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"From the analytical uncertainty to uncertainty in data interpretation"

by D Concordet, JP Braun

The main determinants of biological data interpretation are the clinician experience and the different sources of variations of the data to be interpreted. Some of these sources of variations are of biological nature (e.g. demographic variables, disease, intra and inter individual variations) others, are linked to the metrology properties of the constituent being measured. Imprecision is usually well managed and controlled allowing adequate intra-laboratory comparisons. Accuracy is necessary to ensure proper inter-laboratory transferability, comparison of results, and reference to the literature; unfortunately, accuracy is very often poor, even for the most frequently measured analytes such as plasma creatinine, thus greatly limiting its medical use.

The intrinsic performances of a biological test for the diagnosis of a disease are described by its sensitivity and specificity which represent the percentage of diseased animals having a positive result(true positive) and the percentage of non-diseased animals having a negative result (true negative) respectively. Any other variable that makes the tested analyte vary (whatever its nature) decreases the intrinsic performance of the test. The imprecision in the evaluation of sensitivity and specificity depend on the numbers of subjects tested and for specificity on the characteristics of the population studied (ie. healthy subjects vs. Healthy subjects + subjects having other diseases)
In some cases, it is possible to increase these performances by adjusting the threshold used to declare an animal positive to the identified source of variation.
The predictive value of a positive (negative) result (PVP/PVN) is the probability that an animal testing positive (negative) is sick (healthy). Both depend on the intrinsic performances of the test but also on the clinician's experience. The experience of the clinician can be roughly summarized by its evaluation, before the test, of the probability that the animal is sick in individual medicine or the prevalence of the disease in collective medicine. The diagnostic gain is thus defined as the difference between the positive predictive value and this probability.
Most often estimations of PVP and PVN do not take into account the imprecision in the estimation of sensitivity, specificity of pre-test probability, which can result in overconfidence and possibly in erroneous medical decisions, eg when Se = Sp = 0.80 estimated in groups of 50 healthy and diseased animals respectively, and pre-test probability = 0.25 ± 0.05, then PVP ranges from 0.41 to 0.68, ie from less than coin-tossing to a relatively high probability (2/3).