Clinical Chemistry Trainee Council
Pearls of Laboratory Medicine
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"QC Design: Things You Need to Know" Series

TITLE: Patient-Based Sigma Metric

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Slide 1:
Welcome to "QC Design: Things You Need to Know" series. This is Lakshmi Kuchipudi. I am a senior scientist in Quality Systems Division at Bio-Rad Laboratories. This is the 5th Pearl in this series. In this Pearl, I will discuss a new sigma metric which accurately reflects the capability of an assay with respect to its allowable total error for the patient population served.

Slide 2:
The sigma metric is defined as your allowable total error specification for an analyte…

Slide 3:
…minus any inherent analytical bias in your test method…

Slide 4:
… divided by the stable analytical imprecision of your test method.

Slide 5:
For more information on allowable total error, TE_a, please refer to the 2nd Pearl in this series on "Allowable Total Error." We recommend using biological variation published values for TE_a. CLIA specifications should always be the minimum.

For more information on analytical bias and imprecision, please refer to the 3rd Pearl in this series on "Performance Statistics. "

The sigma metric is a measure of your process capability relative to your quality requirement – it is effectively the number of analytical standard deviations of your test method that fit within your allowable total error specification. For more information on how to use Sigma Metric, please refer to the 4th Pearl in this series on "Sigma Metric."

The sigma metric widely used in clinical diagnostics is treated as a constant, independent of concentration. But this is rarely the case.

Slide 6:
Typically, when sigma metrics are computed at different concentrations, different values are obtained. Let's look at an example. We want to compute sigma metric for Potassium.

Slide 7:
The allowable total error for potassium is 7.44%. This quality specification is based upon biological variation.

Slide 8:
For the purpose of this Pearl, we assume instrument bias is 0.

Slide 9:
If the instrument bias is 0, we can simplify the sigma metric computation as percent TE_a over CV.

Slide 10:
We computed 2 different sigma metric values at 2 different levels of QC.

Slide 11:
Now, which sigma metric value should we use? Level 1 or Level 2 or an average of these 2 levels?

Slide 12:
This is the patient distribution for potassium.

Slide 13:
The red circles show the QC concentration for each level.

Slide 14:
You can see that the level 1 QC concentration represents most of the patient distribution.

Slide 15:
Level 2 QC concentration represents patients in the right tail of the distribution.

Slide 16:
Now back to our question: Which sigma metric value should we use? Level 1 or Level 2?

Slide 17:
A better way is to compute a sigma metric value that uses the entire patient distribution.

Slide 18:
In reality, there is a sigma profile that varies over the concentration range of the analyte. Let's look at our example for Potassium.

Slide 19:
The x-axis shows you the concentration range for potassium.

Slide 20:
If you compute a sigma metric value at each concentration and plot those values,...

Slide 21:
... you get the black curve.

Slide 22:
The red circles are the sigma metric values at QC concentrations.

Slide 23:
A patient-based sigma value is obtained by computing a weighted average of the sigma-values represented in the sigma profile.

Slide 24:
The sigma value at each concentration is weighted by the probability of obtaining a patient result at that concentration based on the frequency distribution of patient results.

Slide 25:
The patient-based sigma metric value for potassium in our example is 5.58.

Slide 26:
You can see the patient-based sigma metric value is closer to the Level 1QC sigma metric value which represents most of the patient distribution.

Slide 27:
Let's look at another example. We want to compute sigma value for Myoglobin. We computed 3 different sigma metric values at 3 different levels of QC.

Slide 28:
Patient-based sigma value in this case is 4.16 and is different from the sigma at any of the QC concentration.

Slide 29:
The patient-based sigma value represents most of the patient distribution.

Slide 30:
Some examples of QC-based and Patient-based Sigma Values for Analytes with 2 QC concentration levels. Depending on the analyte, patient-based sigma metric can be similar to sigma value at one of the QC concentration levels,…

Slide 31:
...near the average of the sigma values computed across QC concentrations, or….

Slide 32:
...substantially different from all sigma values computed at QC concentrations.

Slide 33:
In summary, sigma metric value computed as TE_a minus absolute bias over SD is not a constant but varies with concentration. Sigma metric values computed at different QC concentration levels can be quite different from one another. A patient-based sigma metric value uses the entire patient concentration range and represents the entire patient population.

Slide 34:
In conclusion, a patient-based sigma metric more accurately reflects the quality characteristics of a test method in the patient population.

An accurate estimation of sigma metric provides better guidance in designing laboratory quality control.

Later on in this series, I will discuss designing quality control strategy using sigma metrics. Stay tuned.

Slide 35: References

Slide 36: References

Slide 37: Disclosures

Slide 38: Thank You from www.TraineeCouncil.org

Thank you for joining me on this Pearl of Laboratory Medicine on "Patient-based Sigma Metric" from the "QC Design: Things You Need to Know" series. I am Lakshmi Kuchipudi. These presentations are being created for the Pearls of Laboratory Medicine as part of the *Clinical Chemistry* Trainee Council.