Performance criteria for "qualitative test" procedures

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Performance criteria for qualitative tests

Based on the effect of analytical performance on clinical outcomes

Based on components of biological variation of the measurand

Based on state of the art

What is a "qualitative test" ??

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Are these tests qualitative?

- Pregnancy tests
- Molecular biology tests
- Blood typing
- Tests for drugs of abuse
- Rapid antigen tests for Strep A
- FOB
- Genetic tests
- HPV-test (PCR)

3

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What is a ”qualitative test” ?

- Semi quantitiative test
- Classification test
- Binary test
- Test with results ”yes/no”
- Test with results on an ordinal scale

4

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What is a qualitative test?

IUPAC definition: "*Analysis in which substances are identified or classified on the basis of their chemical or physical properties, such as ...*

The CLSI, in EP12 A2, restrict the use of the term to *".... methods that provide only categorical responses (i.e. positive/negative or yes/no)*

Eurachem (draft definition): *"Classification according to specified criteria"*

5

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Ordinal scale versus nominal scale

Ordinal scale: all types of ***grading***:, +/++/+++, negative/positive if there is an underlying quanity scale

Nominal: all types of ***classification***: disease, molecular specis, gene sequence, blood groups, incuding "yes/no" if there is no underlying quantity scale

6

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What is a qualitative test?

If we dont know what a qualitative test is,

it is impossible to specify performance criteria

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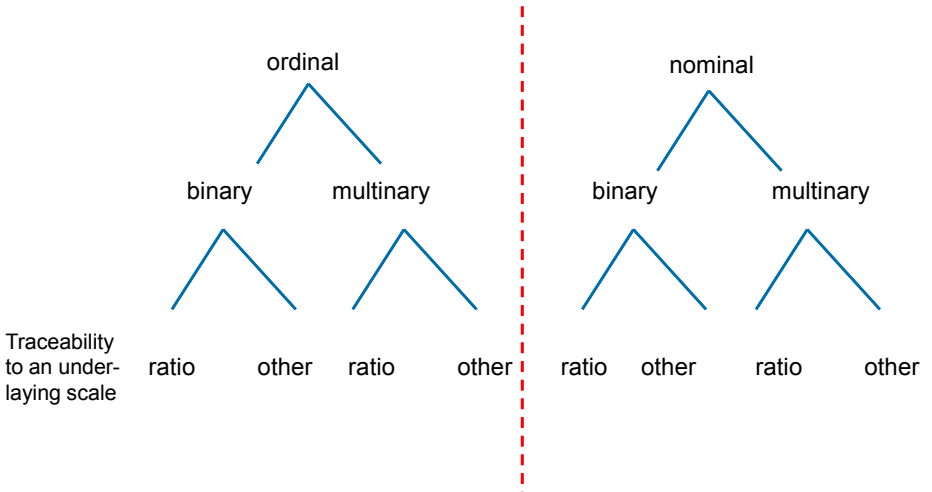
What is a qualitative test?



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Proposal 1: don't use the term qualitative test!

Nominal scale test – e.g. blood typing
Ordinal scale test – e.g. pregnancy test

Differential scale – e.g. HbA1c with NGSP units
Ratio scale – e.g HbA1c with IFCC units

9

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Ordinal <u>measurements</u>

Results for an ordinal quantity are ***measurements***, but the results have no units.

10

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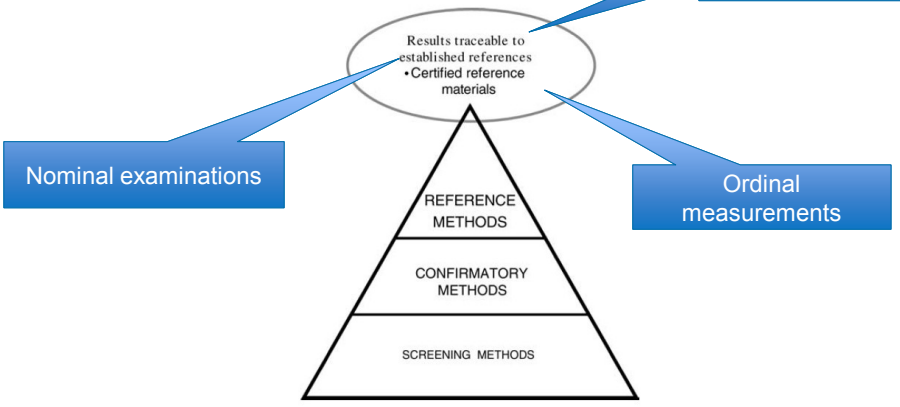
It is not clear how to describe traceability for ordinal test results

Quantitative measurements



Nominal examinations

Ordinal measurements

Fig 1 Hierarchical classification of qualitative methods according to their traceability

Rios et al. Quality assurance of qualitative analysis in the framework of the European project 'MEQUALAN'. Accred Qual Assur (2003) 8:68–77

11

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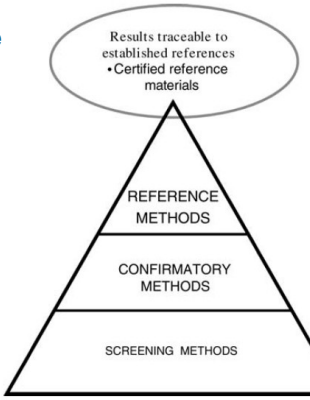
It is not clear how to describe traceability for ordinal test results

Specific and accurate hCG methods



Old studies with old methods based on diseased and non diseased populations

Urine pregnancy test

Serology for infectious diseases

Fig 1 Hierarchical classification of qualitative methods according to their traceability

Rios et al. Quality assurance of qualitative analysis in the framework of the European project 'MEQUALAN'. Accred Qual Assur (2003) 8:68–77

12

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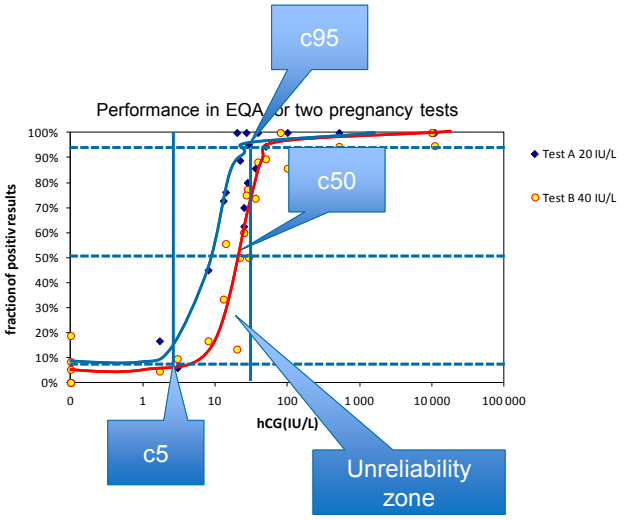
Performance characterstics for pregnancy tests



13

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CLSI EP12-A2

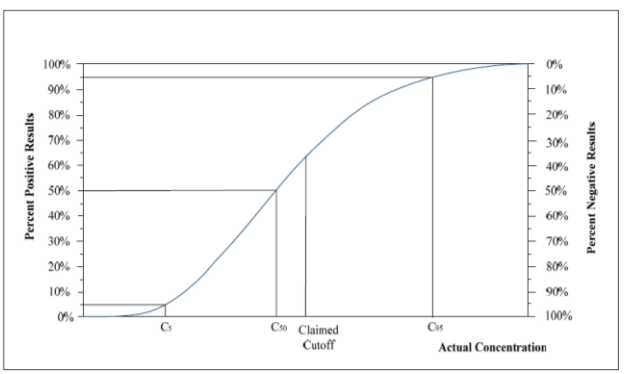

Figure 1. Analyte Concentration Near the Cutoff. The percent of positive and negative results from a large series of test results would be expected to change as a function of the analyte concentration near C_{50}.

14

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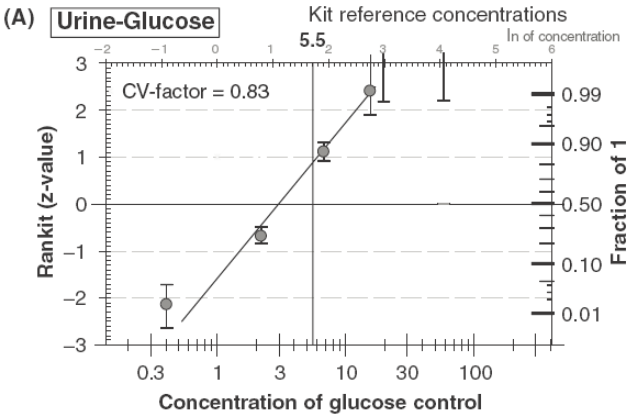
How to draw the line….



Hyltoft Petersen, P., et al. (2008) Scand J Clin Lab Invest 68(4): 298-311.

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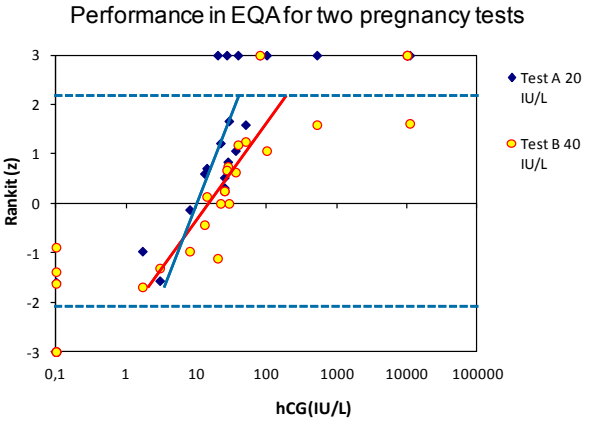
How to draw the line….



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Proposal 2: c5, c50 an c95

For ordinal binary test with a quantitative back ground scale assays should be characterized with the three quantities:

“c5”, ”c50” and ”c95”.

The manunfacturer should declare the c50 value for the assay, and describe the metrological traceability

17

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Performance characteristics for an individual ordinal scale test result

What is ’precision’ on an ordinal scale?

- The ability to repeat a value?
- The positive predictive value (positive/true positive + false positive)
- The interval of concentration where the result is unreliability zone

18

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Measures of repeatability for ordinal results

Define the *total* ordinal variation in the interlaboratory comparison according to (1) as:

$$\hat{h}^2_{(T)} = \frac{1}{(K-1)/4}\sum_{k=1}^{K-1}\hat{F}_{k.}(1-\hat{F}_{k.}), \quad (2)$$

and the *within* m-th laboratory ordinal variation as:

$$\hat{h}^2_{m(\mathrm{W})} = \frac{1}{(K-1)/4}\sum_{k=1}^{K-1}\hat{F}_{km}(1-\hat{F}_{km}). \quad (3)$$

The classic variation of the cumulative frequencies of the k-th category *between* laboratories is

$$\hat{S}^2_{k(\mathrm{B})} = \frac{1}{M}\sum_{m=1}^{M}(\hat{F}_{km}-\hat{F}_{k.})^2. \quad (4)$$

It is possible to split the total ordinal variation with $df_{\mathrm{T}} = N - 1$ degrees of freedom (2) into the "within" and "between" components as follows [20]:

$$\hat{h}^2_{(\mathrm{T})} = \hat{h}^2_{(\mathrm{W})} + \hat{S}^2_{(\mathrm{B})} = \frac{1}{M}\sum_{m=1}^{M}\hat{h}^2_{m(\mathrm{W})} + \frac{1}{(K-1)/4}\sum_{k=1}^{K-1}\hat{S}^2_{k(\mathrm{B})}, \quad (5)$$

Bashkansky et al. Interlaboratory comparison of test results of an ordinal or nominal binary property: analysis of variation. Accred Qual Assur (2012) 17:239–243

$$h^2 = \frac{1}{(K-1)/4}\sum_{k=1}^{K-1}F_k(1-F_k)$$

Blair J, Lacy MG (2000) Statistics of ordinal variation. Sociol Methods Res 28:251–280

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Not clear how to express uncertainty of an ordinal result

Has to be done with a probabilistic statement.

We are not used to communicate this type of uncertainty to requesting doctors or to patients.

"False positive" can be misinterpreted for the laymen – is it sample that should be positive, but became negative – or the reverse ?

20

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Performance characteristic	Expression
False positive rate*	$\frac{FP}{TN+FP}$
False negative rate*	$\frac{FN}{TP+FN}$
Sensitivity*	$\frac{TP}{TP+FN}$
Specificity*	$\frac{TN}{TN+FP}$
Efficiency	$\frac{TP+TN}{TP+TN+FP+FN}$
Youden Index	Sensitivity(%) + Specificity(%) - 100
Likelihood Ratio	$\frac{1-\text{False negative rate}}{\text{False positive rate}}$
Bayes posterior probability	Bayes rule

21

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Not clear how to express the robustness of an ordnal test

Table IV. Compilation of results from the clinical application of on-site drug testing.

		Observed number	Total number
Number of samples with correct result		84 (84%)	100
Correct rate in positive samples		59 (79%)	76
Correct rate in negative samples		23 (96%)	24
Rate of correct analytical result for parameters		881 (98%)	900
Proportion of false negatives of incorrect results		8 (42%)	19
False positive parameters	Amphetamine, benzodiazepines, buprenorphine, methadone, opiates, tramadol		
False negative parameters	Cannabis: 1 sample containing THCCOOH 14 ng/mL Benzodiazepines: 4 samples containing oxazepam 100 ng/mL, clonazepam 120–360 ng/mL, alprazolam 11–770 ng/mL, triazolam 50 ng/mL Opiates: 1 sample containing total morphine < 300 ng/mL Tramadol: 1 sample containing 230 ng/mL		

Beck, O., et al. (2014). "Laboratory and clinical evaluation of on-site urine drug testing." Scand J Clin Lab Invest **74(8): 681-686.**

22

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Proposal 3

We should develop and agree on measures of precision and uncertainty for ordnal test results in order to describe performance criteria

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Internal quality assessment for ordinal tests

<c5	c5 – c95	>c95
FP	-	TP
TN	-	FN

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External quality assessment for ordnal tests

<c5	c5 – c95	>c95
FP	TP	TP
TN	TN	FN

25

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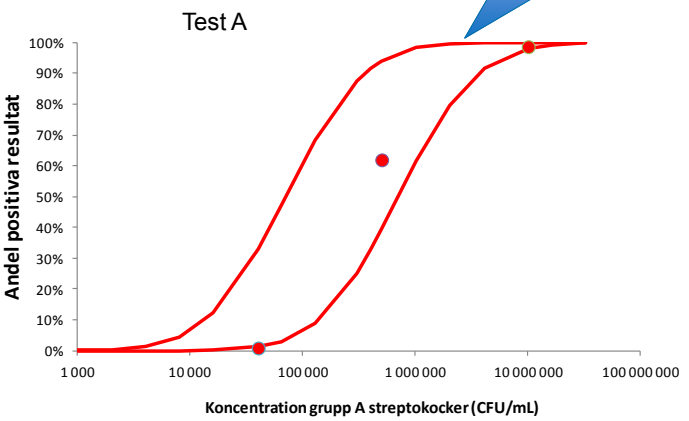
Empirical, ”state of the art” limits for performance



26

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How do we report EQA results

Oversikt

Prov	Komponent	n	Andel med förväntat svar (%)	Förväntat svar	Eget resultat
/1	Grupp A streptokocker	766	99.1	Negativ	Negativ
/2	Grupp A streptokocker	764	100	Negativ el. Positiv	Positiv
/3	Grupp A streptokocker	764	97.5	Positiv	Positiv

Historik

27

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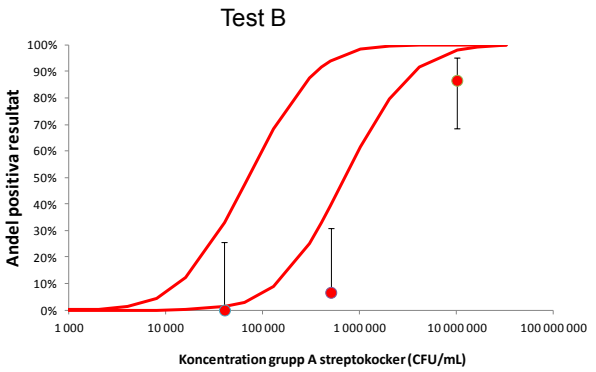
Tests with deviating performance can be revealed



28

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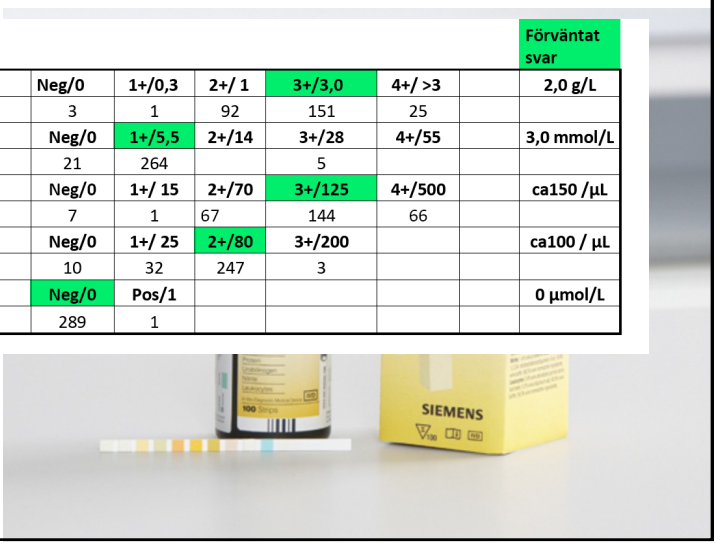
Urine test strips – how do we report the clinical results?

Siemens Multistix							Förväntat svar
U-Albumin g/L	**Neg/0**	**1+/0,3**	**2+/ 1**	**3+/3,0**	**4+/ >3**		**2,0 g/L**
Antal svar	3	1	92	151	25		
U-Glukos mmol/L	**Neg/0**	**1+/5,5**	**2+/14**	**3+/28**	**4+/55**		**3,0 mmol/L**
Antal svar	21	264		5			
U- Leukocyter /µL	**Neg/0**	**1+/ 15**	**2+/70**	**3+/125**	**4+/500**		**ca150 /µL**
Antal svar	7	1	67	144	66		
U-Erytrocyter /µL	**Neg/0**	**1+/ 25**	**2+/80**	**3+/200**			**ca100 / µL**
Antal svar	10	32	247	3			
U-Nitrit	**Neg/0**	**Pos/1**					**0 µmol/L**
Antal svar	289	1					



29

Proposal 4

Harmonizing the way of expressing ordinal test results.

Harmonization will reduce the risk for misinterpretation and simplify secure communication of results

30

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In summary

Proposal 1: Forget about ’qualitative test’

Proposal 2: Use c5, c50 c95 to characterize test performance

Proposal 3: Develop and agree on measures of precision and uncertainty of ordinal test results

Proposal 4: Harmonize the terminology of results

31

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Thank you for the attention

32

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