Bayesian modification of the CUSUM plot to monitor quality of treatment in small patient series with unfinished follow-up

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The CUSUM plot showing the cumulated sum of events in a consecutive series of patients is the simplest control chart for monitoring hospital services. Application may be difficult, however, if the process comprises few patients, if the case mix fluctuates, and if the observation time is long. We have developed adaptations of the plot to monitor outcome of treatment in children with Acute Lymphoblastic Leukemia (ALL) in a low-volume center.

Methods: CUSUM plotting was applied retrospectively to a series of 39 children with ALL treated on the Nordic 1992-2000 protocol. Final results are known (five-year event free survival P(EFS) overall and for children stratified to standard, intermediate and high risk chemotherapy). A plot indicating whether local outcomes were more likely to result from the average Nordic success:failure ratio or from an inferior ratio was incorporated. Each case was considered a test of “healthy” versus “sick” performance, like in Bayesian diagnosis: the likelihood ratio for each observed outcome was weighted by taking log to base 2 and the sequential weights cumulated. Next, plotting was applied prospectively to 30 children on the ongoing Nordic 2008 protocol, for which interim Kaplan-Meier curves are reported every year. Individual P(EFS) values corresponding to follow-up time was read off the appropriate risk group curve, an estimate of expected events being then given by – ln P(EFS).

Results: In the 1992 protocol the overall Nordic success:failure ratio was 78%:22%. In our series 10 events were observed, exceeding the expected 8.6 events. CUSUM (OBS-EXP) showed a “bad run” followed by a “good run”. Correcting for case mix by using risk-group specific P(EFS) values did not change the curve. CUSUM (Weights) reached a nadir of -1.66 after 20 patients, rising thereafter to +0.04, i.e. equivalence between the two hypotheses. In the 2008 series children have been followed for 2-65 months, and so far only one event has occurred. CUSUM (OBS-EXP) shows a “deficit” of 1.85 events, and CUSUM (Weights) is +1.20. Thus, odds favoring acceptable performance are greater than 2:1.

Conclusions: A Bayesian curve monitoring whether treatment results are good or poor can be included in CUSUM plots, and it can be applied prospectively to cohorts with unfinished follow-up.