



Laboratory accreditation

the value of quality improvement

Dr. D. van Loon

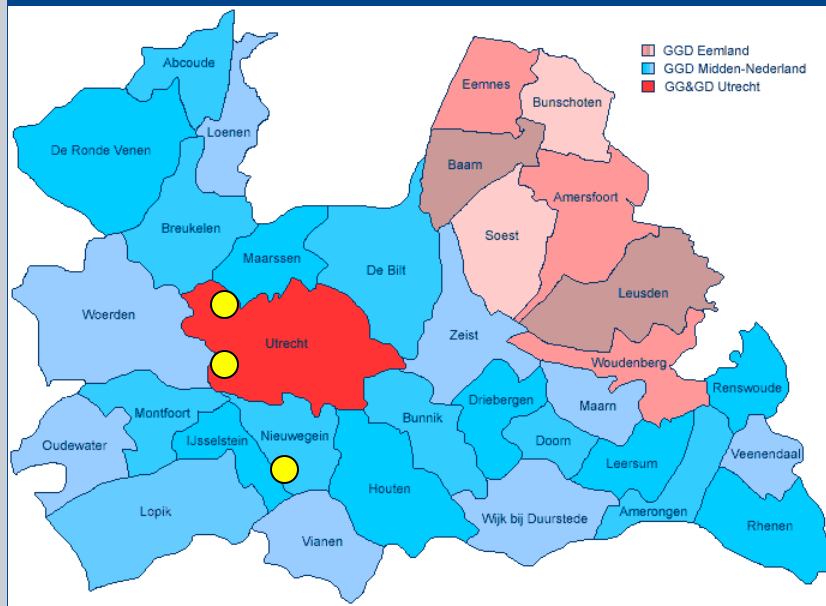
Department of Clinical Chemistry
AntoniusMesosGroep
The Netherlands



AntoniusMesosGroep

St. Antonius Ziekenhuis
Teaching hospital – Supra-regional centre specialised in cardiac surgery
1900 bypass graft and valve replacement procedures p.a.
600 bed acute / high care hospital

Mesos Medisch Centrum
General hospital
300 bed medium / low care hospital





AntoniusMesosGroep

The AntoniusMesosGroep is a combination of St. Antonius Ziekenhuis and Mesos Medisch Centrum

3 locations (Nieuwegein [CCKL R007] and two in Utrecht [CCKL R174])

Identical systems since 1997 (chemistry, immunochemistry, hematology hemostasis and blood gas analysis)

1 location only POCT two locations Rapid Response Laboratory



What is Accreditation?

- Accreditation is the procedure by which an authoritative body gives formal recognition that a body or a person is competent to carry out tasks.
- As a status, accreditation provides public notification that an organization meets standards of quality, set forth by an International Organization



Where are we now?

400 medical laboratories in The Netherlands

299 medical laboratories are registered by the CCKL

220 medical laboratories are accredited bij the RvA/CCKL

Update 8 october 2008



Improvements, consequences of several years of accreditation for the lab

- Use of appropriate methods
- Better service from the instrument and kit suppliers
- Improvement of the service/maintenance contracts
- Better control of traceable elements (temperature, volume, weight)
- More adequate process control on first, second and/or third quality control
Technical and plausibility checks / medical correct results
- General acceptance of an accreditation standard (ISO 15189)



Contineous quality improvement

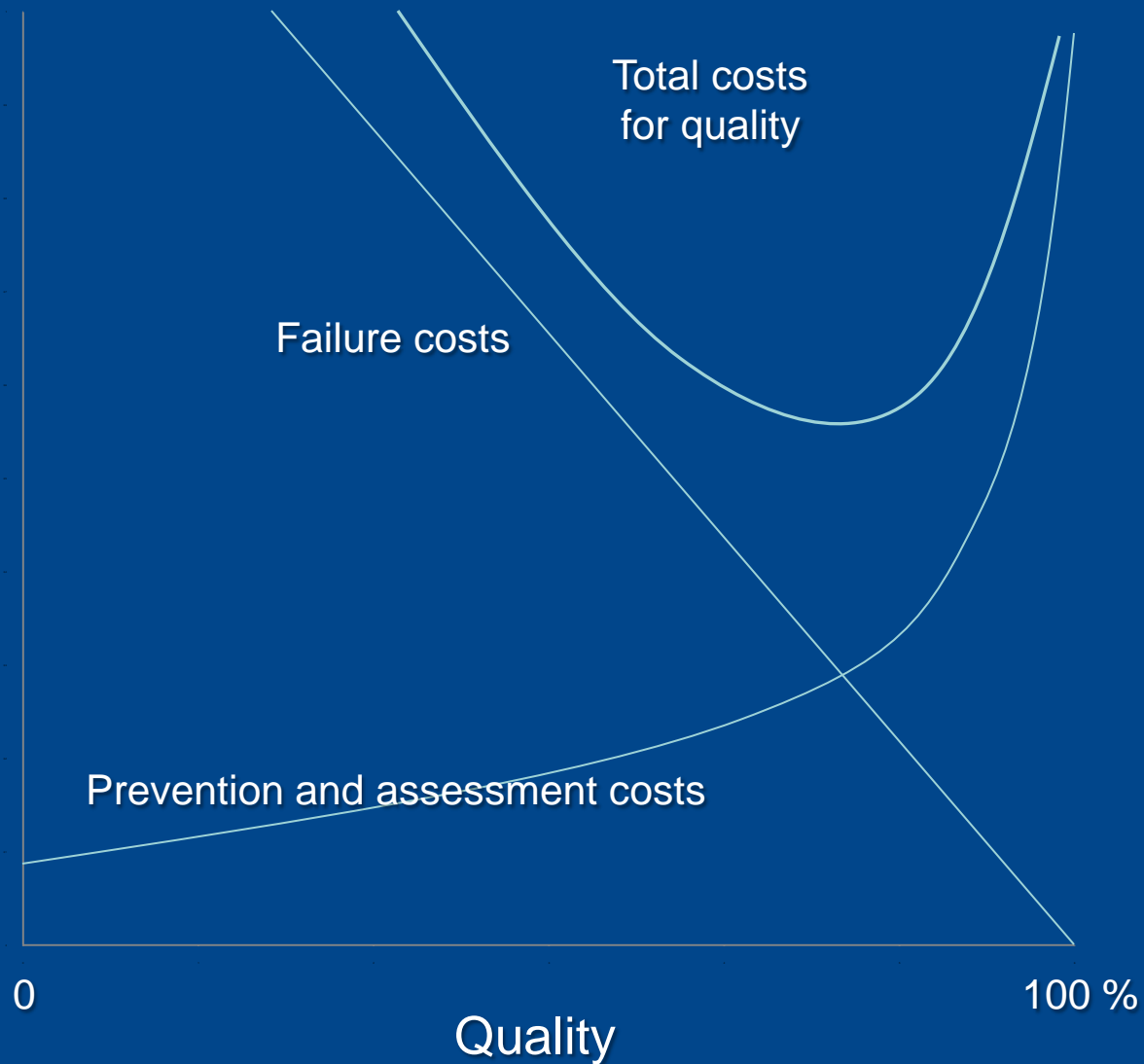
- Improved quality combined with increased productivity and reduced costs
- Application of models from industry

Bell	:	Juran, Shewart
Ford	:	Deming
Toyota	:	Lean
Motorola	:	Six Sigma
Johnson & Johnson	:	DMAI ² C





The Juran quality model





Type of error

Westgard rules

Warning

1_{2s}

Random

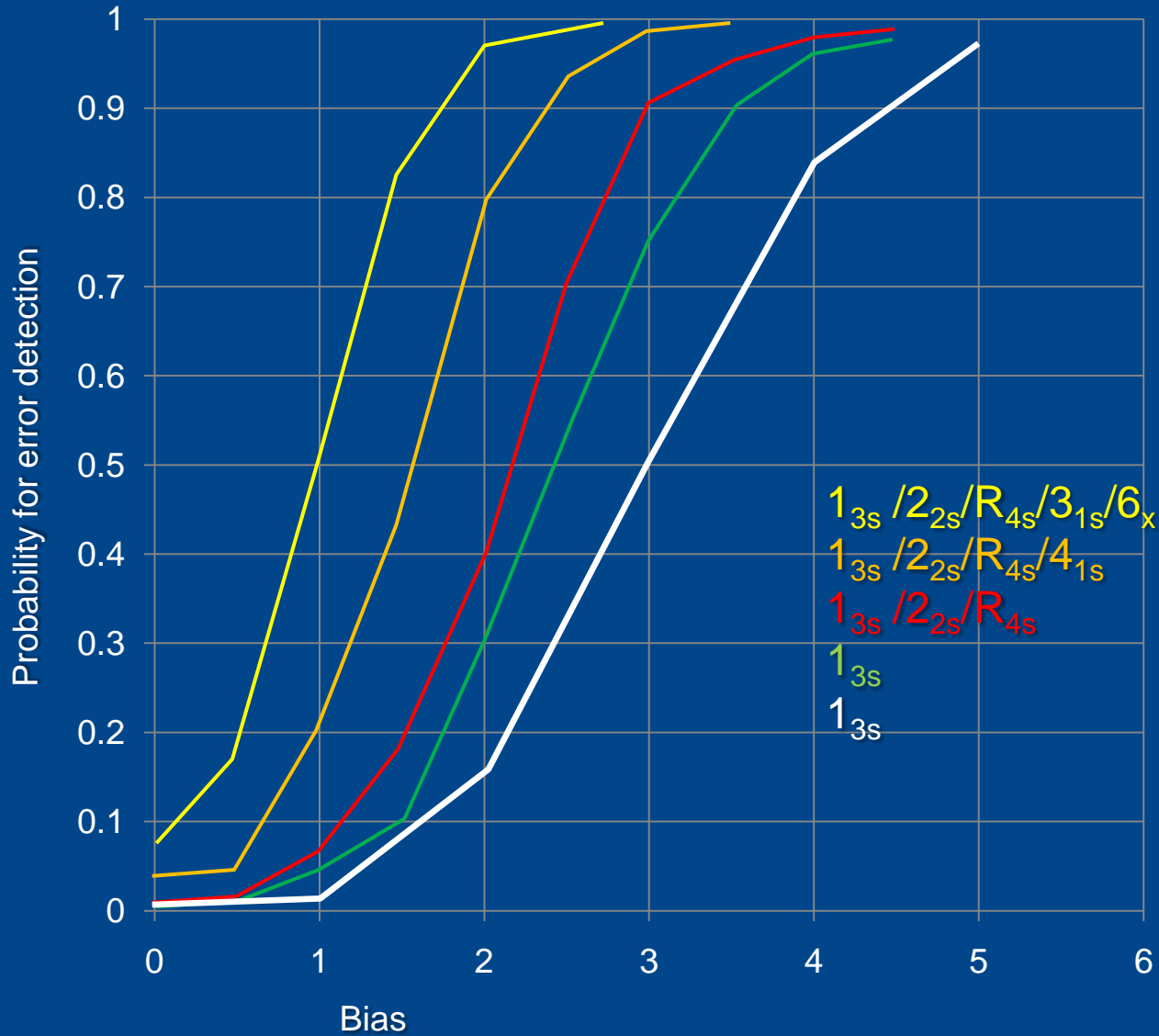
$1_{2.5s}, 1_{3s}, 1_{3.5s}$
 R_{4s}

Systematic

$2_{2s}, 4_{1s}, 2 \text{ of } 3_{2s}, 3_{1s}$
 $6_x, 8_x, 9_x, 10_x, 12_x$
 $\bar{X}_{0.05}, \bar{X}_{0.01}$
cusum



Power curves



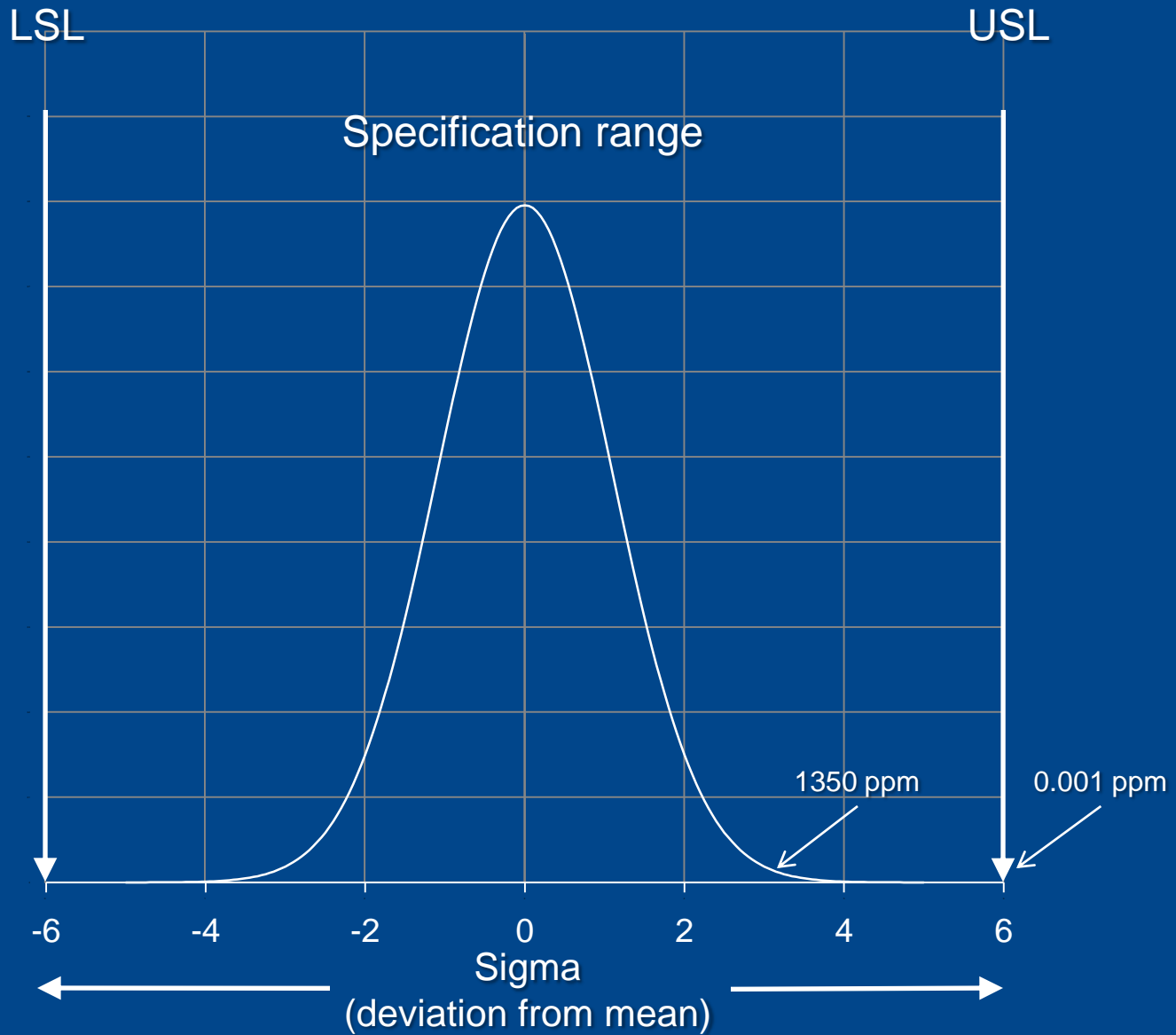
$1_{3s} / 2_{2s} / R_{4s} / 3_{1s} / 6_x$
 $1_{3s} / 2_{2s} / R_{4s} / 4_{1s}$
 $1_{3s} / 2_{2s} / R_{4s}$
 1_{3s}
 1_{3s}

N	R
6	1
4	1
2	1
2	1
1	1



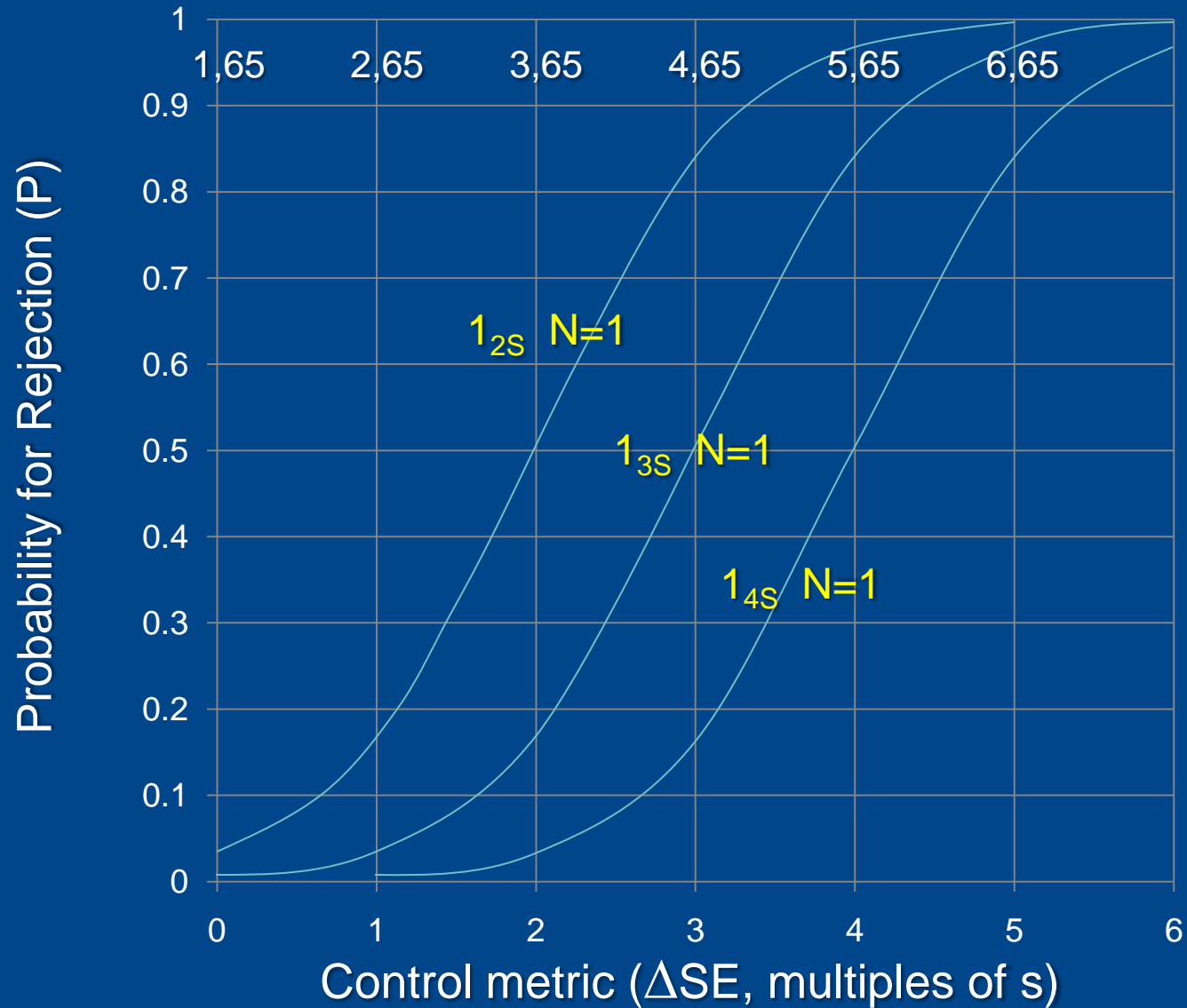
Sigma	Number of defects	
	abs	percentage
1,0	317400	31,7
2,0	45400	4,5
2,5	12419	1,2
3,0	2700	0,3
3,5	465	0,0465
4,0	63	0,0063
4,5	6,8	0,00068
5,0	0,57	0,000057
5,5	0,038	0,0000038
6,0	0,002	0,0000002

$$\text{Sigma score} = (\text{tolerance} - \text{bias}) / \text{CV}$$





Proces metric (Sigma-scale)





Biological variation

$$\text{Sigma score} = [TE_a - \text{bias}] / VC$$

$$CV_a < 0.5 * CV_w$$

$$B(\%) < 0.25 * (CV_w^2 + CV_g^2)^{0.5}$$

enzym	CVw	CVg	I(%)	B(%)	TE(%)
ALAT	24,3	41,6	12,2	12,0	32,1



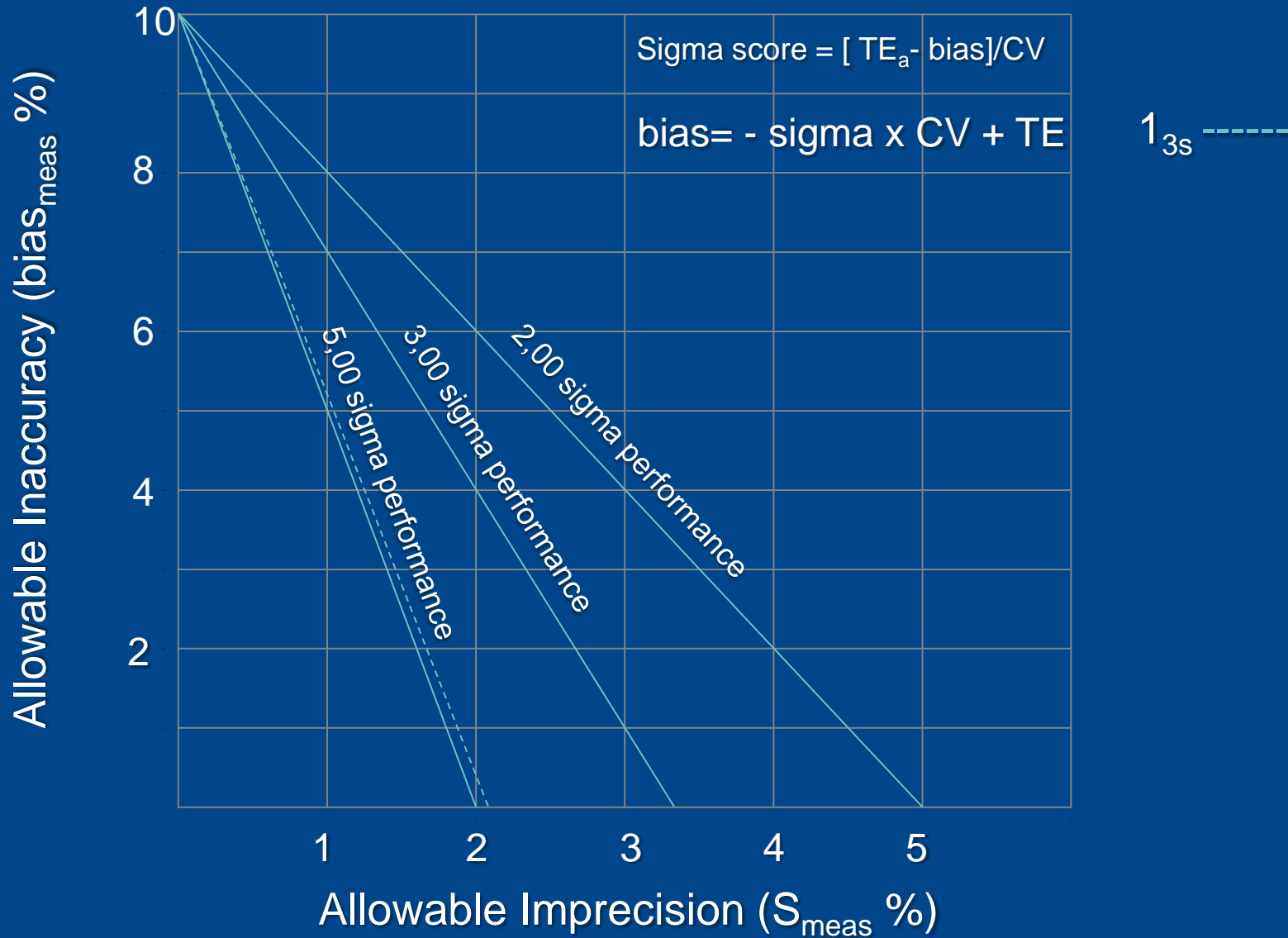
$$TE_a = 1.65 CV_a + B$$

PT	4,0	6,8	2,0	2,0	5,3
aPTT	2,7	8,6	1,4	2,3	4,5
Fibrinogen	10,7	15,8	5,4	4,8	13,6

Lipase	23,1	33,1	11,6	10,1	29,1
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OPSpec Chart TE_a 10% with 90% AQA(SE)





Procedure to design the IQC

- Analytical performance of the test procedure [manufacturer]

Estimate the sigma from TE_a [Ricos Database] based on biological variation (bias = 0)

Sigma < 3 ; EP5a to determine the $CV_{analytical}$

Calculate sigma of the proces (bias = 0)

Method comparison ; EP9

Calculate the control rules for the proces

Set the quality targets for the proces



State of the art?





Prothrombin time : results of EP 5a

	Mean (sec)	Std.dev (sec)	CV (%)
System 1			
level 1	28,9	0,36	1,24 (1,7)
level 2	118,2	2,73	2,31 (2,3)
System 2			
level 1	28,3	0,41	1,45 (1,7)
level 2	118,0	1,91	1,62 (2,3)



Prothrombin time : $TE_a = 5,3\%$

	CV (%)	Sigma	Control rules	P_{fr}	P_{ed}	N
System 1						
level 1	1,24	4,28	$1_{3s}/2$ of $3_{2s}/R_{4s}/3_{1s}$	0,02	0,91	3
level 2	2,31	2,30	max	0,01	0,03	3
System 2						
level 1	1,45	3,67	$1_{3s}/2$ of $3_{2s}/R_{4s}/3_{1s}$	0,02	0,91	3
level 2	1,62	3,28	max	0,01	0,19	3



Activated partial thromboplastine time:results of EP 5a

	Mean (sec)	Std.dev (sec)	CV (%)
System 1			
level 1	34,1	0,74	2,16 (1,6)
level 2	61,3	0,72	1,18 (2,9)
System 2			
level 1	34,7	0,66	1,89 (1,6)
level 2	60,5	0,71	1,17 (2,9)



Activated partial thromboplastine time : $TE_a = 4,5\%$

	CV (%)	Sigma	Control rules	P_{fr}	P_{ed}	N
System 1						
level 1	2,16	2,08	[max QC]	0,01	<0,2	3
level 2	1,18	3,82	$1_{3s}/2$ of $3_{2s}/R_{4s}/3_{1s}$	0,02	0,78	3
System 2						
level 1	1,89	2,38	[max QC]	0,01	<0,2	3
level 2	1,17	3,83	$1_{3s}/2$ of $3_{2s}/R_{4s}/3_{1s}$	0,02	0,79	3



Fibrinogen : results of EP 5a

	Mean (g/L)	Std.dev (g/L)	CV (%)
System 1			
level 1	2,74	0,07	2,39 (3,0)
level 2	1,58	0,04	2,42 (5,0)
System 2			
level 1	2,64	0,06	2,34 (3,0)
level 2	1,54	0,05	3,36 (5,0)



Fibrinogen : TE_a = 13,6%

	CV (%)	Sigma	Control rules	P _{fr}	P _{ed}	N
System 1						
level 1	2,39	5,69	1 _{2,5s}	0,01	>0,94	1
level 2	2,42	5,62	1 _{3s} /2 of 3 _{2s} /R _{4s} /3 _{1s}	0,01	0,94	1
System 2						
level 1	2,34	5,80	1 _{2,5s}	0,01	0,94	1
level 2	3,36	4,05	1 _{3s} /2 of 3 _{2s} /R _{4s} /3 _{1s}	0,02	0,85	3



Activities during the evaluation of a chemistry system

EP5 ; 100 test measurements (2 levels)

EP9 ; 100 test measurements

40 different test procedures

Total of 14.400 tests during 5 to 6 months (at least)

6 months expenses for 2 technical assistants

Depreciation (6 months ~ 7 % of the investment)

Total 65.000 Euro



Desirable Specifications for Total Error, Imprecision, and bias, Derived from Biological Variation

mat	Analyte	CVw	CVg	I(%)	B(%)	TE(%)
S	C-Reactive protein	42.2	76.3	21.1	21.8	56.6
S	Bilirubin conjugated	36.8	43.2	18.4	14.2	44.5
S	ALAT	24.3	41.6	12.2	12	32.1
S	Bilirubin total	25.6	30.5	12.8	10	31.1
S	Iron	26.5	23.2	13.3	8.8	30.7
S	Creatine kinase	22.8	40	11.4	11.5	30.3
S	Lipase	23.1	33.1	11.6	10.1	29.1
S	Triglycerides	20.9	37.2	10.5	10.7	27.9
S	Creatine kinase MB, activity	19.7	24.3	9.9	7.8	24.1
S	Urea	12.3	18.3	6.2	5.5	15.7
S	ASAT	11.9	17.9	6	5.4	15.2
S	a-Amylase	8.7	28.3	4.4	7.4	14.6
S	Urate	8.6	17.2	4.3	4.8	11.9
S	Alkaline phosphatase	6.4	24.8	3.2	6.4	11.7



mat	Analyte	CVw	CVg	I(%)	B(%)	TE(%)
S	LDH	8.6	14.7	4.3	4.3	11.4
S	HDL cholesterol	7.1	19.7	3.6	5.2	11.1
S	Phosphate	8.5	9.4	4.3	3.2	10.2
S	Cholesterol	6	14.9	3	4	9.0
S	Creatinine	4.3	12.9	2.2	3.4	6.9
S	Glucose	5.7	6.9	2.9	2.2	6.9
S	Potassium	4.8	5.6	2.4	1.8	5.8
S	Magnesium	3.6	6.4	1.8	1.8	4.8
S	Albumin	3.1	4.2	1.6	1.3	3.9
S	Transferrin	3	4.3	1.5	1.3	3.8
S	Total Protein	2.7	4	1.4	1.2	3.4
S	Calcium	1.9	2.8	1	0.8	2.4
S	Chloride	1.2	1.5	0.6	0.5	1.5
S	Sodium	0.7	1	0.4	0.3	0.9
B	HbA1c	5.6		2.8		



mat	analyt	unit	level ₁	CV _{L1}	sigma _{L1}	level ₂	CV _{L2}	sigma _{L2}
S	C-Reactive protein	mg/L	10.2	2.9	19.6	44.3	1.6	36.1
S	Lipase	IU/L	32	1.6	18.6	65	0.9	31.5
S	Triglyceride	mMol/L	1.13	2.3	12.1	2.04	1.3	21.1
S	ALAT	IU/L	55	1.5	22.1	168	1.5	20.7
S	ASAT	IU/L	81	2.5	6.2	293	0.8	19.4
S	Bilirubin conj.	μMol/L	19.1	4.5	9.9	63.1	2.5	17.7
S	CK	IU/L	176	1.8	17.2	483	1.7	17.6
S	Iron	μMol/L	14.6	2.1	14.5	35.3	1.9	16.2
S	Amylase	IU/L	98	0.7	20.4	499	1.0	14.9
S	Bilirubin total	μMol/L	30.2	4.6	6.7	94.5	2.9	10.6
S	Urate	mMol/L	0.25	0.8	14.9	0.52	1.2	10.3
S	Urea	mMol/L	5.72	1.6	9.6	18.00	1.6	9.7
S	LDH	mMol/L	168	1.1	10.1	398	1.2	9.5
S	Cholesterol	mMol/L	3.6	0.8	10.8	6.9	1.0	8.9



Mat	Analyt	Unit	Level ₁	CV _{L1}	sigma _{L1}	level ₂	CV _{L2}	sigma _{L2}
S	AF	IU/L	112	2.9	4.0	382	1.4	8.1
S	Phosphate	mMol/L	0.89	2.5	4.1	1.83	1.3	8.1
S	Glucose	mMol/L	4.7	1.5	4.6	18.3	1.0	7.0
S	Potassium	mMol/l	3.63	1.4	4.2	5.75	1.0	5.6
S	Magnesium	mMol/L	0.76	2.0	2.4	1.56	0.9	5.3
S	Albumin	g/L	35.4	2.2	1.8	52.8	1.0	3.8
S	Protein total	g/L	56.6	1.2	2.9	84.5	1.0	3.4
S	HDL cholesterol	mMol/L	0.94	3.8	2.9	1.94	3.9	2.8
S	Creatinine	μMol/L	82.7	3.6	1.9	361.3	2.6	2.7
S	Calcium	mMol/L	1.92	1.5	1.6	2.88	1.3	1.9
S	Transferrin	mg/L	2.21	1.8	2.1	3.38	2.7	1.4
S	Chloride	mMol/L	78.0	1.7	0.9	108.7	1.2	1.3
S	Sodium	mMol/L	125.3	1.1	0.8	157.0	1.2	0.7



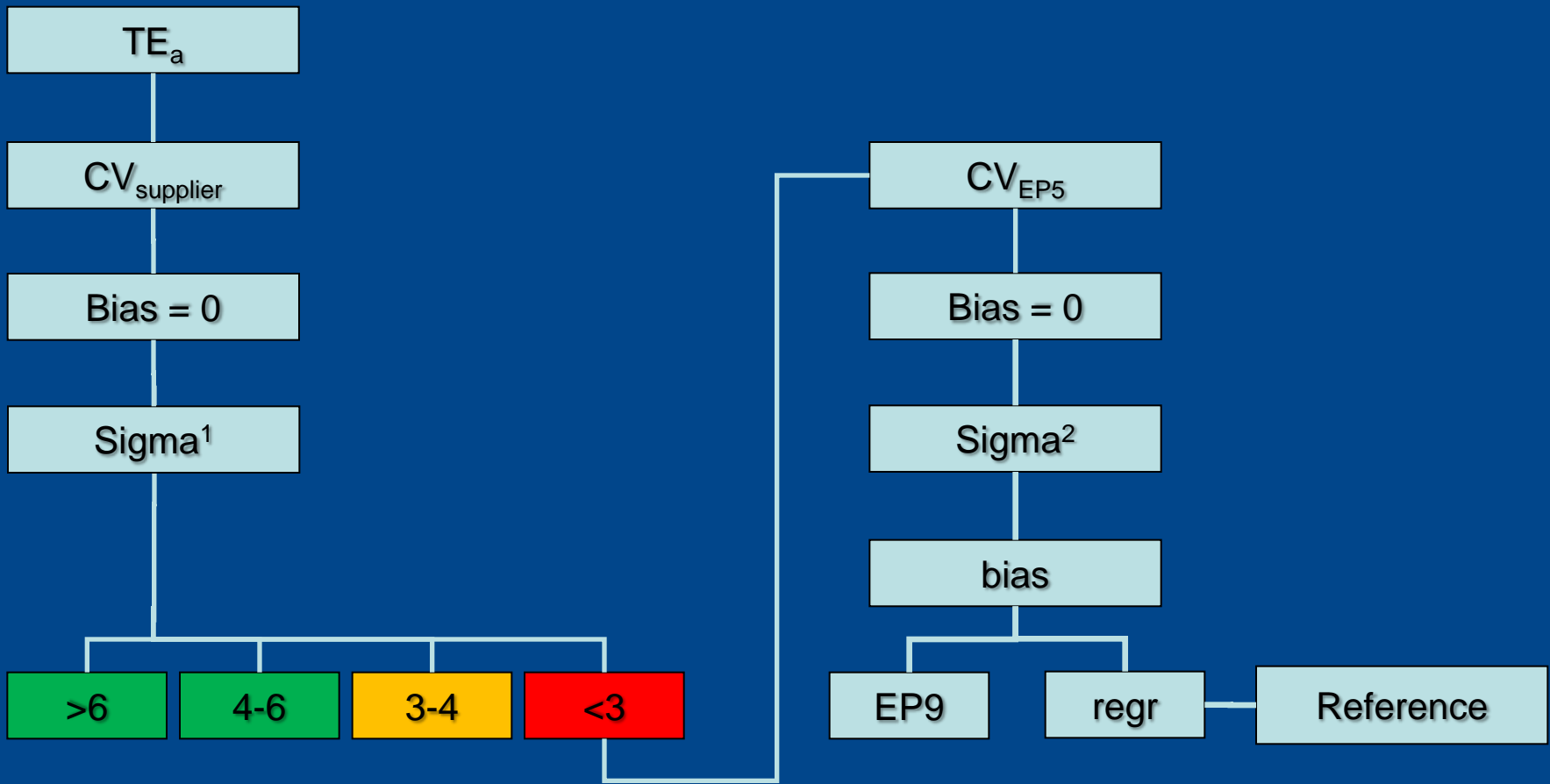
Quality Targets for the Measuring Process

Sigma score	Interpretation
>6	“worldclass” ; 1 controle rule
4 – 6	Fit for intended use
<4 en >3	Fit for intended use, more control rules/ higher frequency
<3	Poor performance, maximal QC



Results of EP5a for poorly performing tests

		level	CV%	target	level	CV%	target	EP5a
Glucose	mmol/l	4,9	1,0	1,4	18,9	0,9	1,4	OK
Protein total	g/l	57,6	1,2	2,1	85,8	1,0	1,8	OK
Creatinine	μmol/l	84,3	2,4	3,3	350	2,1	2,3	OK
ASAT	IU/l	76	1,0	2,0	265	0,5	0,8	OK
Calcium	mmol/l	1,84	1,4	1,4	2,80	1,5	1,3	OK
Potassium	mmol/l	3,5	1,1	1,0	5,7	0,6	0,7	OK
Sodium	mmol/l	122,7	0,9	0,9	150,6	0,8	0,9	OK





TE_a

$Impr_{supplier}$

Bias = 0

Sigma¹

Design of QC / Westgard rules



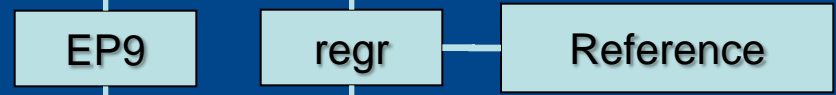
Quality Targets

reference interval

CV_{EP5}

Bias = 0

Sigma²



Calculate Sigma



Activities during the lean evaluation of a chemistry system

EP5 ; 100 test measurements (2 levels)

EP9 ; 100 test measurements

40 different test procedures

8 test procedures EP5

Total of 3000 tests during 2,5 months

2,5 months expenses for 2 technical assistants

Depreciation (2,5 months ~ 3 % of the investment)

Total 22.000 Euro



The value of quality improvement

=

Faster, Lower costs and Better

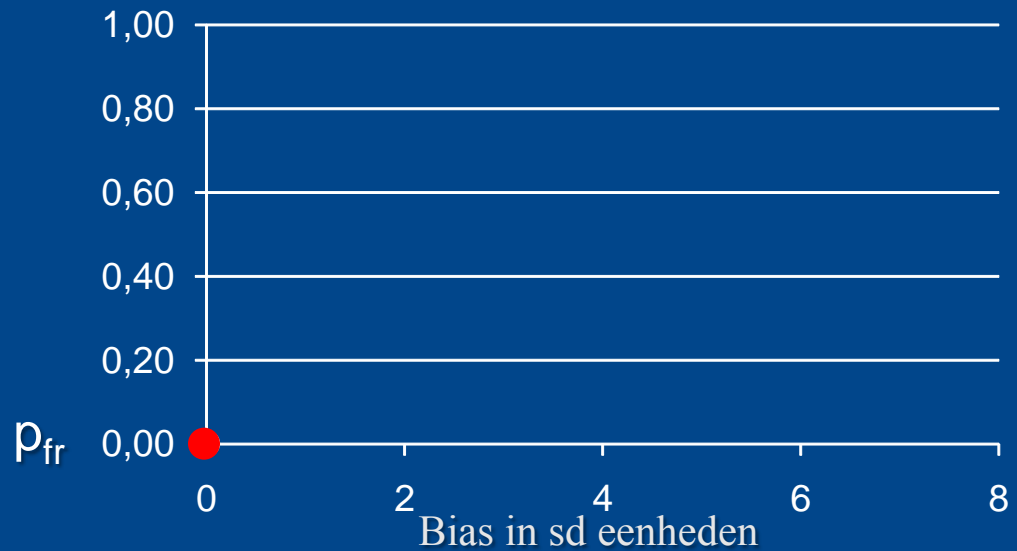
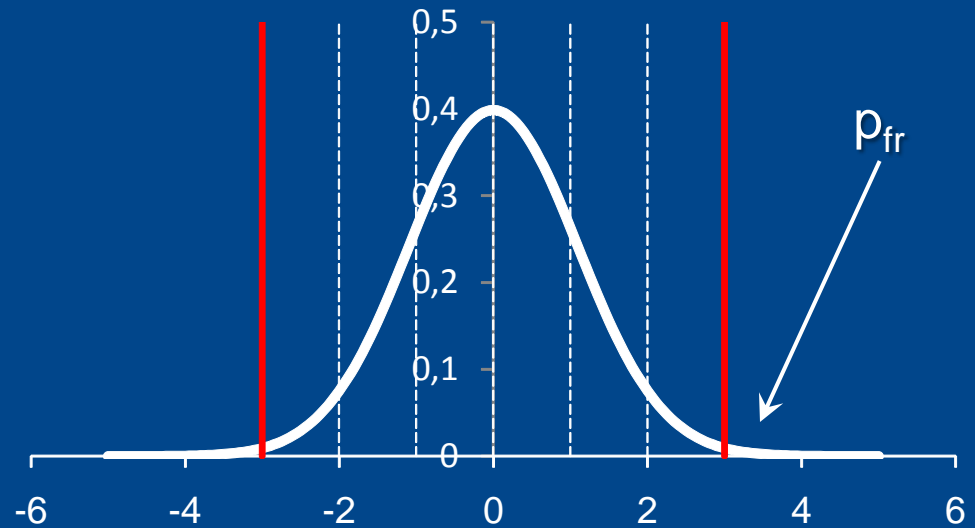
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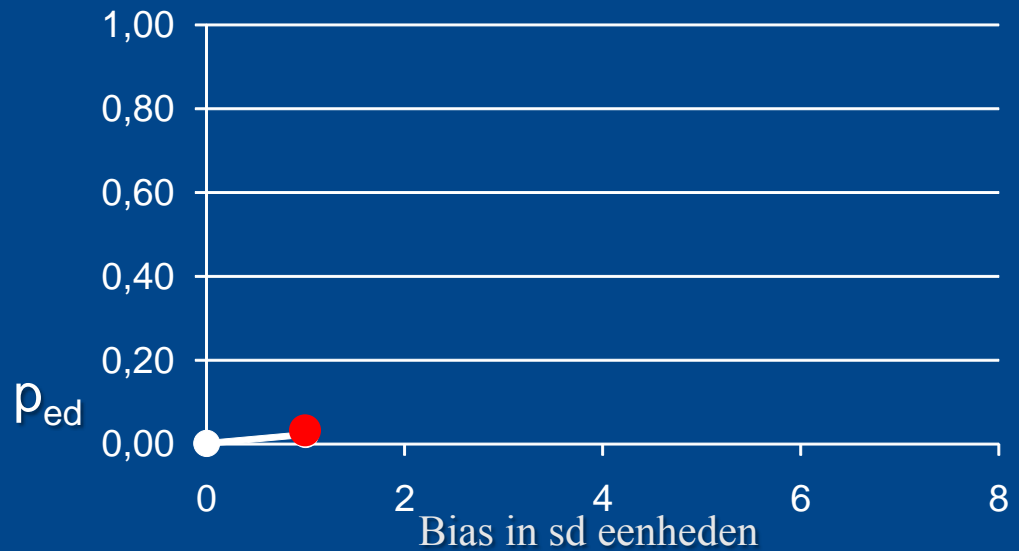
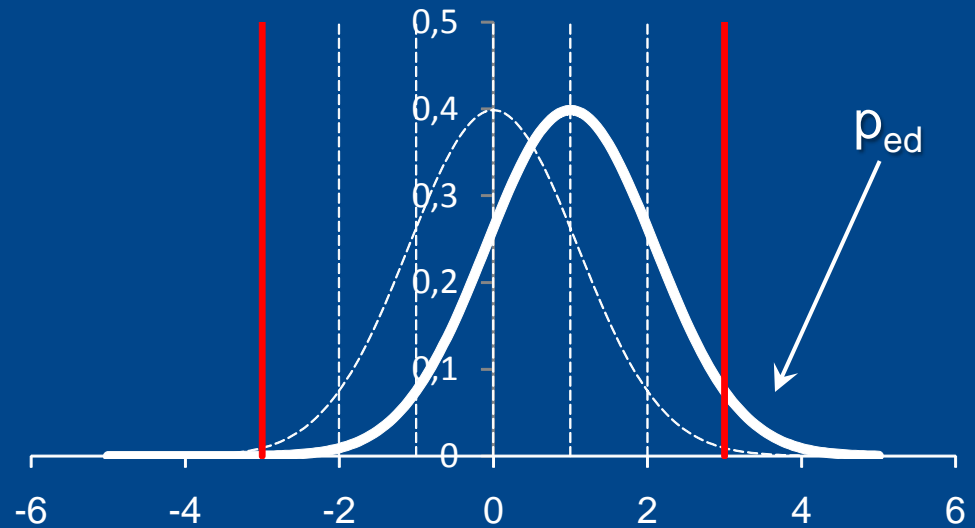


Number of SDs from mean	Area of upper tail	Area below upper tail
0.00	0.5000	0.5000
0.50	0.3085	0.6915
1.00	0.1587	0.8413
1.50	0.0668	0.9332
1.65	0.0495	0.9505
2.00	0.0228	0.9772
2.50	0.0062	0.9938
3.00	0.0013	0.9987
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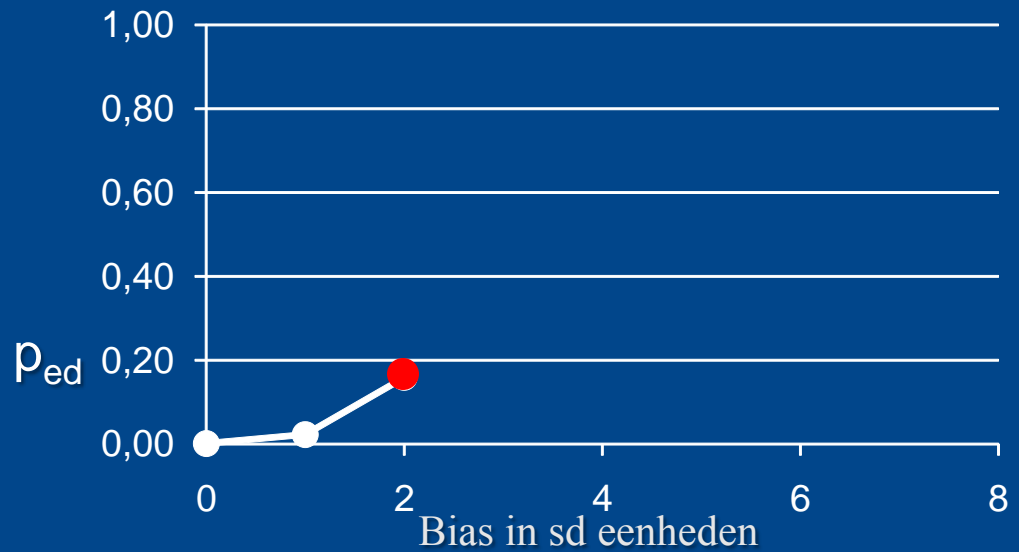
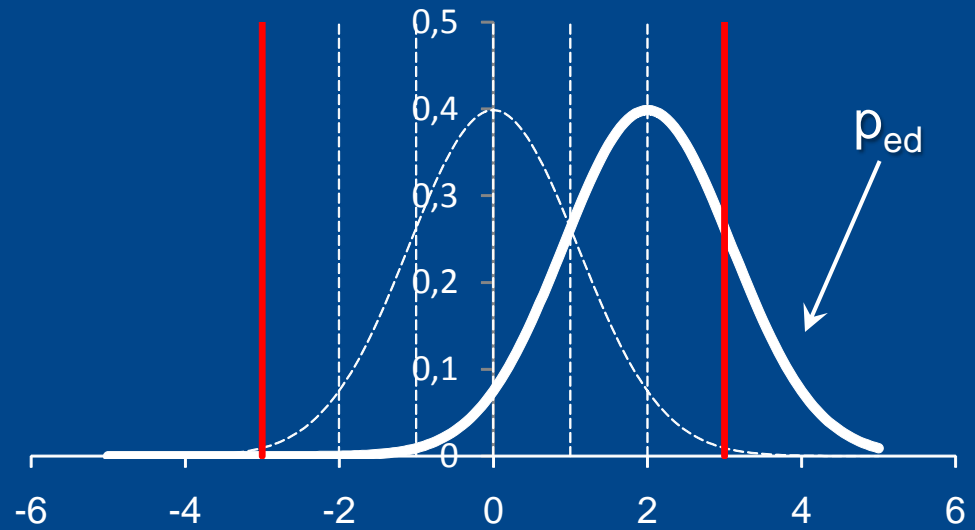


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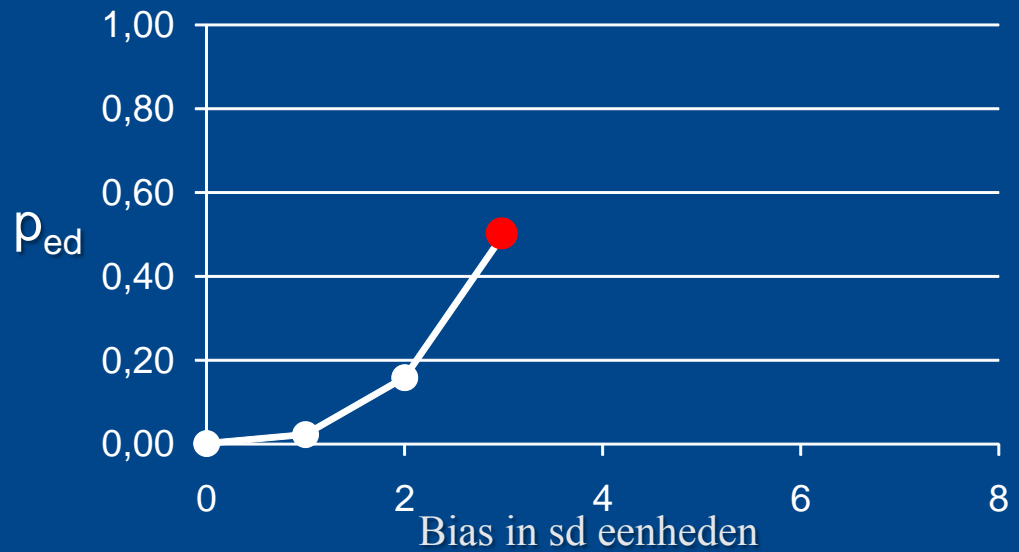
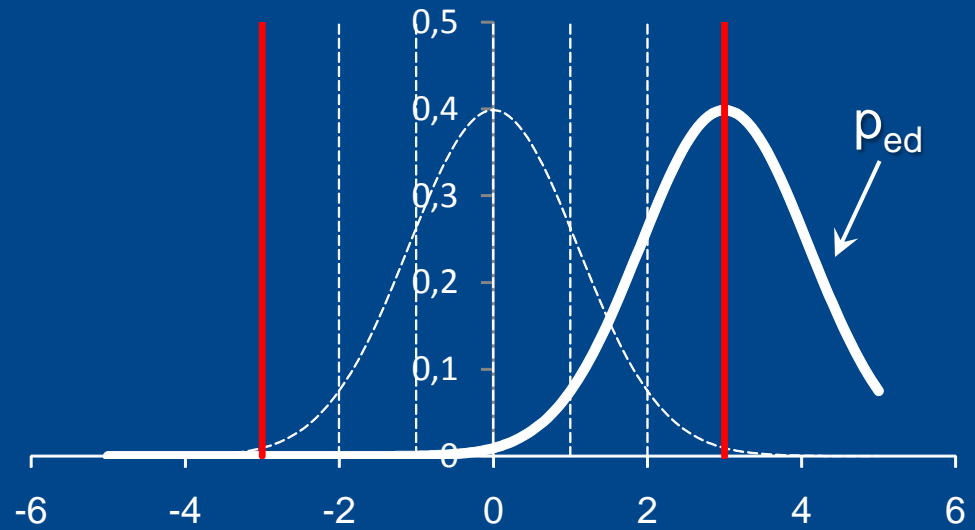
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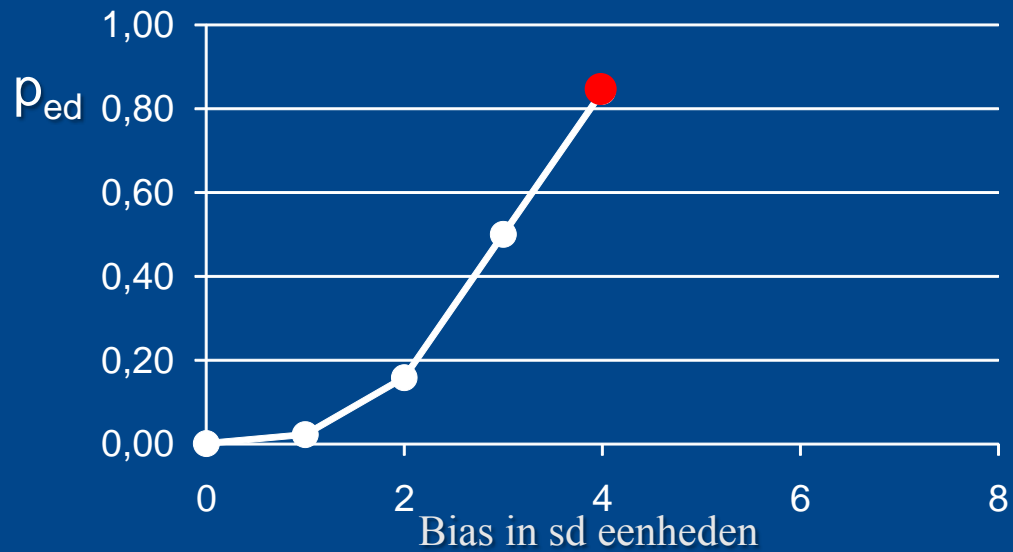
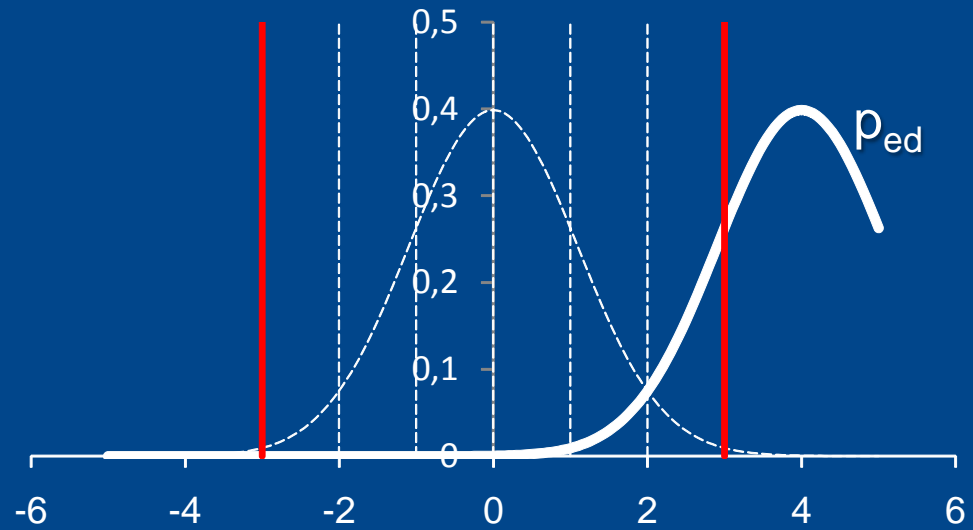
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