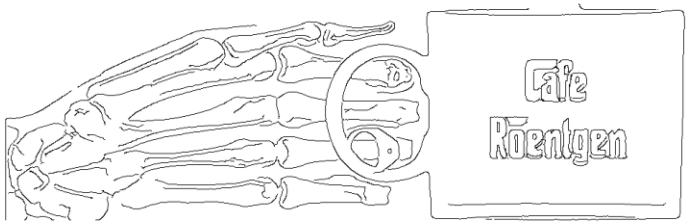
TATA MEDICAL CENTER



Diagnostic tests and how to test them

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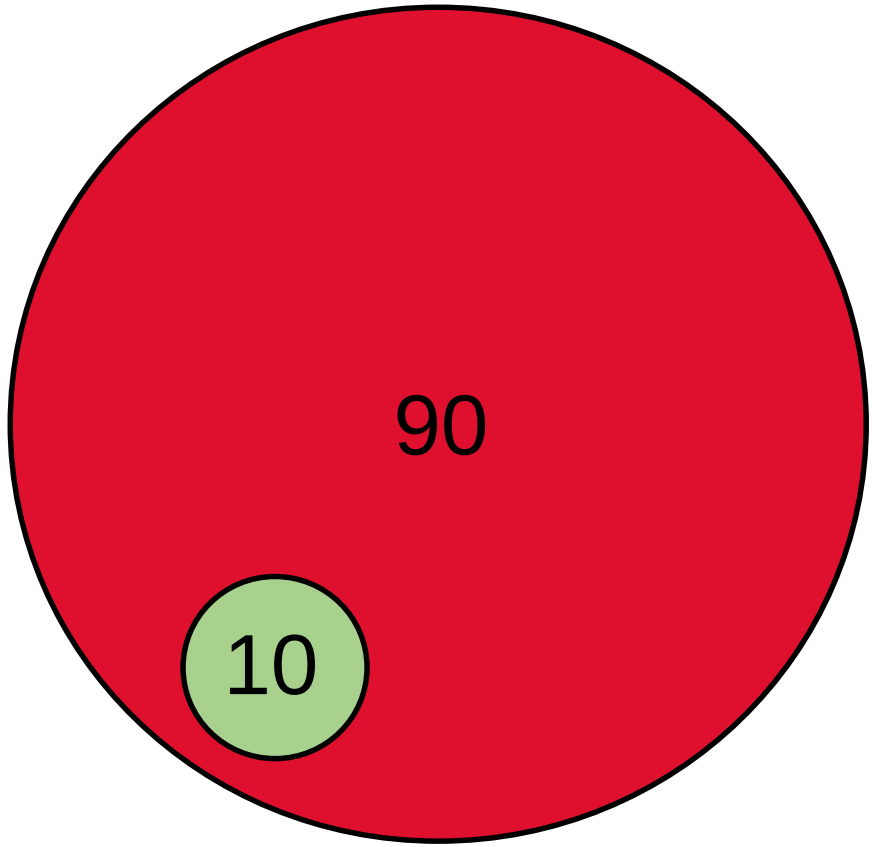
Gold standard:

- Must be more elaborate/ risky/ time consuming/ expensive.
- Must have least error/ bias
- Must be different from the test in question!

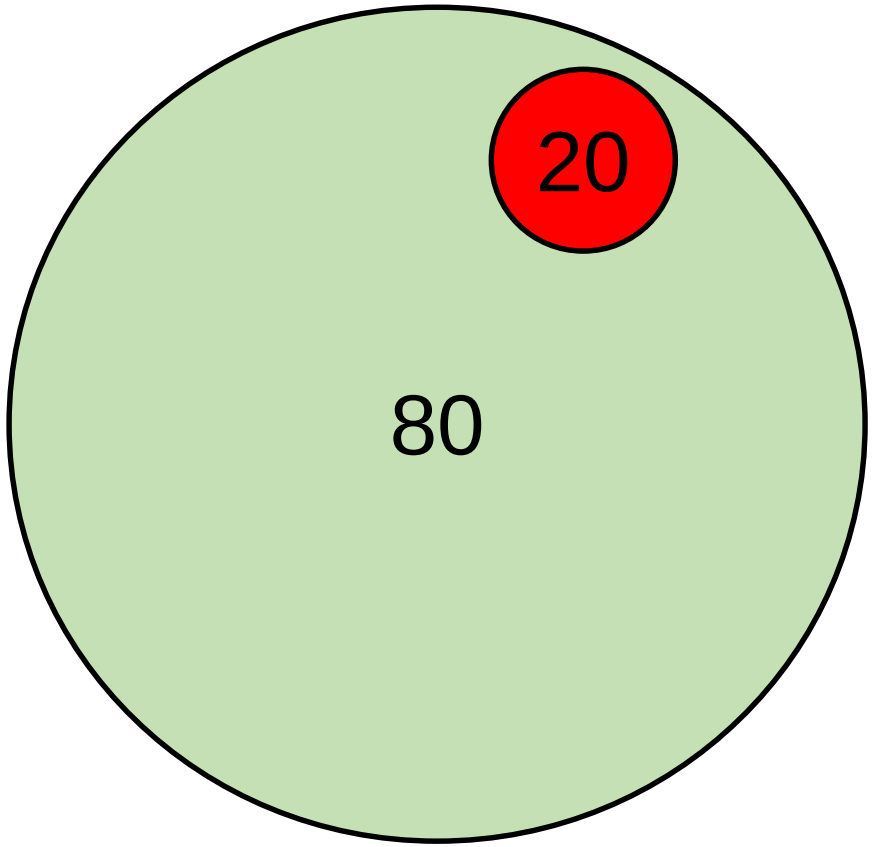
How good is the diagnostic test?

- How many diseased and non-diseased can be correctly identified?
  - If I perform this test on 100 diseased persons how many will be positive?
  - If I perform this test on 100 normal persons how many will be negative?
- The diagnosis of “diseased” vs “not diseased” is obviously made by the Gold/ reference standard.

How good is the diagnostic test?



100 people with disease



100 people without disease

How good is the diagnostic test?

	Disease present (D+)	Disease absent (D-)	Total
Test positive (T+)	90	20	110
Test negative (T-)	10	80	90
Total	100	100	200

How many diseased and non-diseased can be correctly identified?

- Sensitivity tells you if you perform this test on 100 diseased people how many will be positive?
- Sensitivity = True positive/ Total diseased.
- Specificity tell you if you perform this test on 100 normal people how many will be negative?
- Specificity = True negative/ Total non-diseased.

How good is the diagnostic test?

- Sensitivity and specificity are indicators how good a test is compared to a gold standard.
- Sensitivity and specificity describe test performance in people with ***known disease status***.
- These are ***not dependent on disease prevalence***.
- It tells you nothing about how likely disease is present in a particular patient.

How sure are you that disease is present?

	Disease present (D+)	Disease absent (D-)	Total
Test positive (T+)	90	20	110
Test negative (T-)	10	80	90
Total	100	100	200

- Positive predictive value tells you if 100 people are positive how many will have the disease?
- PPV = True positive/Total positive
- Negative predictive value tells you if 100 people are negative how many will not have the disease?
- NPV = True negative/ total negative

How sure are you that disease is present?

- PPV and NPV are indicators how well the test performs in real world.
- PPV and NPV describe test performance in people with ***unknown disease status***.
- These are ***dependent on disease prevalence.***

	Disease present (D+)	Disease absent (D-)	Total
Test positive (T+)	True positive	False positive	Total positive
Test negative (T-)	False negative	True negative	Total Negative
Total	Total disease	Total normal	Total population

"Snout" = **s**ensitive - **n**egative - **out**.

"Spin" = **s**pecific - **p**ositive - **in**

Sensitivity ignores false positives.

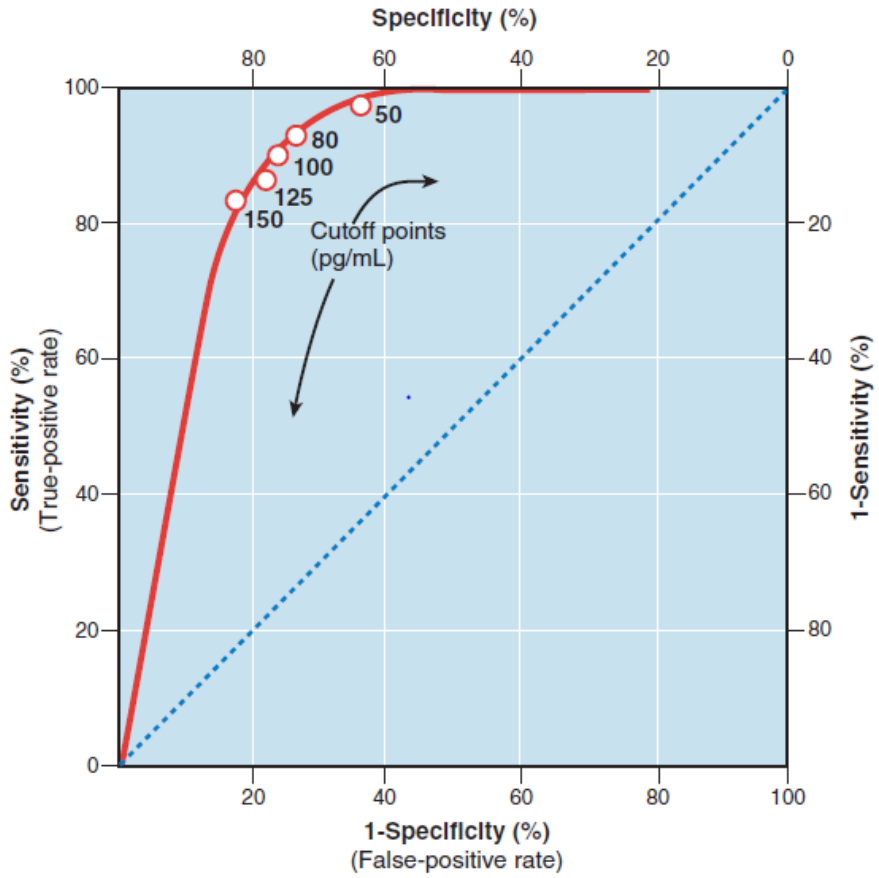
Specificity ignores false negatives.

However, in real life, if true positives are very high in number, false negative number approaches zero. So a very sensitive test tend to have very low false negative and consequently very high NPV.

How to calculate predictive value from prevalence?

- PPV = (Sensitivity x prevalence)/ [Sensitivity x prevalence + (1-specificity)x (1-prevalence)]
- NPV = [Specificity x (100-prevalence)]/[(100-sensitivity) x prevalence + Specificity x (100-prevalence)]

Dichotomy and cut-off



- Calculation of sensitivity, specificity and predictive value requires dichotomising of data [yes/no or disease present/absent].
- For test with continuous/ interval measurements ROC curve helps in selecting cut-off.

Summary

- How many will be positive if 100 diseased people are tested?

Sensitivity

- How many will be negative if 100 non-diseased people are tested?

Specificity

- How many among 100 test positives will have the disease?

PPV

- How many among 100 test negative do not have the disease?

NPV

Likelihood Ratio

Probability versus Odds

- Probability:
  - Rate of occurrence of an event
- Odds:
  - Probability of an event happening divided by the probability of the event not happening.

If a horse wins 80 out of 100 races, the probability of it winning the next race is 80% but the Odds of it winning the next race is (probability of winning ~ 80%)/(probability of not winning ~20%), i.e. 4 to 1. So if you bet against the horse you will get 4 rupees for every 1 rupees.

Probability = 80% and Odds = 4 or 4:1

Probability versus Odds

Probability

$$\frac{\text{Number of occurence of event under question}}{\text{Total number of events}}$$

Odds

$$\frac{\text{Probability of the event of occuring}}{\text{Probability of the event not occuring}}$$

$$=$$

$$\frac{\text{Probability}}{\text{1 - probability}}$$

$$\text{Probability} = \frac{\text{Odds}}{\text{1 + Odds}}$$

Probability versus Odds

$$\text{Pre test Odds} = \frac{\text{Pre test probability}}{1 - \text{pre test probability}}$$

Likelihood ratio

	Disease present (D+)	Disease absent (D-)	Total
Test positive (T+)	A	B	Total positive
Test negative (T-)	C	D	Total Negative
Total	Total disease	Total normal	Total population

- **Positive likelihood ratio [LR+]:**
  - Probability of a test being positive in a diseased person vs Probability of a test being positive in a non-diseased person.
  - (LR+) = [Probability of positive test in diseased] ÷ [Probability of positive test in non-diseased]

    = [A/(A+C)] ÷ [B/(B+D)]

    = Sensitivity/(1 - specificity).

[D/(B+D) = Specificity, hence, B/(B+D) = 1 - specificty]

Likelihood ratio

	Disease present (D+)	Disease absent (D-)	Total
Test positive (T+)	A	B	Total positive
Test negative (T-)	C	D	Total Negative
Total	Total disease	Total normal	Total population

- **Negative likelihood ratio [LR+]:**
  - Probability of a test being negative in a diseased person vs probability of a test being negative in a non-diseased person.
  - (LR+) = [Probability of negative test in diseased] ÷ [Probability of negative test in non-diseased]

    = [C/(A+C)] ÷ [D/(B+D)]

    = (1- sensitivity)/Specificity.

Meaning of likelihood ratio

- ***(LR+) = 5*** means if we run a test a positive result is 5 times more likely in presence of disease than in the absence of disease.
- ***(LR-) = 0.5*** means if we run a test a negative result is twice more likely in absence of the disease than in the presence of disease.

Pre-test Odds x Likelihood ratio = Post-test Odds

Calculation of pre-test and post-test probability

- Pre test probability means probability of having the disease even before any test is done. This usually means prevalence.
- Post – test probability means probability of having the disease after the test is done.
- Positive predictive value = post-test probability.

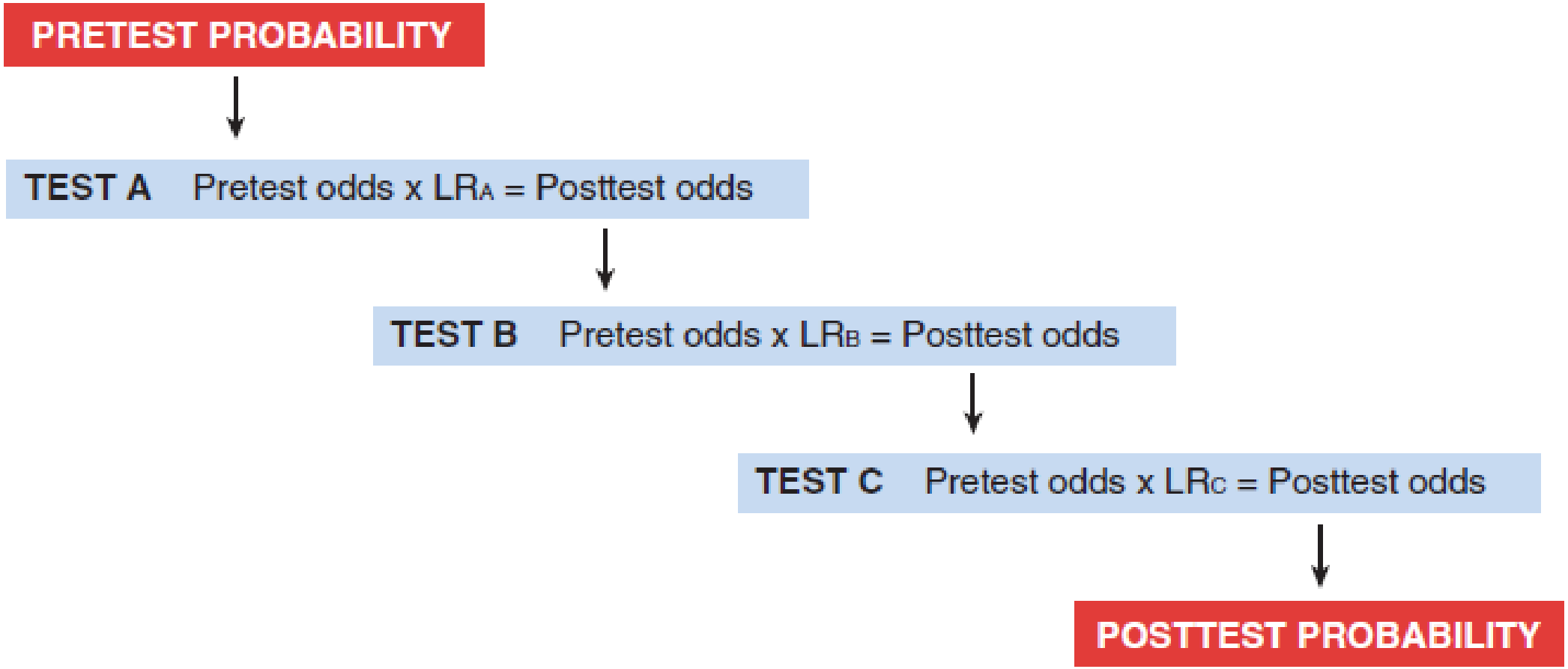
Calculation of post-test probability from LR:

- Prevalence of disease = pre-test probability [p]
- Pre-test Odds [d] = p/(1-p)
- Pre – test Odds x (LR+) = Post-test Odds [d’]
- Post – test probability (p’) = d’/(1+d’)

Advantages of likelihood ratio

- Can be applied at different levels of the same test. Does not require the dichotomous cut-off of sensitivity and specificity.
- Can be applied to serial tests to calculate the post-test probability after an entire battery of tests.

Advantages of likelihood ratio



Diagnostic tests

Inaccurate assessment of sensitivity and specificity

- Incorrect gold standard.
- Spectrum of patients:
  - Sensitivity is high in presence of severe disease.
  - Specificity is high in screening population.
- Bias.
  - Gold standard and index test should be different, independent of each other and blinded to each other.
- Statistical uncertainty/ chance
  - Always look at 95% confidence interval while reading a study.

Determinants of predictive value

- Sensitivity
- Specificity
- Prevalence

Always determine prevalence before performing the test to know the post-test probability.

- **How to increase pre-test probability?**
  - Specifics of clinical situation [History, examination, risk factors].
  - Demographics [GB cancer more likely in North India].
  - Referral process [rare diseases more common in teaching hospital].

Take home points

- Sensitivity and specificity tells you how good a test is.
- PPV and NPV tells how likely disease is present.
- Likelihood ratio helps you calculate probability of disease at multiple levels of same tests and after serial tests.
- While reading a paper check for chance and biases.
- Before ordering a test increase the pre-test probability.
- Never forget what is the prevalence of the disease in question – never expect a zebra when you hear hooves.