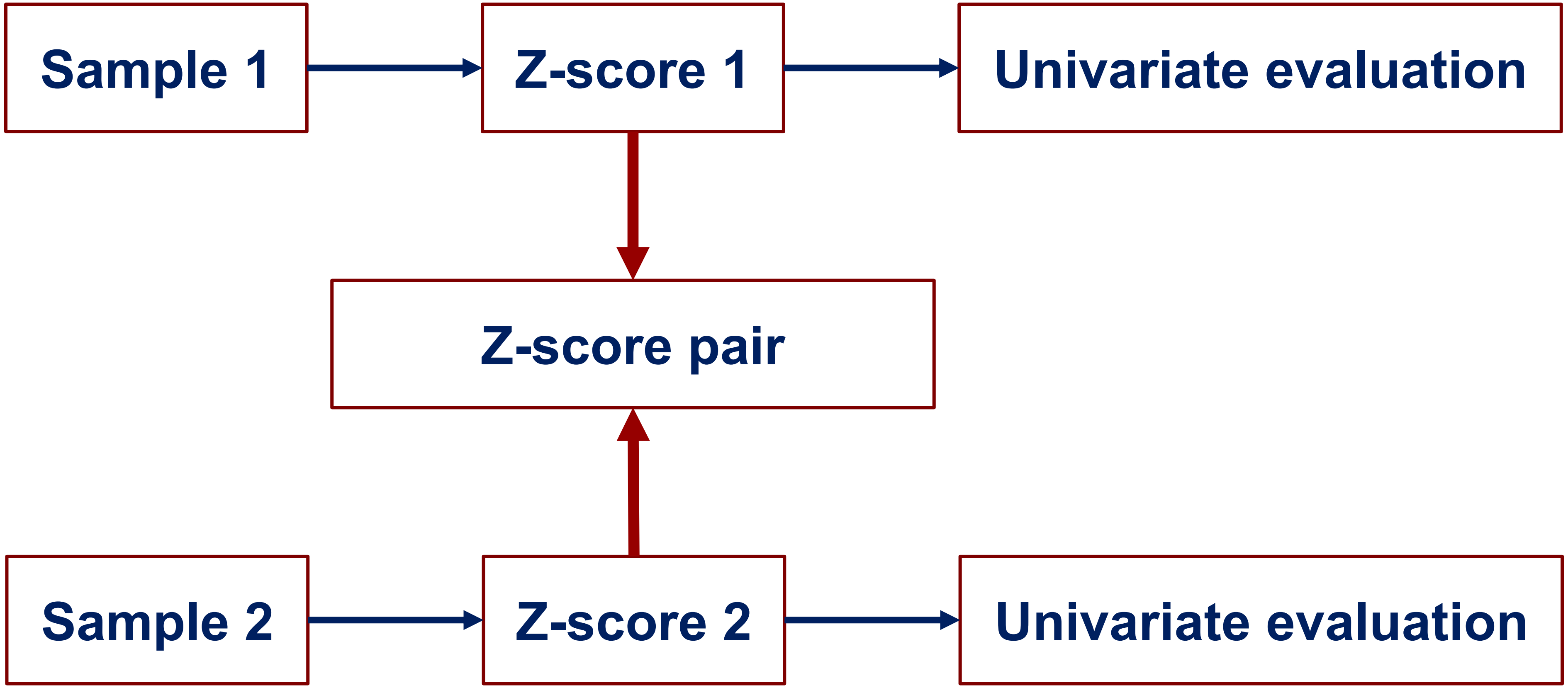


EXTERNAL QUALITY CONTROL TOOLBOX

- Univariate Z-score analysis (per survey)
- Bivariate Z-score analysis (per survey)
- Predictive Control Chart (PCC) on longitudinal Z-scores (multiple surveys)


Univariate evaluation
Z-SCORE
Longitudinal
Predictive Control Chart
Bivariate evaluation

Univariate Z-score analysis


Sample 1
Z-score 1
Univariate evaluation
Z-score pair
Sample 2
Z-score 2
Univariate evaluation

Z-score

INTERNATIONAL STANDARD

ISO/IEC 17043

First edition
2010-02-01

Conformity assessment — General requirements for proficiency testing

Évaluation de la conformité — Exigences générales concernant les essais d'aptitude

$-2 \geq$ Z-score ≤ 2

Satisfactory

No signal

$-3 \leq$ Z-score < -2

$2 <$ Z-score ≤ 3

Questionable

Warning signal

Z-score < -3

Z-score > 3

Unsatisfactory

Action signal

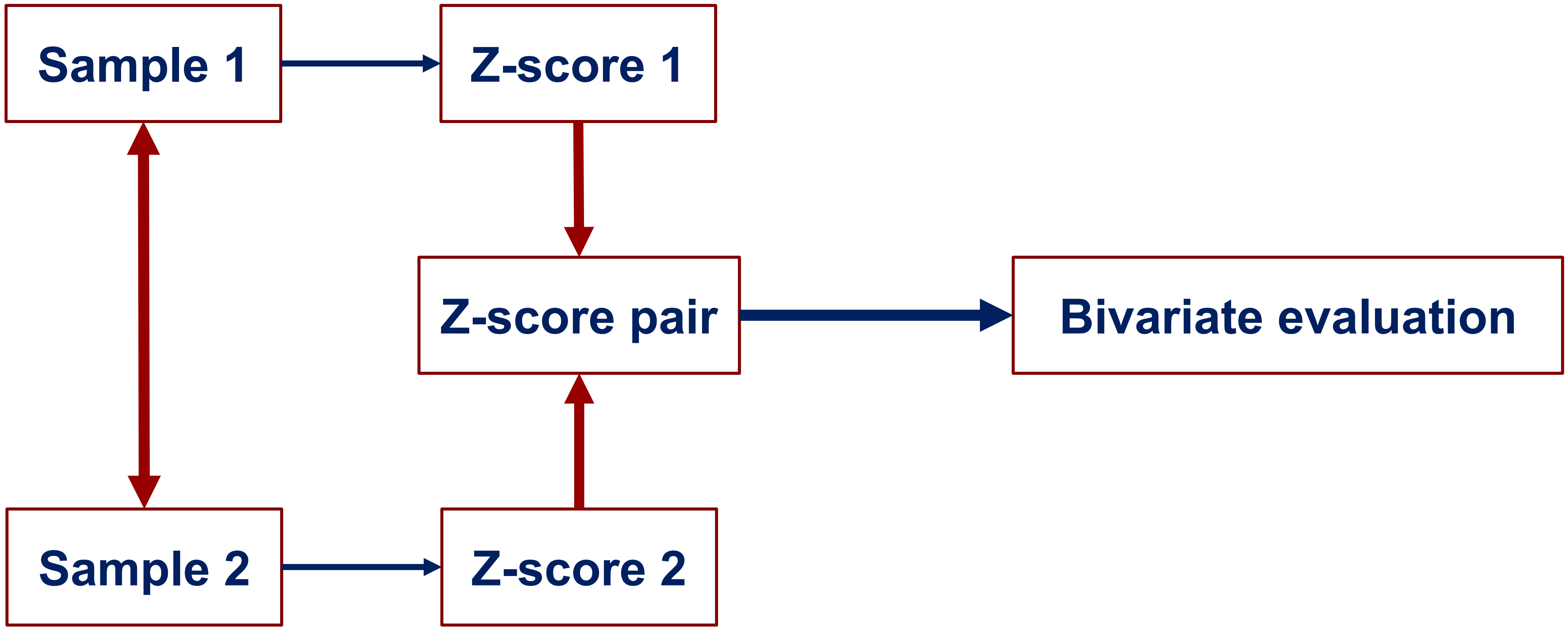
Single Survey

- Univariate analysis.
- Assessment of deviation from target value per sample.

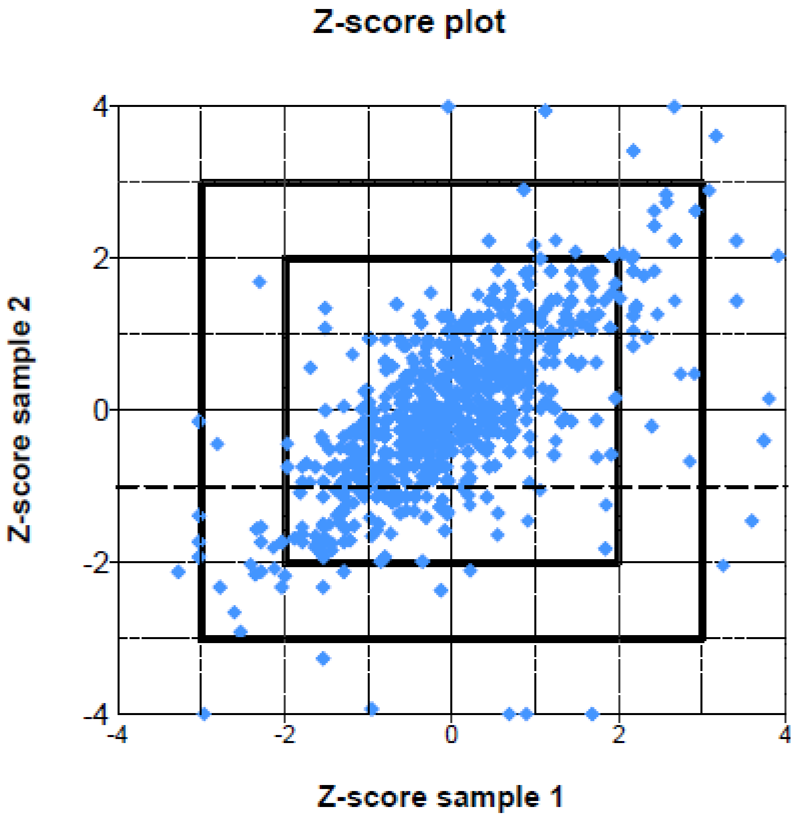
Module	Parameter	Sample	Test System	Total	Assay	Method
Coagulation Factor - I	Factor XI	23.146	3	-0.52	-0.52	-0.10
		23.147	3	1.98	1.97	1.39
Coagulation Factor - I	Factor XII	23.146	3	-0.80	-0.79	-0.26
		23.147	3	-1.09	-1.08	-0.36
Coagulation Factor - II	Factor II	23.148	3	3.37	3.37	2.87
		23.149	3	1.10	1.10	-0.33
Coagulation Factor - II	Factor V	23.148	3	-2.14	-2.14	-3.24
		23.149	3	-0.36	-0.36	-1.97
Coagulation Factor - II	Factor VII	23.148	3	0.31	0.31	0.31
		23.149	3	-1.30	-1.30	-2.24
Coagulation Factor - II	Factor X	23.148	3	-0.87	-0.87	-0.27

- Investigate potential causes for significant deviation.

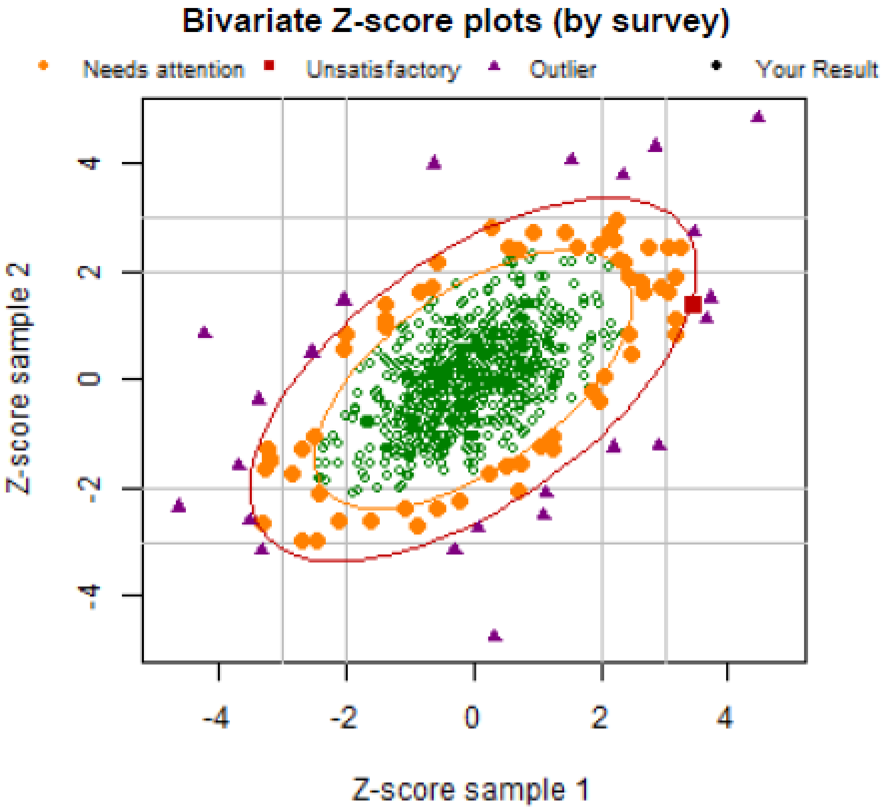
Bivariate Z-score analysis


Sample 1
Z-score 1
Z-score pair
Bivariate evaluation
Sample 2
Z-score 2

Classical Youden plot



Bivariate Z-score analysis



Clin Chem Lab Med 2024; 62(8): 1548–1556 DE GRUYTER

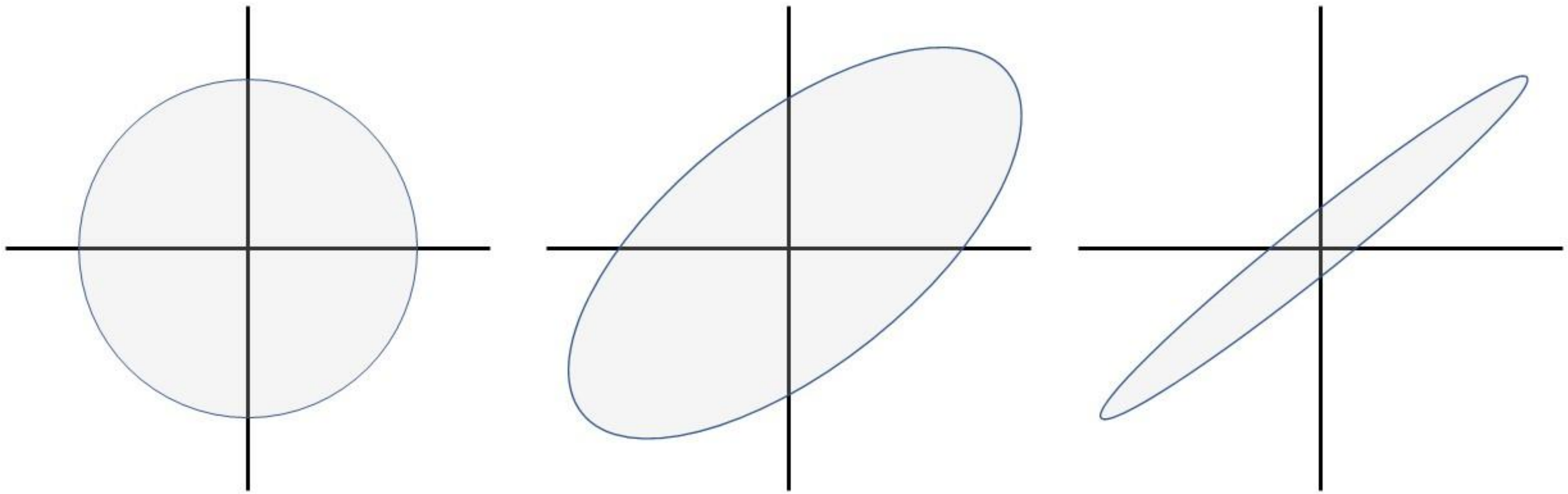
Piet Meijer*, Frederic Sobas and Panagiotis Tsiamyrtzis

Assessment of accuracy of laboratory testing results, relative to peer group consensus values in external quality control, by bivariate z-score analysis: the example of D-Dimer

Conclusions: The use of the bivariate z-score analysis is of major importance when multiple samples are distributed around in the same survey and dependency of the results is likely. Important lessons can be drawn from the shape of the ellipse with respect to random and systematic deviations, while individual laboratories have been informed about their position in the state-of-the-art distribution and whether they have to deal with systematic and/or random deviations.

https://www.degruyter.com/document/doi/10.1515/cclm-2023-0835/html

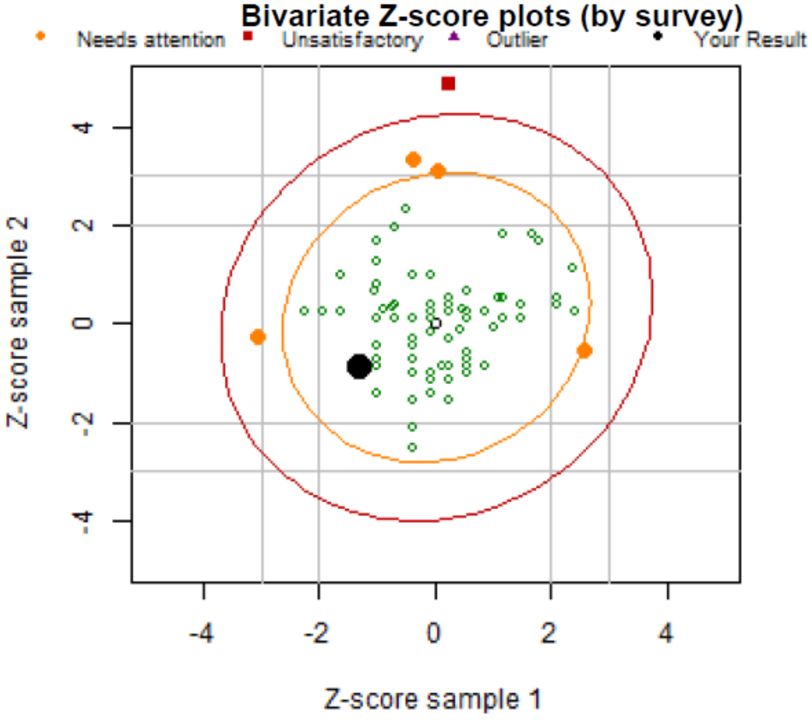
Bivariate Z-score analyse



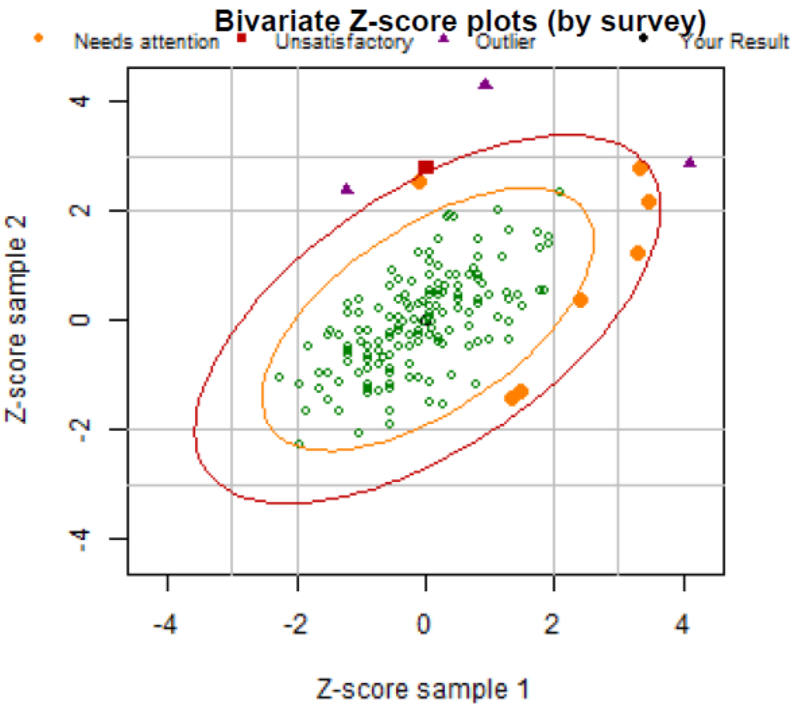
No correlation Moderate correlation High correlation

Examples Bivariate Z-score analyse

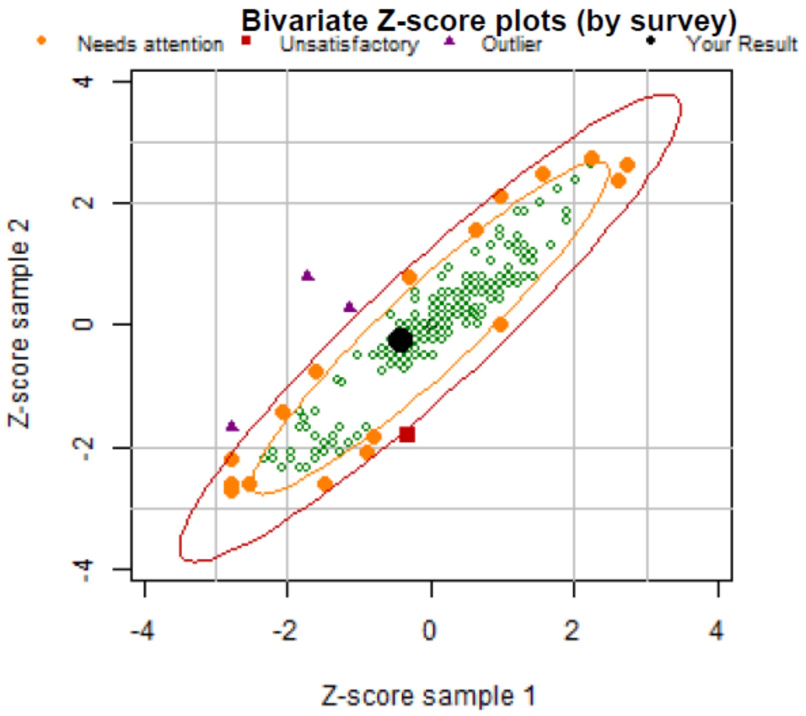
PC Clot



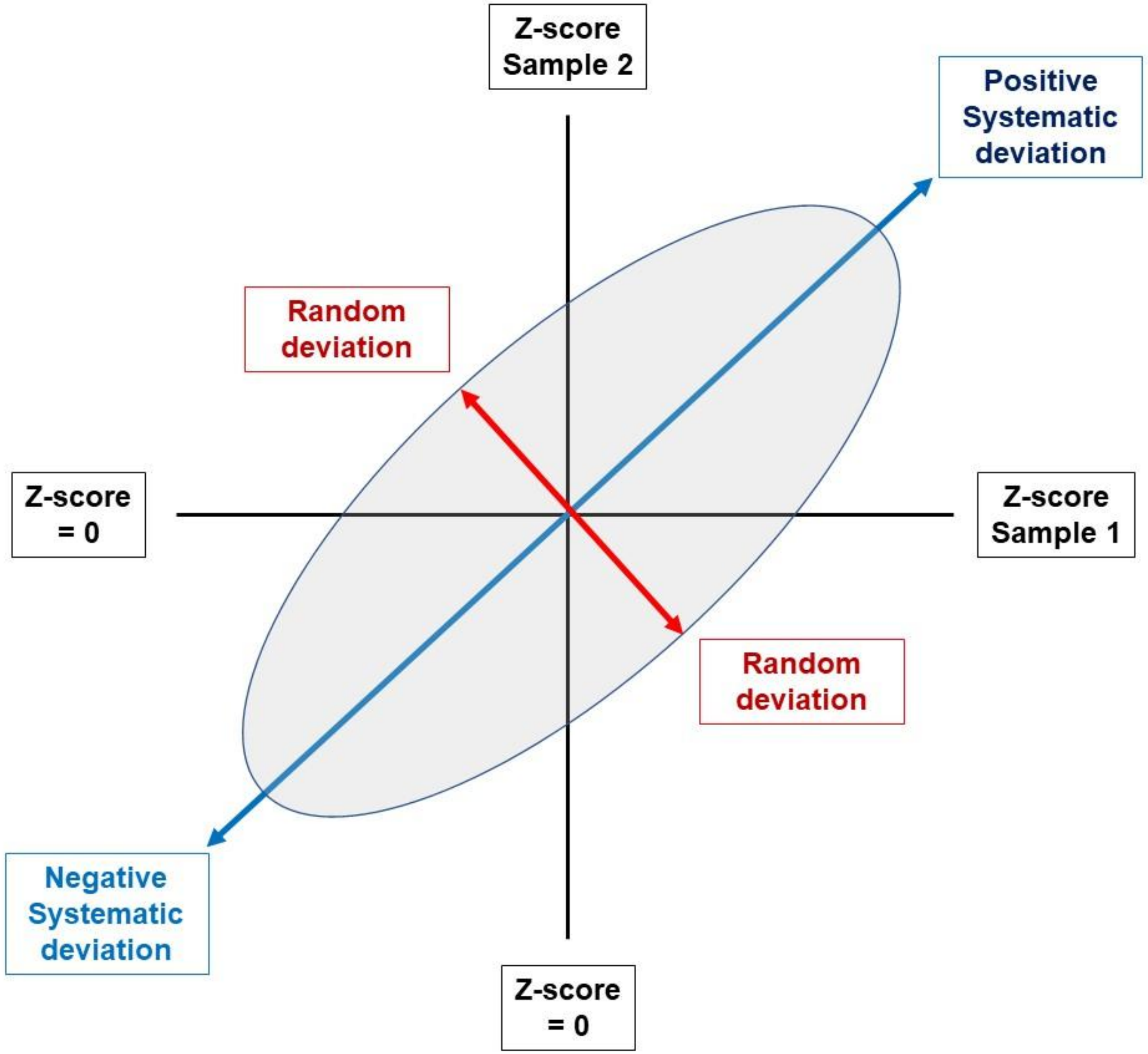
PS Clot



UFH



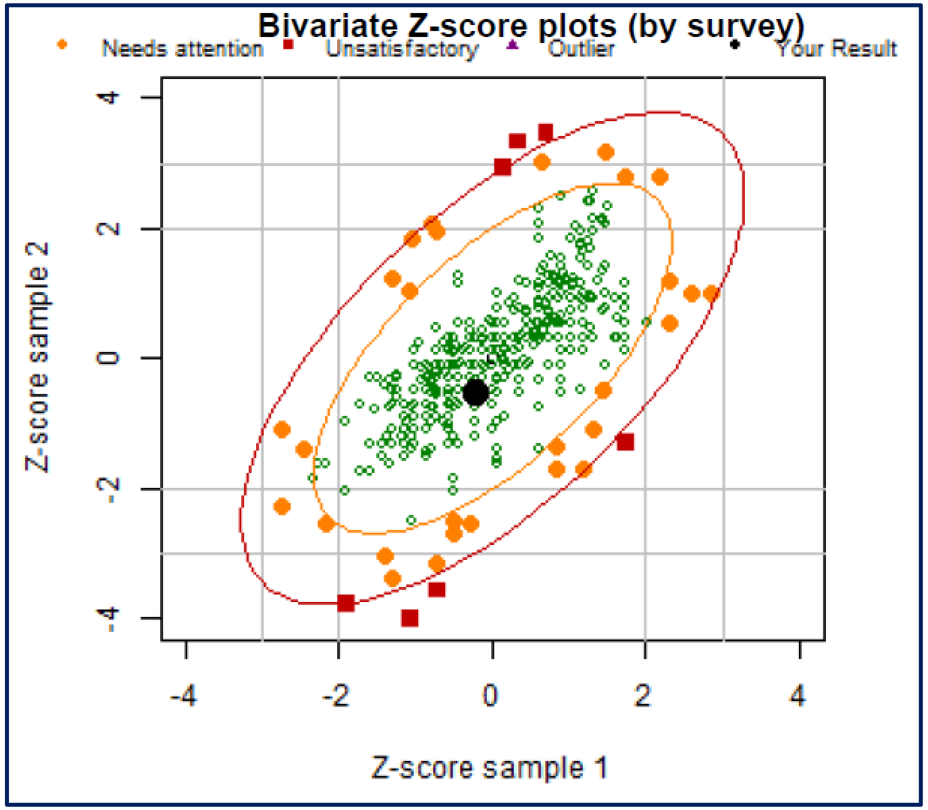
Bivariate Z-score analyse



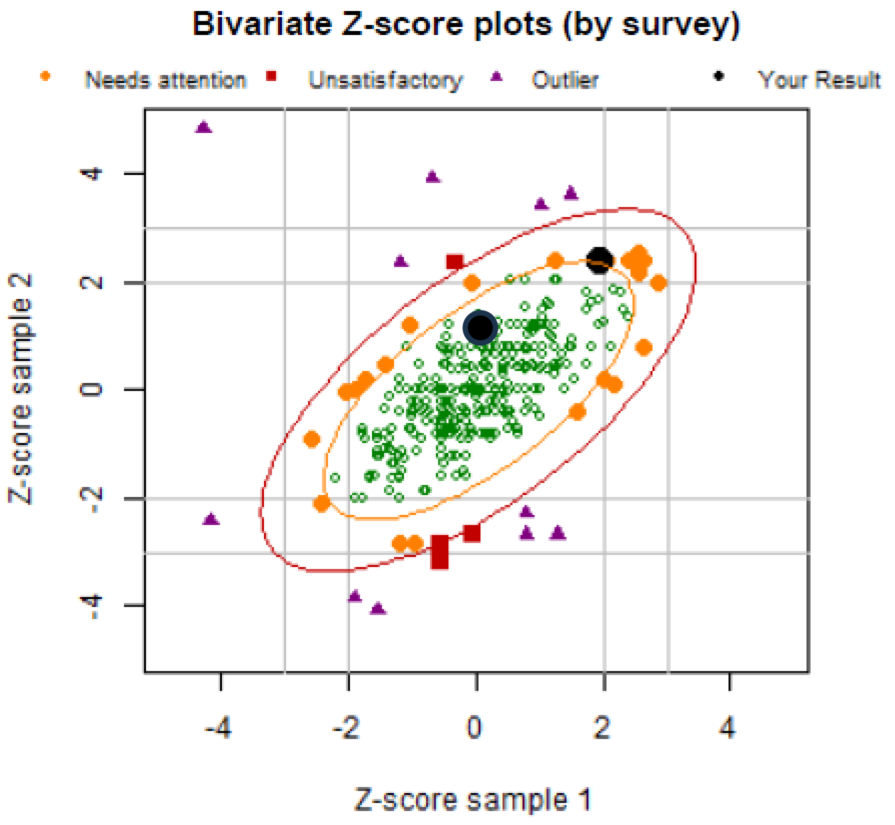
Single Survey

- Bivariate analysis.
- Position of your own Z-score pair in total distribution of Z-score pairs.

The use of the bivariate z-score analysis is of major importance when multiple samples are distributed around in the same survey and dependency of the results is likely. Important lessons can be drawn from the shape of the ellipse with respect to random and systematic deviations, while individual laboratories have been informed about their position in the state-of-the-art distribution and whether they have to deal with systematic and/or random deviations.



Example 1 | Prothrombin Time / INR



Z-score pair in the higher right quadrant corresponding to an increase of systematic error.

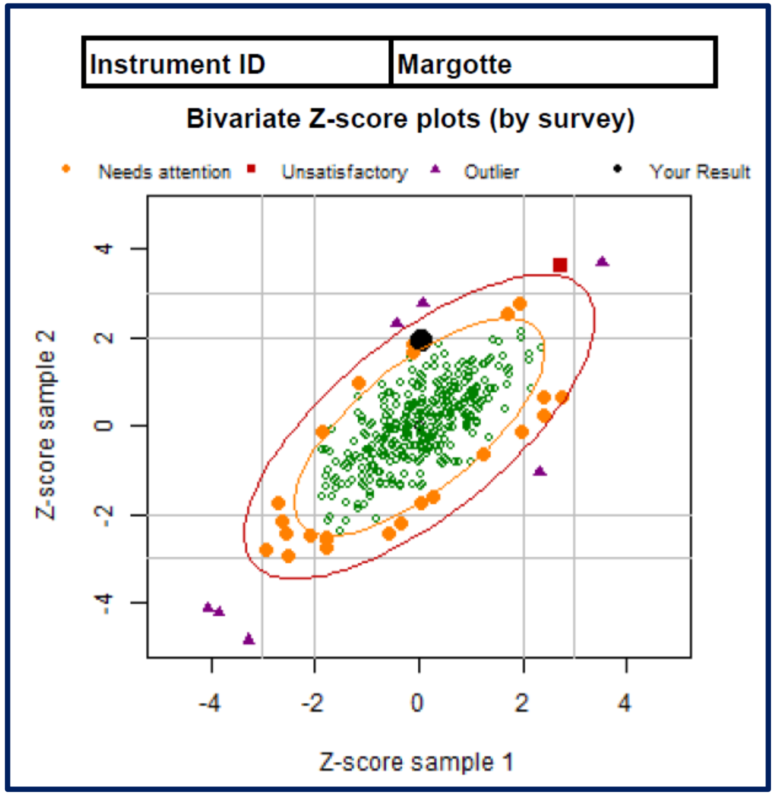
There was a delay in preventive maintenance in combination with the end of the current batch of thromboplastin.

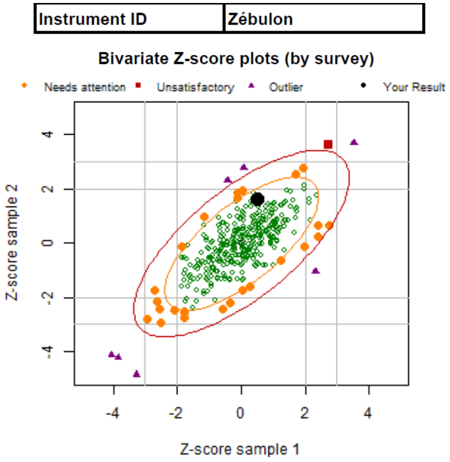
After maintenance and also change of reagent batch the z-scores became 0.22 - 0.81. The instrument went back to the green area by eluding the increase of systematic error thanks to the z-scores bivariate analysis !!

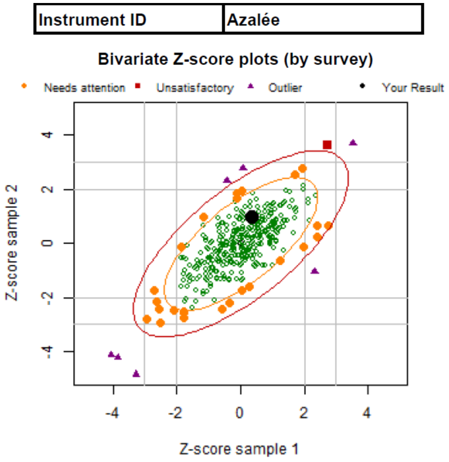
Example 2

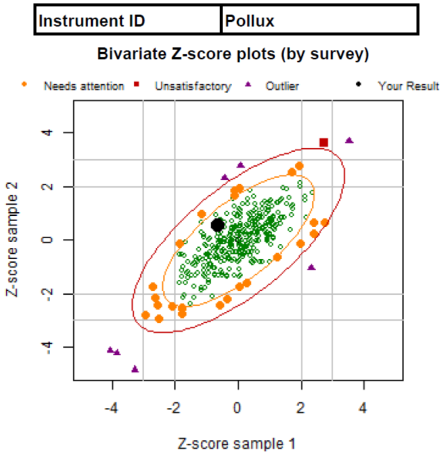
Fibrinogen

				Univarate Analysis		Bivarate Analysis
				Reagent	Reagent/Equipment	
Screen - I	Fibrinogen (Clauss)	24.05	Margotte	0.04	0.04	
			Zébulon	0.49	0.49	
		24.06	Margotte	1.94	1.94	
			Zébulon	1.64	1.64	
Screen - I	Fibrinogen (Clauss)	24.05	Azalée	0.34	0.34	
			Pollux	-0.67	-0.67	
		24.06	Azalée	0.99	0.99	
			Pollux	0.57	0.57	









Instrument	Inter-assay CV
Margotte	**± 6.0%**
Zebulon	± 4.3%
Azalee	± 4.3%
Pollux	± 4.3%

Z-score analyse per survey

Univariate	Bivariate
Individual evaluation of deviation from target value	Evaluation of position of Z-score pair within the full correlation of Z-scores pairs
↓	↓
Within laboratory	Between laboratories

Predictive Control Chart (PCC) on longitudinal Z-scores

Longitudinal Z-score analyse

Survey 1

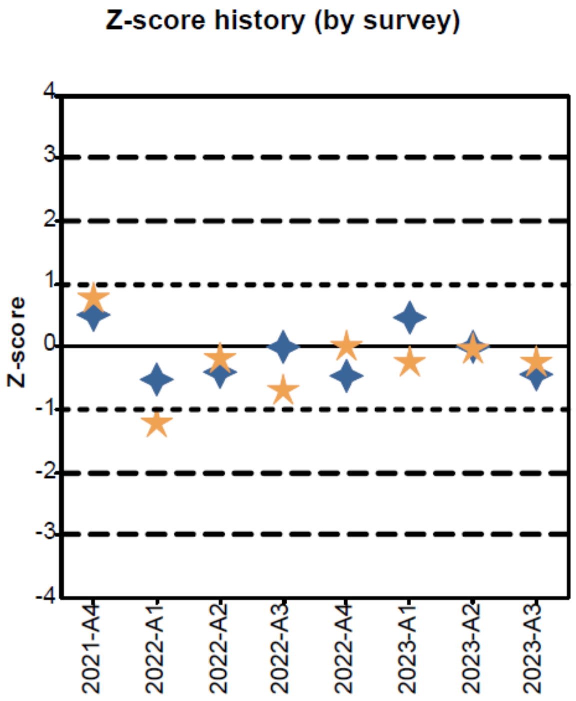
Survey 2

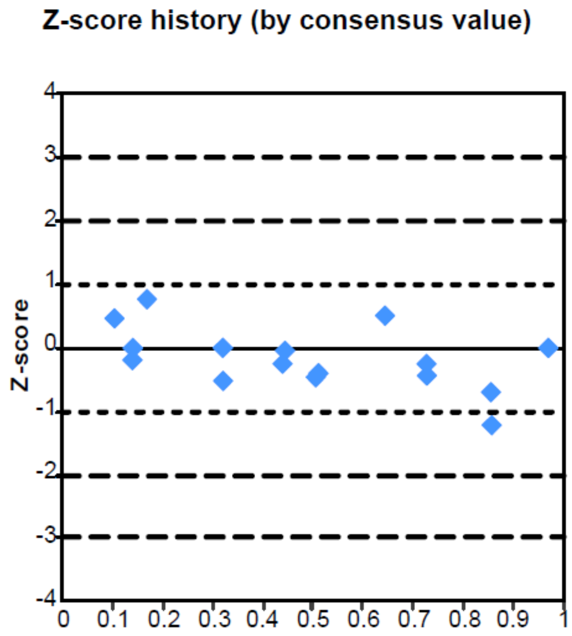
Survey 3

Survey 4

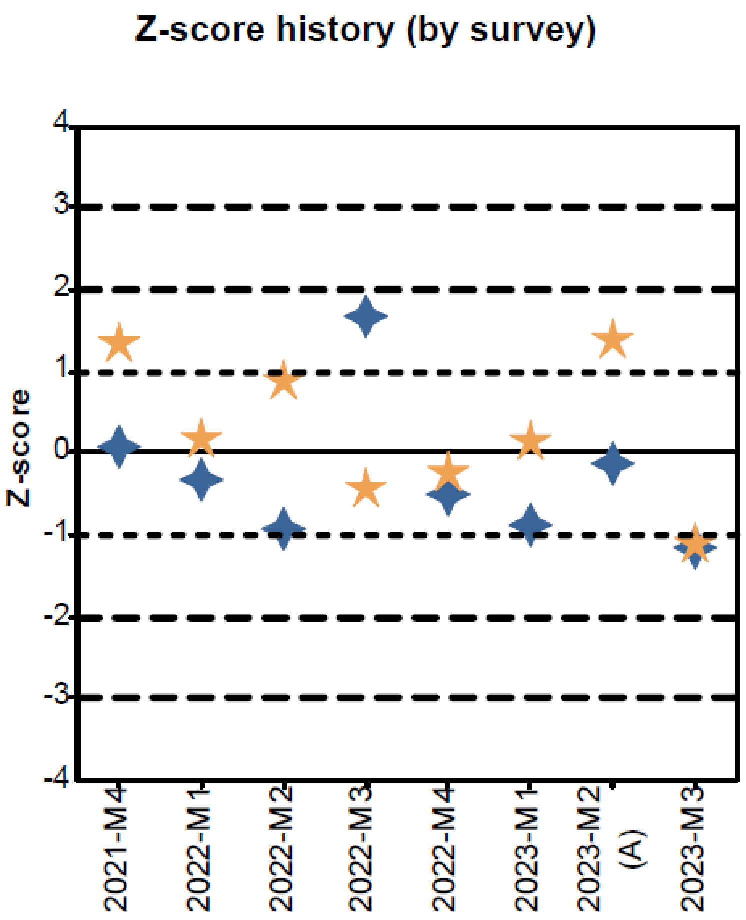
Survey 5

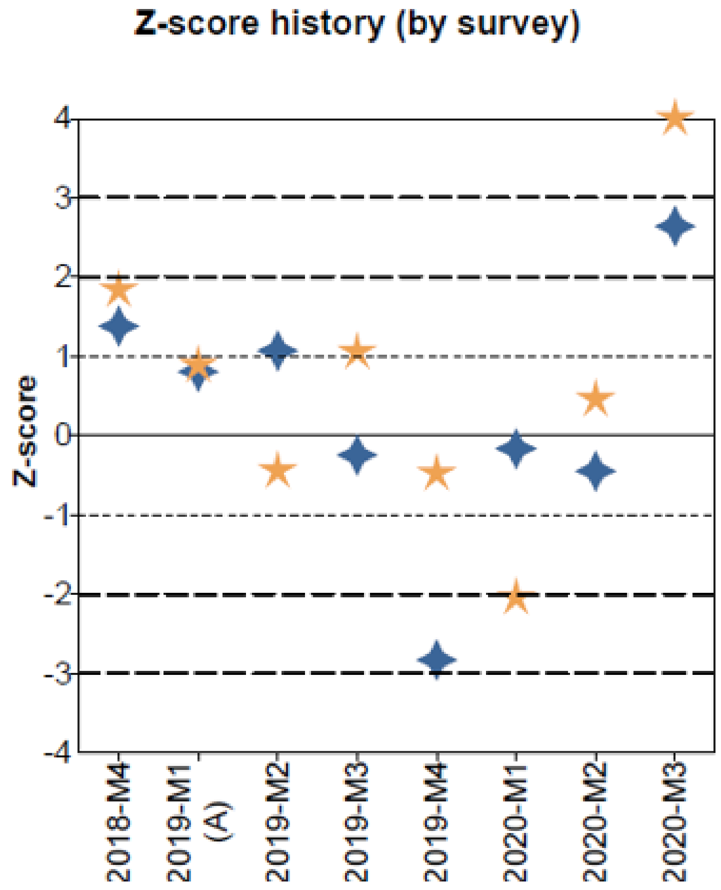
Trend in Z-scores between surveys

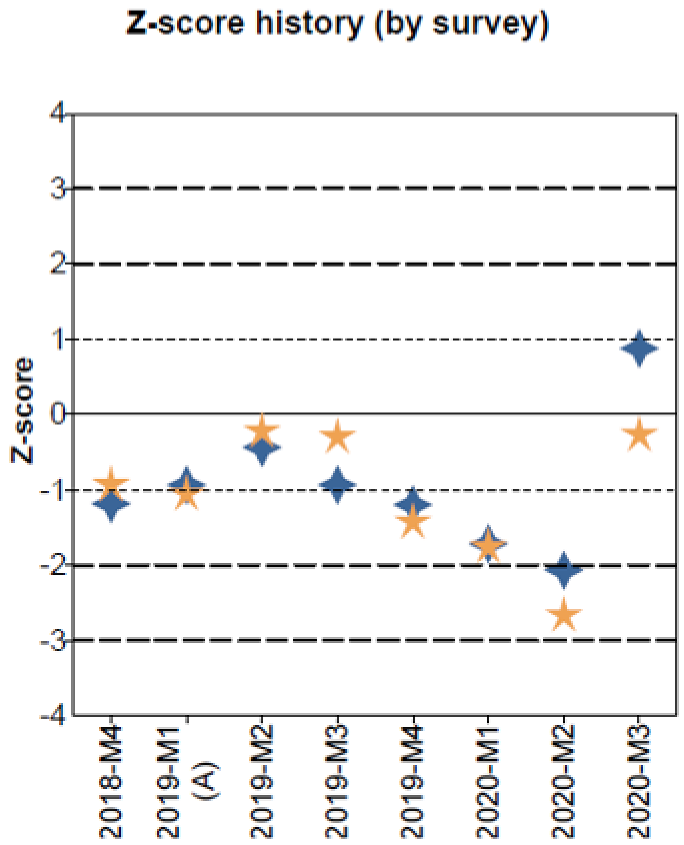




Longitudinal Z-score analyse







Longitudinal Z-score analyse

- Currently only a graphical representation.
- Personal interpretation about trends.
- Valuable for recognising systematic and / or random deviations.

HOWEVER!!!

A sophisticated modern evaluation based on Bayesian Statistical Process Control is lacking!

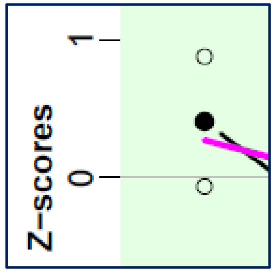
THE KEY OF BAYESIAN STATISTICAL PROCESS CONTROL:

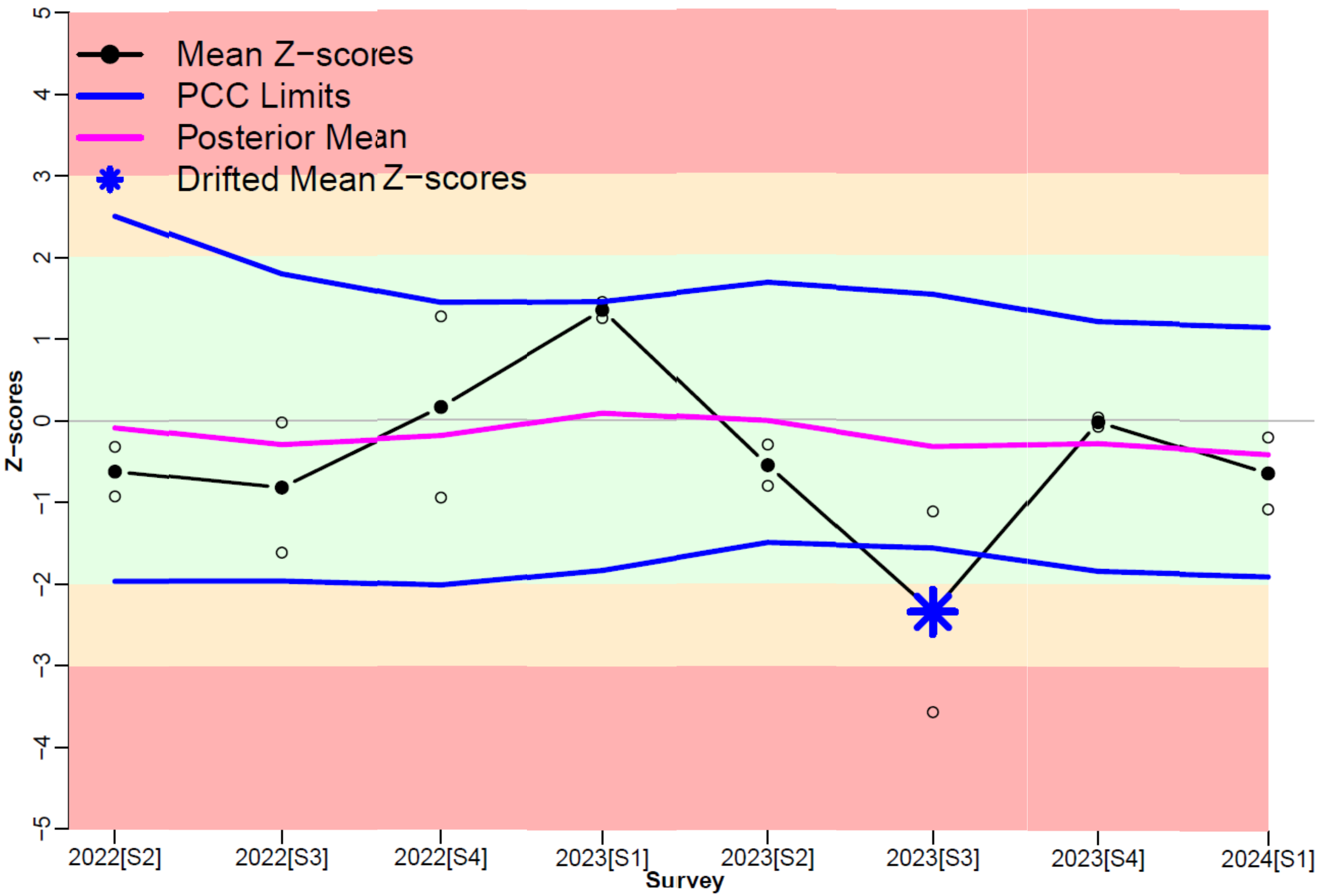
Use of prior information!
In EQA: prior Z-scores

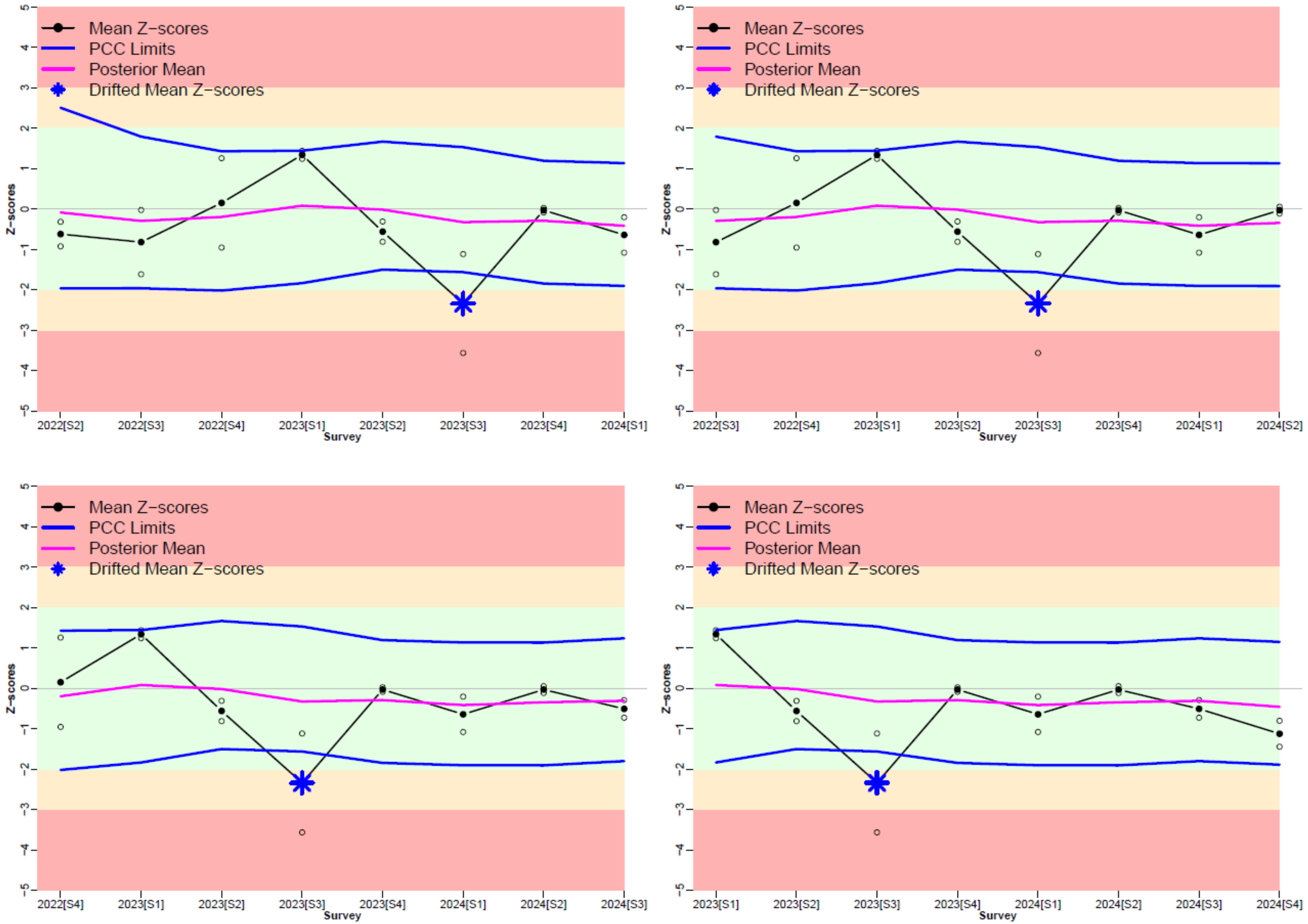
Bayesian-driven Z-score predictive control chart

Prior Information

Z-score distribution







Mean Z−scores
PCC Limits
Posterior Mean
Drifted Mean Z−scores
Z−scores
5
4
3
2
1
0
−1
−2
−3
−4
−5
2022[S2] 2022[S3] 2022[S4] 2023[S1] 2023[S2] 2023[S3] 2023[S4] 2024[S1]
Survey
Mean Z−scores
PCC Limits
Posterior Mean
Drifted Mean Z−scores
Z−scores
2022[S3] 2022[S4] 2023[S1] 2023[S2] 2023[S3] 2023[S4] 2024[S1] 2024[S2]
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Mean Z−scores
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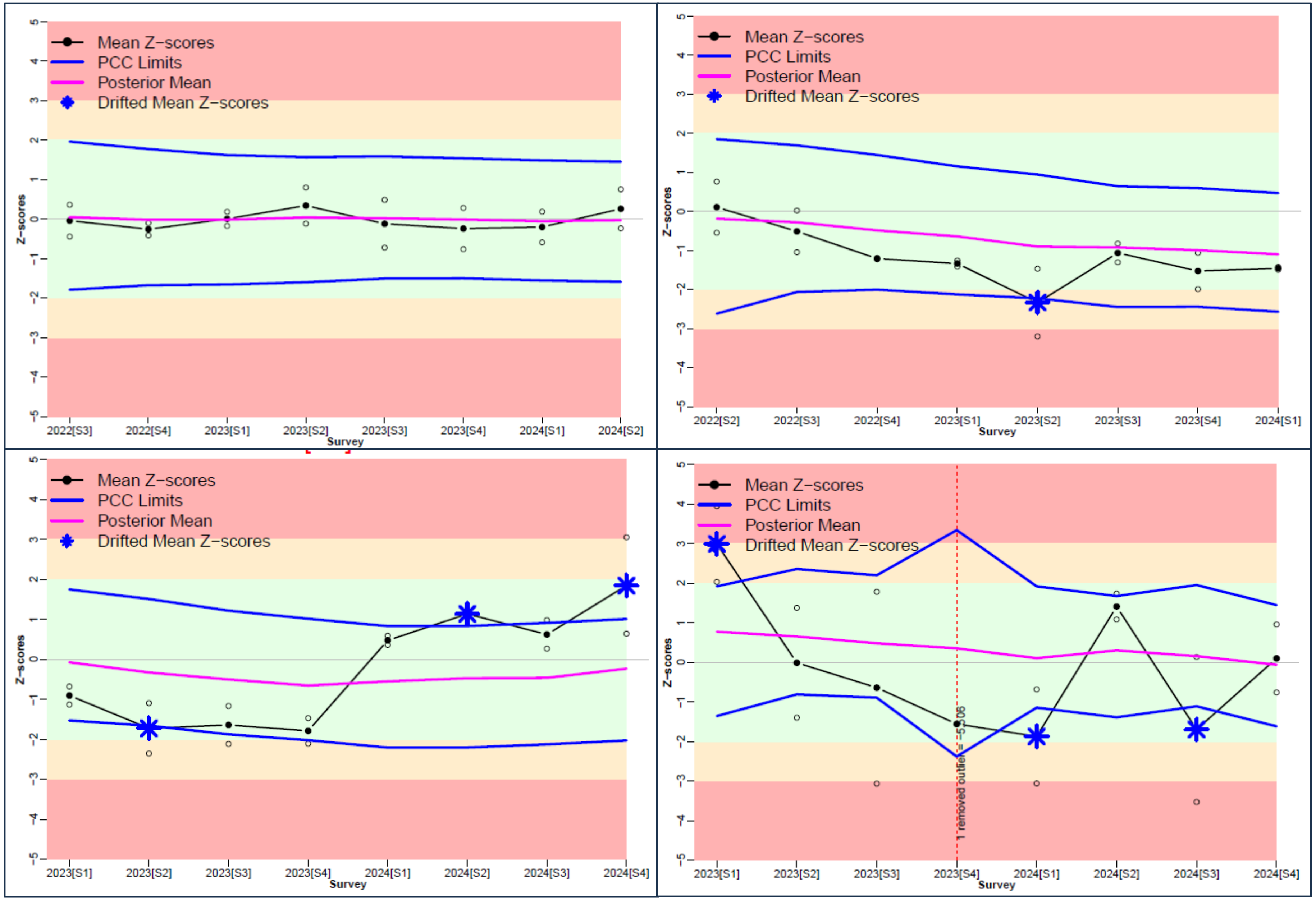
2023[S1] 2023[S2] 2023[S3] 2023[S4] 2024[S1] 2024[S2] 2024[S3] 2024[S4]
Survey



Mean Z−scores
PCC Limits
Posterior Mean
Drifted Mean Z−scores
Z−scores
Survey
1 removed outlier = −5.06

Longitudinal Z-score analyse

Bayesian PCC

- Performance over time
- Trends
- Shifts
- Transient deviations

Within laboratory

Univariate

Individual evaluation of deviation from target value

→ Within laboratory

Bivariate

Evaluation of position of Z-score pair within the full correlation of Z-scores pairs

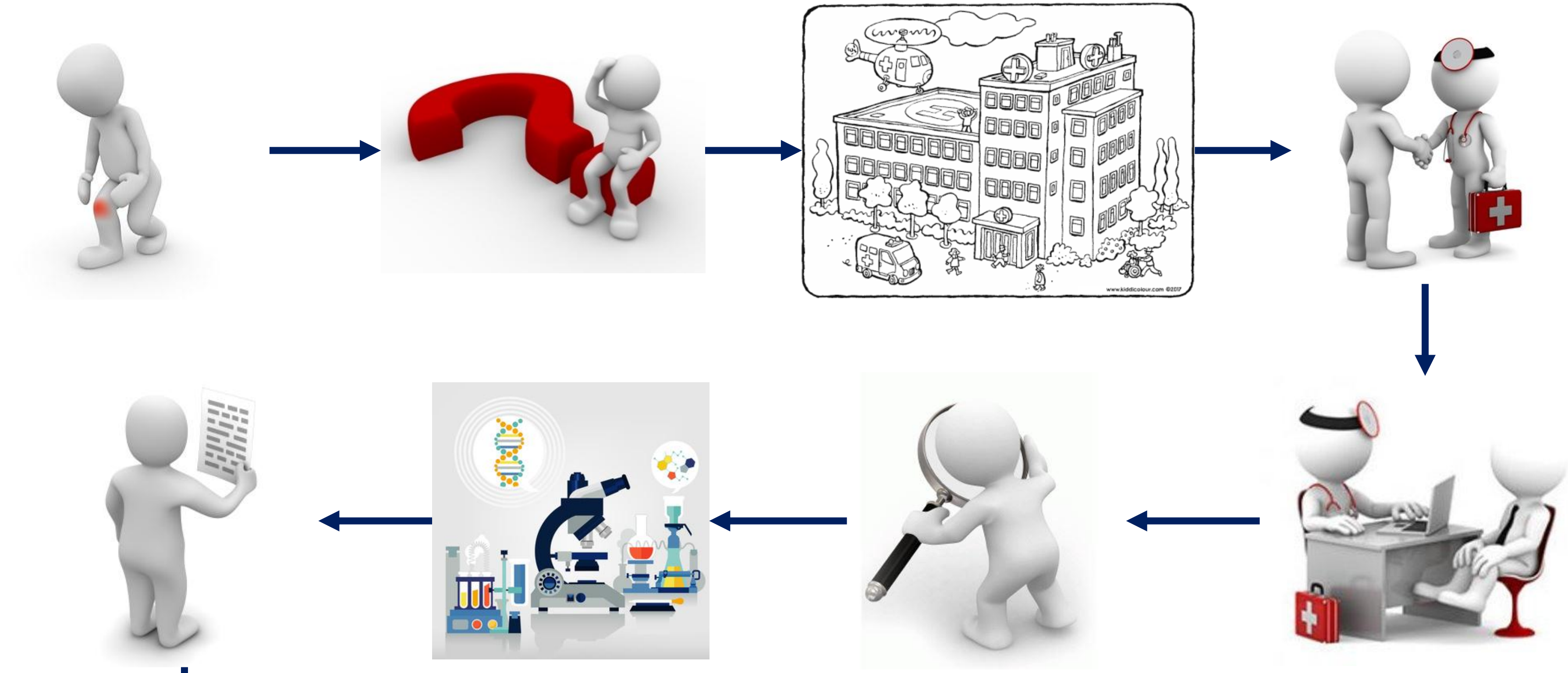
→ Between laboratories

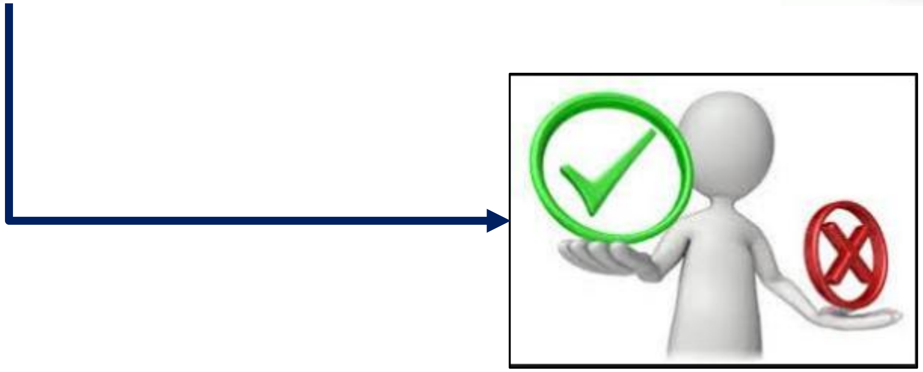
Bayesian PCC

- Performance over time
- Trends
- Shifts
- Transient deviations

→ Within laboratory

The story of the patient





The laboratory should deliver reliable results to the physician to make proper decision-making possible.

Acknowledgement

- Werfen
- Frederic Sobas (Lyon, France)
- Panagiotis Tsiamyrtzis (Athens, Greece)
- Participants in ECAT programme

Quality of coagulation testing for the benefit of the patient

Thank you for your attention

Merci beaucoup pour votre attention