Managing twinned analysers in clinical chemistry laboratories

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Analysers in medical laboratories are often doubled either to increase the analytical throughput or to guarantee the customer a constant turnaround time in spite of unavoidable breakdowns or halts for maintenance. Using two different instruments for the same test means that successive samples from a given patient may be randomly assayed on anyone of the two instruments. For example, this configuration of twinned analysers is implemented in the authorôs laboratory for

- Blood gas
- Emergency immunochemistry (chiefly cardiac markers)
- Basic chemistry

The obvious drawback of twinned analysers is the bias that is likely to occur between them. The calibration process of the presently marketed clinical chemistry analysers is very far from a genuine metrological procedure. Calibration assays are generally repeated only twice which leads to a significant uncertainty of set points.

In routine work, twinned analysers are independently calibrated so that each one is affected by a random and independent error of its set point. We cannot therefore rely upon calibration to equalize them. A variable bias between the two instruments is unforgiving. The discrepancy may range within an interval of [± 3 SD] (where SD is the standard deviation of each instrument). This potential error is unacceptable for low capability analytical methods.

Managing twinned analysers requires not only an efficient separate QC but also a continuous monitoring of the bias between instruments. Any significant deviation should be corrected as soon as possible by adjusting one set point or both. Three inappropriate practices must be discarded :

- Setting up as twinned analysers two instruments of different brands, that are not using the same reagents and the same calibrators. Some clinical chemists are wrongly thinking that they can rely upon a slope and an intercept resulting from a method comparison to cancel out the bias between their analysers. This computation surely cancels out the average bias between instruments but not the individual difference of biases for every patient.

- Planning weekly or monthly reviews of the means of control material to decide whether the twinned analysers were equalized or not. This a posteriori control is much too late.

- Comparing the Levey-Jennings charts of the twinned tests: This comparison is not very informative even when both QC plots are painted on the same screen. QC points are too much scattered on the plots to provide an efficient visual indicator of the difference between set points.

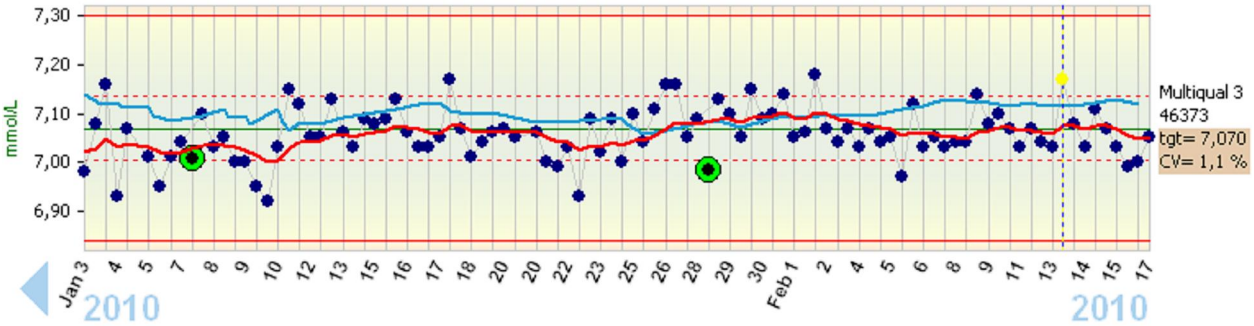
The paired moving averages

MultiQC7 proposes an alternative way to monitor the bias of twinned analysers : The paired exponentially weighted moving averages (PEWMA) of control materials : At first, twinned analytes must be controlled with the same materials. Then the two moving averages are simultaneously plotted on the same chart. They are paired on the basis of the same date.

The exponentially weighted moving average (EWMA) is a cumulative score that weights the earlier observations successively less than subsequent observations in such a way as to automatically phase out distant observations almost entirely. The EWMA is both

- a statistical process-monitoring tool: It detects the presence of assignable causes that result in a process shift (*bias*).
- a forecast of where the process will be at the next time period. An estimate of the bias of a method is given by the difference between the EWMA and the target. This estimate can be used as the basis for a dynamic process-control algorithm to determine how much adjustment is necessary.

For every analyte MultiQC draws the EWMA line (red in the picture below) superimposed over the regular Levey-Jennings chart. When the analyte is twinned with another one, a second EWMA line (light blue below) is added to the main chart to provide the clinical chemist with a simultaneous and real time display of both individual biases (the distance of each EWMA line to the target line) and of the bias between tests (distance between the two EWMA lines).



K^+ assay on twinned analysers

Main analyser
- QC points
- EQA target flags
- EWMA
- Control limits of the EWMA

Twin analyser
- EWMA

Remarks

- The QC assays for an analyte are not necessarily done at the same time as those of its twin. Furthermore an analyte may be controlled twice or thrice whilst its twin is controlled once or vice versa. Time scales do not coincide. To be able to pair the two EWMA lines, MultiQC must therefore locally expand/shrink the time scale of the twin before inserting it in the time scale of the main analyte.

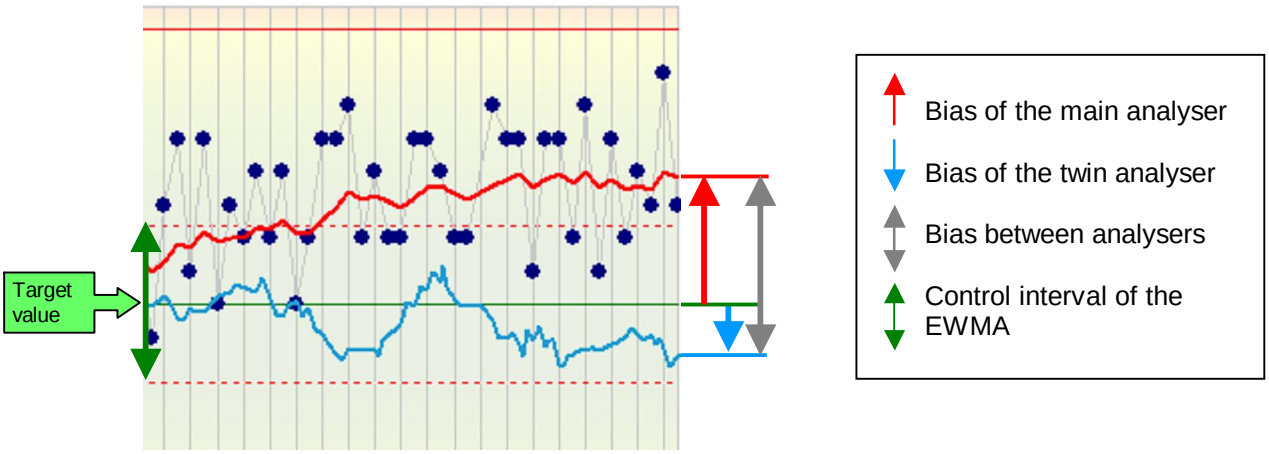
- The plot of paired moving averages only shows the QC points of the main analyte. The QC points of the twin analyte are hidden not to cram the chart with useless marks.

- The smoothing factor λ of the main analyte is applied to both EWMA lines, even if the twin analyte has a different factor. Thus the red and the blue lines are comparable because equally smoothed.

Equalizing twinned analysers

The paired moving averages are aimed at monitoring the bias of twinned analytes and at suggesting calibration adjustments as soon as the gap becomes too high. In the picture below, the bias reaches about 2 SD (grey double arrow). Such a discrepancy is too big for a low capability method. It

should trigger a corrective action. The twin analyser (blue curve) is pretty much stable whilst the main one (red curve) has drifted of about +1.5 SD from its target value.



The EWMA of the main analyser (red line) has drifted out of the control interval whereas the twin analyser (blue line) is more stable. Equalizing the twinned analysers may be necessary if the capability of the analytical method is low.

Because of the uncertainty of the calibration process mentioned above, it would be fruitless to try to reset the main analyser to its genuine set point thanks to another calibration. This might equally either improve or worsen the situation. Presently sold analysers are not able to guarantee calibration biases less than ±2.0 SD (in good conditions).

The only way to equalize the main analyser with its twin is to manually tune the calibration factor in an engineering process control fashion. The drift of the EWMA provides us with the precise value of the required adjustment. Unfortunately, direct access to calibration factors is rarely available on todayôs medical laboratories instruments. Manufacturers are more and more forbidding what they call ñfudge correctionsò hoping to guarantee a floor level of (poor) analytical quality with unskilled operators. If you are a skilled and perfectionist clinical chemist you have to purchase another instrument that allows feedback adjustments of calibration factors.

Software of clinical chemistry analysers often have entry fields named *Slope* and *Intercept*. These coefficients cannot help us because they are intended for a definitive change of analytical methods. They are used for adjustment factors that create permanent shifts. The best example is the compensation of creatinine Jaffe assay to match the ID-MS method.

What we need is a direct access to the calibration factors to be able to slightly adjust them when the EWMA shows that a feedback action is necessary. This adjustment is provisional. It must disappear with the next calibration.

further reading : www.multiqc.com