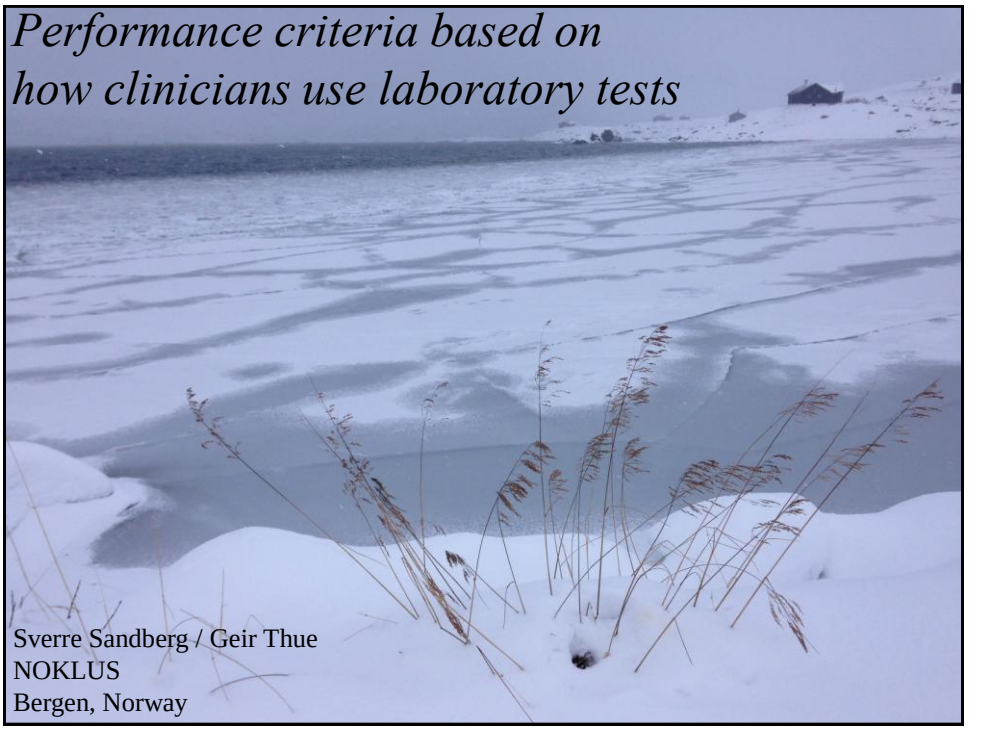


What is this talk about?

- Theoretical basis for setting goals from clinicians´opinion
- Examples on how to use the concept
- Pro / Con for this model
- Conclusion

First of all

If you ask clinicians about performance criteria or quality specifications for laboratory tests, they will not have a clue since they think laboratory tests are correct.

So therefore, you have to ask them indirectly – that is, how do they use the tests?

Opinions of clinicians and patients

- ✓A method to discover how the clinicians are using the tests.
- ✓It is then possible to extract what analytical quality they presuppose that they have.
- ✓This can then be used to set quality specifications.
- ✓The quality specificaitons will mirror how clinicians/patients use the tests

How to find the ”opinions” of the clinicians ?

1. *To examine the medical journals to see what the physicians do in the real life situation*
2. *To distribute case histories to simulate the real life situation*

What analytical quality does clinicians think laboratories have - *ask about a critical difference*

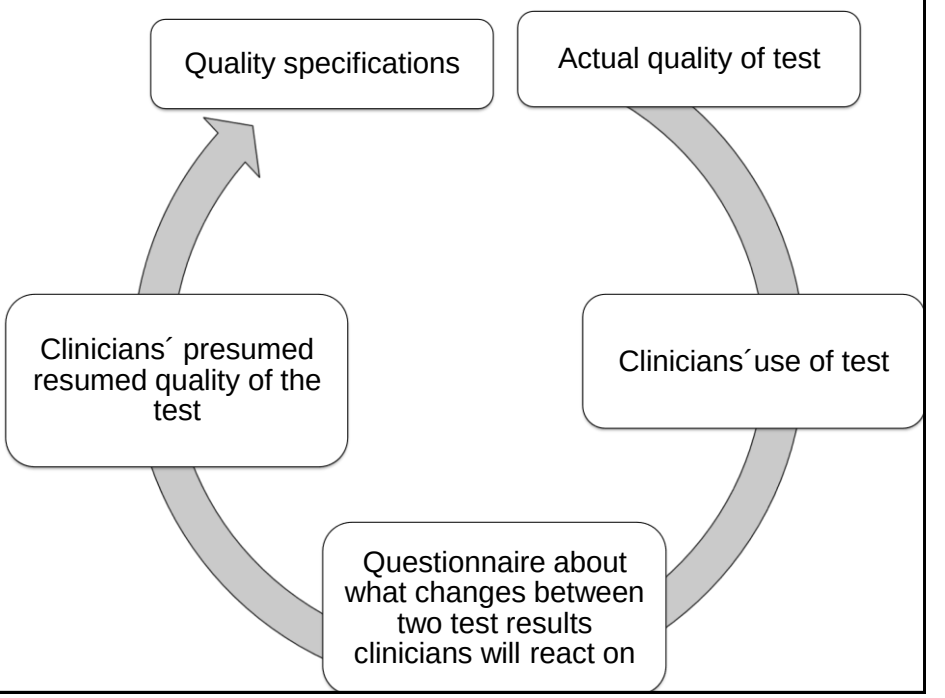
If we ask clinians/patients what difference between two results they will react on, we can calculate what analytical quality they presume that their laboratory have for this specific test.

Critical difference

The differences between the two results given is the medical critical difference (CD) that should be detected by the actual measurement method.

Dependent on the question, the CD can comprise:

- pre-analytical variation
- imprecision under defined reproducibility conditions
- within-subject variation
- bias



However

There is often a discrepancy by the actual quality of the test and the quality that the clnician presume that the test has..

Clinicians more often think that the test is ”better” than it actually is.

When to use the method

Only for an analyte in a specific clinical situation.

Only for analytes that have a main role in the monitoring and/or diagnosing the patient.

This limit the number of analytes

Examples

Ellion Gerritzen - 1979

Suppose you find under your treatment the first laboratory results given in the table, You follow the course of the patient and/or the effect of treatment: Please circle the value that would represent a significant change.

Hb: 9.0 next result

9.5 10.0 10.5 11.0

Skendzel 1985

A 41 year old man with a history of bleeding ulcer is currently asymptomatic. The hemoglobin is 14 g/dL. The test is repeated a week later. Indicate the lowest value that would convince you bleeding has recurred.

Calculations of the critical difference (CD) and reproducibility (CVa)

$$CD = bias + z^* \sqrt{2^* CV_a}$$

$$CV_a = (CD - bias) / (z \times \sqrt{2})$$

In most cases, the bias is assumed to be = 0

$$CD = z^* \sqrt{2} * CV_a$$

$$CV_a = CD / (z \times \sqrt{2})$$

However, a difference between two results can also be influenced by the within-subject biological variation. This must also be taken into account.

Including the within-subject biological variation makes the calculations a litte more complicated

$$CD = bias + z^* \sqrt{2^*} \sqrt{CV_{ws}^2 + CV_a^2}$$

- And the CVa

$$CD = bias + z \times \sqrt{2} \times \sqrt{CV_{ws}^2 + CV_a^2}$$

$$CV_a = \sqrt{((CD - bias)/z \times \sqrt{2})^2 - CV_{ws}^2}$$

- But – again – in most calculations, bias is set to zero

$$CD = z \times \sqrt{2} \times \sqrt{CV_{ws}^2 + CV_a^2}$$

$$CV_a = \sqrt{(CD / z \times \sqrt{2})^2 - CV_{ws}^2}$$

Clinical quality specifications for haemoglobin in general practice

12 case stories about Hb

273 general practitioners (10% randomized sample)

76% response rate (207 general practitioners)

Thue et al. Scand J Clin Inves 1991; 51 453-9

Case 6

A 37 years old man has suffered from duodenal ulcer twice previously. The first time he was sent to a hospital because of bleeding, but was not operated on. Last month his indigestion has recurred, and it has become a great deal worse this last week. Five weeks ago his haemoglobin was 111 g/l

State how low your haemoglobin must be (at least) before you take action: ..... g/l.

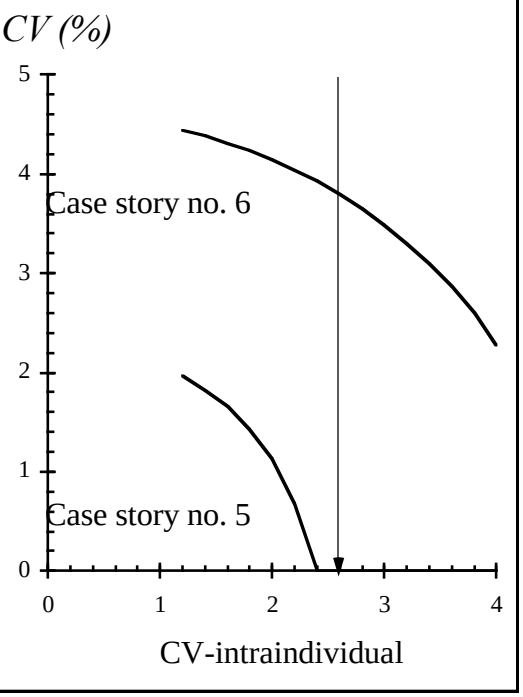
Calculated CVa between-clinician variation (10-50-90 percentile)

CVa%: 2.6 – 4 - 6.3

Limitation no 1:
Variation between clinicians

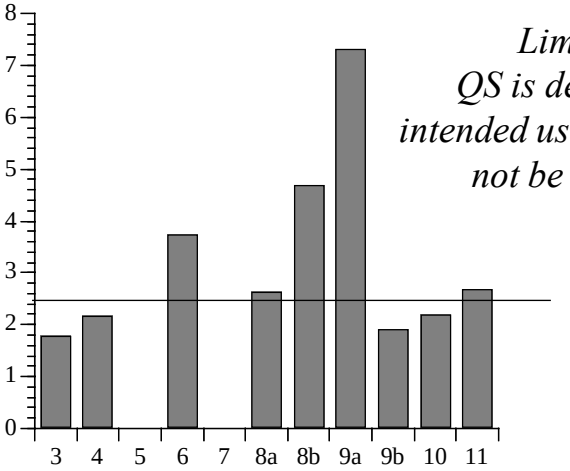
Effect of within-subject biological variation on the estimation of quality specifications

Limitation no 2:
Estimation of within-subject biological variation not good enough



Quality spesifications for Hb (CV) based on different case stories

Ellion Gerrittzen: 4.6
Skendzel: 4.9%



Limitation no 3
QS is dependent on the intended use and can therefore not be general for the analyte

Example: Current use of HbA1c and glucose

- Case stories distributed in
  - Hungary
  - Norway
  - Sweden
  - The Netherlands
  - Australia
  - Spain
  - South-Africa

Physicians: HbA1c

A 45 year-old, considerably overweight woman with 5 children. She was diagnosed with type II diabetes 4 years ago and you are her physician. Her diabetes treatment was a total daily dose of 7 mg glibenclamide and 500 mg metformine. She has a tight every-day schedule paying little attention to her diet and without time for exercise.

HbA1c

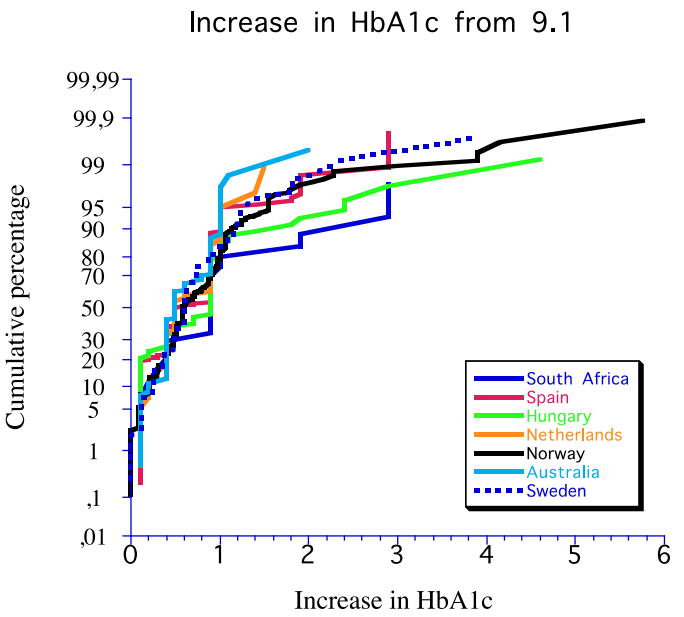
By consultation now the HbA1c is 9.1 % (DCCT value)

You do what you find appropriate.

What do you mean the HbA1c test-result should be at the next consultation for the value to indicate:

A. *Better diabetes control*:
HbA1c value must have decreased to at least ……%

B. *Poorer diabetes control:*
HbA1c value must have increased to at least …….%



HbA1c
– results from 7 countries

Median percentage change in HbA1c to indicate poorer or better control was 0.7 % (0.5 – 0.9) which corresponds to a 8% (0.7/9.1) change in HbA1c from 9.1

Quality specifications set by GPs and patients

Constituent	Quality specification CVa	Ref
Hb	2.8 %	*SJCLI. 1991;51:453*
SR	10 mm	*SJCLI. 1994;54:291*
HbA1c - GPs	1-3%	*Clin Chem. 2005;51:1145*
HbA1c - patients	3%	*Clin Chem. 2001;47:1212*
Glucose GPs	3%	*Clin Chem. 2005;51:1145*
Glucose pat. norm	7%	*Clin Chem. 2001;47:67*
Glucose pat. hypo	3%	*Clin Chem. 2001;47:67*
PT-INR	15%	*Clin Chem. 2006;52:1871*
U-albumin	14%	*Clin Chem. 2008;54:1630*

Limitations of the method

”Inter-clinician” variation can be large

The obtained specification is dependent on a specific clinical situation

The obtained specifications will be influenced by the actual quality of the test

Different populations of clinicians will (probably) act differently

The within-subject variation data is not good enough

Strengths of this method

The obtained QS reflects how the clinicians will use the analyte in clinical practice

Using such QSs will optimize the use of laboratory tests

The method is easy to perform

Potential improvement

Examine for homogeneity of the responding physicians.

The results could only be used within the homogenous group.

Improve biological variation data

Thank you

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Spain
Croatia
Denmark
Sweden
France
The Netherlands
Hungary
Estonia
Australia
Austria
Norway

Participation

Case history sent to about 10 000 GPs

Analytical quality specifications for A/C ratio based on a starting value of 15 mg albumin/mmol creatinine

	CD (%)	CVa (%)
INCREASE	**50th pecentile**	**50th percentile**
Denmark	**33**	**8.6**
Estonia	**100**	**41.3**
Norway	**33**	**8.6**
Spain	**100**	**41.3**
Sweden	**33**	**8.6**
DECREASE		
Denmark	**33**	**8.6**
Estonia	**77**	**31.2**
Norway	**33**	**8.6**
Spain	**33**	**8.6**
Sweden	**33**	**8.6**

Analytical quality specifications for A/C ratio based on a starting value of 15 mg albumin/mmol creatinine and a CVws of 11%.

	CD (%)			CVa based on CDs stated					
				95 % confidence			80% confidence		
Deterioration (n)	25th percentile	50th percentile	75th percentile	25th percentile	50th percentile	75th percentile	25th percentile	50th percentile	75th percentile
Denmark (27)	33	33	100	8,6	8,6	41,6	25,4	25,4	83,4
Estonia (18)	1	100	126	NC	41,6	53,1	NC	83,4	105,5
Norway (494)	33	33	100	8,6	8,6	41,6	25,4	25,4	83,4
Spain (34)	33	100	102	8,6	41,6	42,5	25,4	83,4	85,1
Sweden (57)	1	33	100	NC	8,6	41,6	NC	25,4	83,4
Improvement (n)									
Denmark (26)	30	33	39	6,3	8,6	12,5	22,6	25,4	30,8
Estonia (19)	13	77	81	NC	31,2	33,0	NC	63,8	67,2
Norway (430)	33	33	67	8,6	8,6	26,6	25,4	25,4	55,3
Spain (24)	7	33	33	NC	8,6	8,6	NC	25,4	25,4
Sweden (62)	33	33	67	8,6	8,6	26,6	25,4	25,4	55,3