The Impact of TEa Selection

Zoe C. Brooks, ART, AWEsome Numbers Inc. Sudbury, ON, Canada; George Sweeney, MLS(ASCP)CM, M.O.R.E. Quality Consultant, USA

Objectives:

1. To demonstrate the relationship between the laboratory selection of **TEa** (total error allowable) limits, patient risk and clinical costs.
2. To compare QC (quality control) data for calcium to CLIA (Clinical Laboratory Improvement Amendments) limits, BV (Biological Variation) and NIST (National Institutes of Standards and Technology) medical goal.[3]

Background:

TEa (allowable error) is "equivalent to the error that does not significantly contribute to wrong clinical decisions." (ISO 15189:2012 Medical laboratories – Requirements for Quality and Competence). To evaluate risk, laboratories must "compare the estimated risk against given risk criteria to determine the acceptability of the risk" (CLSI Guideline EP23-A).
Current TEa limits are typically selected within the laboratory as CLIA or BV limits. Neither of these may be appropriate as a 'limit of medical utility". Selection of TEa limits drives the perceived and factual acceptability of patient risk. Medical goals represent best practice.

Methodology:

We created 3 data sets of recently
1. Measured mean;
2. Measured SD; and
3. Peer Mean with sigma values of 5.7, 5.2 and 3.3.

We entered the data in CatalystQC™ software with
1. CLIA limits of 0.25 mmol/L (1.0 mg/dL),
2. NIST-recommended Medical goal of 0.125 mmol/L (0.5 mg/dL) mg/dL, and
3. Biological variation desirable TEa of 2.55%

We calculated a z-value as (|measured mean – TEa limit|)/SD) – equivalent to sigma metric as (TEa-|bias|)/SD
We converted the z-value to percent risk level plus the number and clinical/legal cost of medically-unreliable results (MURs)/year at this level of accuracy and precision.

We compared the interpretation of acceptability of quality and probable action based on the selected TEa limits.

Results:

We see that by only changing TEa values there is a significant change in patient risk and clinical cost. Looking at case 1 as an example, the medical and legal cost can go from $0 with a TEa of 1.0 mg/dL using CLIA limits to a cost of **$320,900** for the year using biological variation desirable TEa of 2.55%. [Due to changes we made in the estimated coast at each level, these numbers are not reflected in the cases shown.]

The patient risk goes from a predicted 0 medically-unreliable results with CLIA to 3,209 patients at risk using the biological variation TEa. Comparing the results of evaluation with CLIA, Medical, and Biological Variance demonstrates that the value selected for TEa will play a major role in clinical acceptability, patient risk, and cost due to medically unacceptable errors.

The TEa should be validated to be certain that the risk and cost is minimized.

"**Incorrect result** – result that does not meet the requirements for its intended medical use; NOTE 1: In the case of quantitative test procedures, a result with a failure of measurement that exceeds a limit based on medical utility." [2] (CLSI EP 23-A)

Analytical performance specifications
Model 1. Based on the effect of analytical performance on clinical outcomes. This can, in principle, be done using different types of studies:
1. Direct outcome studies – investigating the impact of analytical performance of the test on clinical outcomes[1]

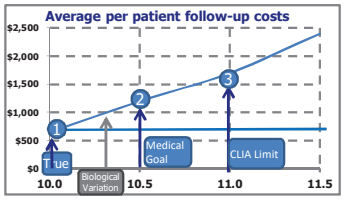
Milan Consensus International Federation of Clinical Chemistry and Laboratory Medicine Clinical Chemistry and Laboratory Medicine

"**Evaluate the potential costs** both in terms of the patient's well-being and in terms of financial liability of the treating parties vs known benefits to the patient." [2] (CLSI EP 23-A)

What is the cost of analytical error in calcium results?

The Impact of Calibration Error in Medical Decision Making
"Based on analysis of over 89,000 patients receiving serum calcium tests at the Mayo Clinic in 1998–1999, we find that the number of follow-up procedures, and hence health care costs, is directly related to initial calcium test values." [3]

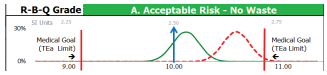
"For an analytical bias of 0.5 mg/dL ... the potential health care cost increase ranged from $34 to $89 per patient having a calcium test. With approximately 3.55 million patients per year receiving screening serum calcium tests being affected by systematic bias, the potential economic impacts range from $60 million to $199 million per year for analytic biases of 0.1 and 0.5 mg/dL, respectively."[3]



1. "If patient result is 10.0, the average follow-up costs are about $650.
2. If this sample is reported as 10.5 mg/dL would, on average, receive an additional $550 in follow-up tests.
3. If reported as 11.0 mg/dL, this error causes an additional $1150 in follow-up tests."

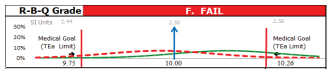
This study analyzed only the cost of follow up tests. (They applied the term bias as total error: inaccuracy/bias of a single sample.) In our study, we conservatively estimated clinical/legal cost of error of 0.5 mg/d/L (0.125 mmol/L) at $100; 1.0 mg/d/L (0.250 mmol/L) at $200 and 0.255 mg/dL (0.06 mmol/L) at $50.

	A. Baseline 5.7 sigma (z-value)	B. Change TEa to BV	C. Change TEa to Medical	What is this?	Where Does it come from
Evaluation of Analytical Process Quality	**PASS**	**FAIL**	**PASS**	**Evaluation**	Calculated by software
# Patient Samples /Yr. controlled mainly by this QC sample	63,581	63,581	63,581	Risk Driver	Available records
True Value of this QC Sample	10.00	10.00	10.00	Risk Driver	From source in lab policy
Medical Goal (Limit of Medical Utility) or TEa Limit	**1.0**	**0.255**	**0.5**	Standard	Laboratory Policy
Measured Mean in this time period	10.1	10.1	10.1	Risk Driver	From measured data
Measured SD in this time period	0.150	0.150	0.150	Risk Driver	From measured data
Avg. Clinical/Legal cost /Medically-Unreliable result	**$200**	**$50**	**$100**	Estimate	Clinical input or studies
Acceptable Risk Criteria (ARC) as # MUR / Year	1,446	1,446	1,446	Standard	Laboratory Policy
# MUR/Year - with performance of this time period	0	11,260	436	**Risk Metric**	Calculated by software
Acceptable Risk as Clinical/Legal Cost of MUR/Year	**$289,200**	**$72,300**	**$144,600**	Standard	Laboratory Policy
Clinical/legal cost MUR currently reported /year.	**$0**	**$563,000**	**$43,600**	**Risk Metric**	Calculated by software
Margin for Error [# SD from mean to Unacceptable Risk]	**3.70**	**-1.27**	**0.37**	**Risk Metric**	Calculated by software
z-value (sigma from measured values [(TEa – |bias|)/SD]	**5.70**	**0.73**	**2.37**	Statistic	Calculated by software
QC Summary Review - Acceptable Risk Criteria as %	2.275%	2.275%	2.275%	Statistic	Calculated by software
Evaluation of QC Process Effectiveness:	**PASS**	**FAIL**	**PASS**	**Evaluation**	Calculated by software



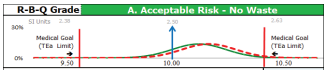
M.O.R.E. Auto-Action to Lower Risk and Cost:
Lower Medical Goal or Acceptable Risk Criteria to reduce risk
Use OptimiZed QC Process
No change in QC frequency

What to do	QC Reject Rule	Sample Frequency/Day	Chart Review: Front Line	Chart Review: Supervisor	Change existing QCP?: Rule	Chart	Freq	Review	Improve - if possible: Accuracy	Precision
	1- 3.5 s	1	1x / Week	1x / 4 Weeks	Yes	No	No	No	No	No



M.O.R.E. Auto-Action to Lower Risk and/or Cost:
Analytical process quality fails acceptable risk criteria
Stop now and ACT to mitigate and reduce risk
Refer to Risk Management Procedure

What to do	STOP	STOP! Improve Method	Improve - if possible: Accuracy	Precision
			Yes	Yes



M.O.R.E. Auto-Action to Lower Risk and/or Cost:
Improve method accuracy & precision
Use OptimiZed QC Process
Increase QC frequency

What to do	QC Reject Rule	Sample Frequency/Day	Chart Review: Front Line	Chart Review: Supervisor	Change existing QCP?: Rule	Chart	Freq	Review	Improve - if possible: Accuracy	Precision
	1- 2.0 s	2	2x / Week	1x / Week	Yes	No	Yes	Yes	Yes	Yes

Discussion:

"Risk is the combination of [A] the probability of occurrence of harm and [B] the severity of that harm" (ISO/IEC Guide 51).

You can control severity of harm by setting limits of medical utility (medical goals) – and the associated cost of failure to meet those goals - for each analyte by clinical setting.

You can control probability of harm by setting acceptable risk criteria as the number and cost of Medically-Unreliable Results reported, routinely at method review and if the method fails.

M.O.R.E. Quality™ will design a QC process and guide staff to meet these standards or act as per your procedures.
Risk management and Mathematically-OptimiZed Risk Evaluation™ are based on medical goals and acceptable risk criteria by the local laboratory director – and patients, institutes, physicians, and society ("The PIPS").

Conclusions:

In these case studies the best source for TEa was the CLIA limit throughout. Best practice would be to validate any TEa that is used prior to starting to report patient results. This would save money and reduce patient risk.

References:

1. Milan Consensus International Federation of Clinical Chemistry and Laboratory Medicine 2014
2. Clinical & Laboratory Standards Institute. Guideline EP23-A Laboratory quality control based on risk management. Wayne, PA. 2011
3. Gallaher M, Mobley LR, Klee G, and Schryver P. The impact of calibration error in medical decision making. Prepared for National Institute of Standards and Technology Chemical Science and Technology Laboratory. Planning report 04-1; May 2004.
4. Brooks, Zoe. Managing Acceptable Risk Level 1: Risk Assessor. AWEsome Numbers, Inc. Sudbury, Ontario, Canada. 2016.

Contact Information:
Zoe: Zoe@awesome-numbers.org
George: gwsweeney@gmail.com

Zoe Brooks is CEO and Director of Innovation and Research at AWEsome Numbers, Inc. George Sweeney has no financial interest in the company.