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Editorials

Planning Statistical Quality Control to Minimize Patient Risk: It's About Time

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The purpose of statistical quality control (SQC)[2] in the clinical laboratory is to assure that reported patient results are fit for their intended use, not only when a measurement procedure is operating in its stable incontrol state, but also when out-of-control conditions occur. The value of quality-control principles and practices in the laboratory has been well recognized and appreciated for many decades. The Clinical and Laboratory Standards Institute (CLSI; then known as the NCCLS) published its first approved guideline on statistical quality-control principles and definitions for quantitative measurement procedures in 1991 *(1)*. The fourth edition of the guideline appeared last year *(2)*.

For many years SQC design primarily involved choosing how many quality control (QC) samples to measure and what QC rules to apply to the QC results. This approach originated in an era when batch testing was common. QC samples were placed in the batch along with patient specimens. The QC sample results were used to decide if the patient results in the batch were acceptable. The goal was for the QC rule to have a low probability of rejection when the batch was in control (probability of false rejection, P_{fr}) and a high probability of rejection when the batch was out-of-control (probability of error detection, P_{ed}) *(3)*.

When continuous-production analyzers became prevalent in the laboratory, a new QC planning question arose: When should QC samples be measured? In batch testing, the answer was to measure QC samples with each batch. However, with continuous-production analyzers a link between QC results and patient results within a batch no longer exists. Instead, QC results simply reflect the current state of the measurement procedure at the time they are measured. Unfortunately, the traditional QC performance measures, P_{fr} and P_{ed}, only indicate how likely it is that a QC rule will reject when the QC rule is evaluated; they aren't affected by how frequently QC evaluations occur.

Another important trend affecting laboratory QC planning has been the increased attention to risk-management principles as exemplified in the publication of CLSI EP23-A, titled *Laboratory Quality Control Based on Risk Management; Approved Guideline (4)*. Risk-management principles place the focus of QC planning on the patient, not the laboratory's measurement procedures. The goal of laboratory QC should be to mitigate patient risk. The laboratory mitigates patient risk by designing QC strategies to assure that laboratory measurement procedures are operating in their stable incontrol state, but the measures used to assess the effectiveness of the laboratory QC strategies should be in terms of their impact on the risk of harm to patients.

Some of the substantive changes in the fourth edition of CLSI's C24 document reflect the importance of QC scheduling in the modern laboratory and the need to evaluate the effectiveness of a QC strategy more directly in terms of patient risk *(5)*. Among other things, the fourth edition introduces several additional performance measures for assessing quality-control performance. One in particular is the expected number of erroneous patient results produced and reported during the existence of an out-of-control condition before it is detected. The expected number of erroneous patient results produced because of an out-of-control condition will depend on the quality requirement (erroneous results contain measurement errors that exceed the quality requirement), the power of the laboratory's QC rule (P_{ed}), the laboratory's QC schedule (frequency of QC evaluations), and the magnitude of the out-of-control condition. Thus, it is a measure that more directly relates to patient risk and depends on both the power of the laboratory's QC rules as well as how often QC samples are evaluated.

Computation of the expected number of erroneous patient results produced because of an out-of-control condition has been described in the literature in which it has been referred to as the expected number of unacceptable results or the expected number of unreliable results *(6, 7)*. The terms "unacceptable" and "unreliable" are synonymous with the term "erroneous" and refer to results containing measurement errors that exceed the

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[2] Nonstandard abbreviations: SQC, statistical quality control; QC, quality control; CLSI, Clinical and Laboratory Standards Institute; P_{fr}, probability of false rejection; P_{ed}, probability of error detection; MaxE(Nuf), maximum expected number of unreliable final patient results.

quality requirement. The computation of the expected number of erroneous patient results can be divided into 2 components: the expected number reported and never corrected (final results), and the expected number that were either being held at the time the out-of-control condition was detected, or were reported but then corrected before being acted on (correctable results). Final erroneous patient results create hazardous situations for patients and may lead to patient harm. Correctable erroneous patient results are a quality cost to the laboratory *(8)*.

In this issue of *Clinical Chemistry*, Westgard et al. seek to provide laboratories with some practical guidance for planning risk-based SQC schedules *(9)*. The authors correctly point out that CLSI C24, fourth edition, stresses the importance of QC scheduling and its impact on patient risk, but because its purpose is to provide a general roadmap for designing QC strategies based on quality control and risk-management principles, it refrains from proposing or endorsing any specific methodology for choosing an appropriate QC schedule. The approach proposed and described by the authors is to find a QC rule, number of QC measurements, and frequency of QC evaluations such that the maximum expected number of unreliable final results due to an out-of-control condition, termed MaxE(Nuf), is less than or equal to 1. They provide nomograms to help determine the number of patient specimens that can be measured between QC events to limit MaxE(Nuf) to <1 on the basis of the QC rule used and number of QC measurements evaluated at each QC event.

The various QC rule power curves employed by the authors appear to be based on 400–1000 simulated trials at 7–9 different magnitudes of out-of-control conditions that were performed over 35 years ago *(10)*. Instead of taking advantage of modern computing power to produce more complete power curves based on significantly larger numbers of simulated trials, the authors fit polynomial curves to the limited and dated simulation data to estimate MaxE(Nuf) values *(11)*. However, even with these shortcomings the nomograms should provide some useful guidance regarding how many patient specimens can reasonably be examined between QC evaluations to be assured that not too many erroneous patient results are reported when out-of-control conditions occur in a measurement procedure.

While planning a QC strategy to limit the maximum expected number of erroneous patient results reported owing to the occurrence of an out-of-control condition in the measurement procedure is an important step forward in more directly relating laboratory QC to patient risk, such planning does not get us all the way there. Reporting an erroneous patient result creates a hazardous situation for the patient that may lead to patient harm, but it is not the same thing as patient risk. Risk-management guidelines define patient risk as the combination of the probability of occurrence of patient harm and the severity of the harm. The probability of occurrence of patient harm not only depends on the number of erroneous patient results that are reported owing to the occurrence of an out-of-control condition in the measurement procedure, but also on how often out-of-control conditions in the measurement procedure occur (measurement procedure reliability) and how likely it is that an erroneous reported patient result leads to an inappropriate medical decision or action that causes patient harm.

Many of the new QC planning parameters that impact patient risk are about time: the length of time between QC evaluations, the expected time between occurrences of out-of-control conditions, and the expected time required to identify and correct erroneous patient results before they are acted on. Incorporating these additional parameters into a full patient-risk model is the next step in planning statistical QC strategies to minimize patient risk; and it's about time.

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