DETECTING TRENDS IN NOISY DATA SERIES: APPLICATION TO THE DETECTION OF PSA FAILURE, DEFINED AS THREE CONSECUTIVE PSA RISES IN MEN TREATED FOR PROSTATE CANCER

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When studying longitudinal data, it is common to define an event based on a sustained rise (or decline) of the observations. However, data may be subject to variability independent of the event, and appropriate statistical methods are necessary to account for these extraneous variations. We propose a method to evaluate rules that define events based on consecutive increases (or decreases) of observations, given the presence of extra-variability. We illustrate our approach using post-radiotherapy series of prostate-specific antigen (PSA).
PSA is used as a monitoring tool for prostate cancer recurrence following radiotherapy. The ASTRO criterion defines PSA failure as three consecutive PSA increases. This *rule of three* is widely used, but has been criticized for its low classification performances.
We carried out a numerical validation study of this criterion, and examined its short-term performance in correctly identifying a truly rising PSA trajectory (sensitivity), and how often it can recognize a truly stable series for what it is (specificity). Our method relies on the simulation of realistic, sophisticated data sets that accurately reflect the systematic and random variations observed in such series. We first fitted an appropriate model to real PSA series, and then simulated new data from this model. These flexible *empirically based simulations* allow one to evaluate various biochemical failure rules, and measurement schedules. The approach can be applied to evaluate other rules that purport to rapidly and accurately detect up (down) turns in noisy series, such as in other medical data, and data series used to monitor economic trends.