# CLINICAL PERFORMANCE CHARACTERISTICS

## A. Definitions

### 1. Diagnostic sensitivity and specificity

The **diagnostic sensitivity** (true positive rate) indicates the effectiveness of an IVD medical device in correctly identifying patients who have a particular disease or condition.

The **diagnostic specificity** (true negative rate) indicates the effectiveness of an IVD medical device in correctly classifying patients that do not have a particular disease or condition.

**NOTE:** The diagnostic sensitivity and diagnostic specificity depend on the choice of a cut-off value (e.g. to separate negative from positive values).

Prevalence of the disease targeted has a high impact on the accuracy of screening tests and diagnostic tests. A new biomarker test for a rare disease would have to be extremely accurate (specific) in order to not produce many false positive results amongst the high excess of not-affected people.

For example: The prevalence of a disease is about 20 cases/100 000 individuals, all of whom belong in the target population of the test. If you use an assay with 99 % diagnostic sensitivity and 99 % specificity, and test all the 100 000 individuals, you will probably catch all the 20 cases with the disease. However, if the diagnostic specificity of your assay is 99 %, you will get 1 % of false positive results, which is 1 000 cases. This means 50 false positives for each true positive case. If your diagnostic specificity is 95 %, you will get 5 % false positives, which is 5 000 cases, 250 for each true positive.

### 2. Diagnostic accuracy

The **accuracy** is the overall probability that a patient will be correctly classified.

### 3. Predictive Value

The **positive predictive value** indicates the effectiveness of an IVD medical device in separating true positive results from false positive results for a given attribute in a given population.

The **negative predictive value** indicates the effectiveness of an IVD medical device in separating true negative results from false negative results for a given attribute in a given population.

**NOTE:** The expected predictive value depends on the prevalence[1] of the disease or condition in the population of interest.

If the sample sizes in the positive (disease present) and the negative (disease absent) groups do not reflect the real prevalence of the disease, then the positive and negative predicted values, and accucary, cannot be estimated and you should ignore those values.

Alternatively, when the disease prevalence is known then the expected positive and negative predictive values can be calculated.

[1] i.e. the percentage of a population that is affected with a particular disease at a given time

## B. Calculations

| Disease / Test | Present (n) | Absent (n) | **Total** |
|---|---|---|---|
| Positive | True positive (a) | False positive (c) | $\boldsymbol{a+c}$ |
| Negative | False negative (b) | True negative (d) | $\boldsymbol{b+d}$ |
| **total** | $\boldsymbol{a+b}$ | $\boldsymbol{c+d}$ | $\boldsymbol{a+b+c+d}$ |

| ***Clinical performance characteristic*** | ***Formula*** |
|---|---|
| **diagnostic sensitivity (true positive rate)** | $\frac{a}{a+b}$ |
| **diagnostic specificity (true negative rate)** | $\frac{d}{c+d}$ |
| **false positive rate** | $\frac{c}{c+d} = 1 - sensitivity$ |
| **false negative rate** | $\frac{b}{a+b} = 1 - specificity$ |
| **detected positive predictive value in the cohort[2]** | $\frac{a}{a+c}$ |
| **detected negative predictive value in the cohort[2]** | $\frac{d}{b+d}$ |
| **expected positive predictive value[2]** | $\frac{sensitivity \times prevalence}{sensitivity \times prevalence + (1-specificity) \times (1-prevalence)}$ |
| **expected negative predictive value[2]** | $\frac{specificity \times (1-prevalence)}{specificity \times (1-prevalence) + (1-sensitivity) \times prevalence}$ |
| **diagnostic accuracy** | $\frac{a+d}{a+b+c+d}$ |

[2] If the sample sizes in the positive (Disease present) and the negative (Disease absent) groups do not reflect the real prevalence of the disease, then the Positive and Negative predicted values, and Accucary, cannot be estimated and you should ignore those values.
Alternatively, when the disease prevalence is known then the expected positive and negative predictive values can be calculated.