Sensitivity and Rates

Specificity and Rates

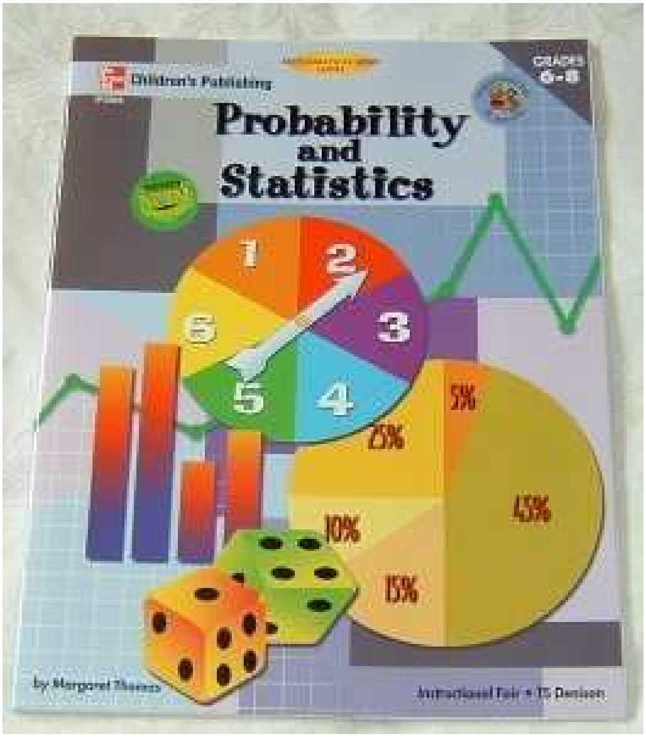
Receiver operator characteristics and Cut-Off points

Bonferroni

Prevalence

Likelihood ratios

Snnout and Sppin



Sensitivity

Test result	Sub-population known to be positive	Sub-population known to be negative
+ve	A True positives	B False positives
-ve	C False negatives	D True negatives

Answers the following question:-

• What proportion of those patients who have the disease will have a positive result?

Calculated as follows:

• True positives / (total patients with disease)

• Also known as true positive rate.

• Complement is (1 - false negatives)

• Requires enough information to be able to create a 'four-fold' table.

• The key property when the goal is to exclude a disease.

Rates

Note that sensitivity was referred to as the 'true positive rate'

Why talk about rates?

• First, sensitivity itself is a rate.

i.e.- chances out of 100 that someone with the disease will have a positive test.

• Second, it is the first step in freeing sensitivity from the effects of prevalence, which makes it a much more useful property as will be discussed later.

• Third, it leads to useful derivations such as the complement. i.e. 1 minus the false negative rate

In this case, 1 equals 100%

Consequently, if the sensitivity was 85%, the true positive rate would be 0.85 and the false negative rate 0.15.

Specificity

Test result	Sub-population known to be positive	Sub-population known to be negative
+ve	A True positives	B False positives
-ve	C False negatives	D True negatives

Answers the following question:
What proportion of those patients who do not have the disease will have a negative result?

Calculated as follows:
True negatives / (total patients without disease)

- Also know as true negative rate.
- Complement is (1 - false positives)
- Requires enough information to be able to create a four-fold' table.
- The key property when the goal is to confirm a disease.

Rates again

Note that specificity was referred to as the 'true negative rate'
Why talk about rates, again?

- Again, specificity itself is a rate.

i.e.- chances out of 100 that someone without the disease will have a negative test result.

- Second, it is the first step in freeing specificity from the effects of prevalance, which makes it a much more useful property and will be discussed later.
- Third, it leads to useful derivations such as the complement. i.e. 1 minus the false positive Rate

In this case, 1 equals 100%

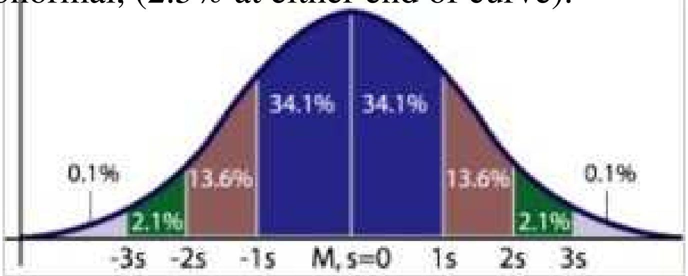
Consequently, if the specificity was 87%, the true negative rate would be 0.87 and the false positive rate 0.13.

Receiver operator characteristics

• As the sensitivity, or true positive rate, increases so does the false positive rate. • Some believe (erroneously) that sensitivity can be increased without increasing false positive rate.
• But, for any test cut-off point, the true positive rate can be plotted against the false positive rate to produce a receiver operator curve.
• These graphs show that as sensitivity is increased, so is number of false positives. Conversely, any manipulation to reduce the number of false positives reduces sensitivity.

Cut-Off Points

• The cut-off point or value for any test is critical to sensitivity and specificity. The lower the point, the higher the sensitivity and the lower the specificity, and vice versa.
• Cut-off points are totally arbitrary but are usually based on a curve of normal distribution.
• Arbitrarily, "normal" is defined as within two standard deviations from the mean, automatically defining 5% of the population as abnormal, (2.5% at either end of curve).



Dark blue is less than one standard deviation from the mean. For the normal distribution, this accounts for 68% of the set while two standard deviations from the mean (blue and brown) account for 95% and three standard deviations (blue, brown and green) account for 99.7%.

Cut-Off Points

Although this methodology is in universal use, there are significant disadvantages

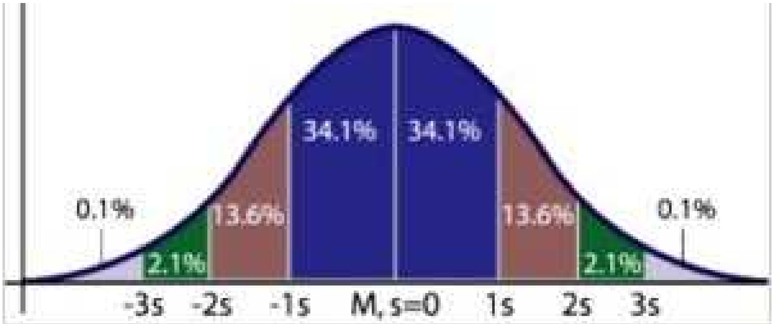
• 5% of population will test "abnormal" but be potentially disease-free.

• Population from which test values initially derived not necessarily disease-free.

• Distribution of most biological substances follow skewed rather than normal curve.

• Most labs do not adjust values for age, gender, diet, time of day, activity etc.

Consequently, you must understand limitations of testing before rushing to accept results.



Dark blue is less than one standard deviation from the mean. For the normal distribution, this accounts for 68% of the set while two standard deviations from the mean (blue and brown) account for 95% and three standard deviations (blue, brown and green) account for 99.7%.

Bonferroni

A mathematician with important contributions to the theory of probability. He created a formula for adjusting the p number (statistical significance) for those situations in which over-exuberant researchers carried out multiple investigations on the same data set. (Sound familiar?)

- Bonferroni's phenomenon allows the forecast of an abnormal result, based simply on the number of tests ordered.
- In the age of multi channel and parallel investigations, there will likely be a greater chance of laboratory abnormality than not, based simply on testing having taken place.

Specimen calculation

1 - (.95)12

= 1 - (.54)

= (.46)

= 46% probability that a healthy, asymptomatic person will have an abnormality on SMA12

Prevalence

Exercise stress testing

ETT	Disease present 900	Disease absent 100	PPV*
+ve	774	23	97%
-ve	126	77	62%
	Sens 86%	Spec 77%	

* Positive predictive value

Sensitivity and specificity are fixed properties that do not change once the cut-off point has been fixed. However, the ability of a test to predict the true state of affairs changes constantly dependent on the prevalence of the disease in question.

• In the examples, note that sensitivity and specificity remain unchanged at 86% and 77% respectively.
• However, positive predictive value is tested at disease prevalence of 90% and 10% with wildly differing results, 97% and 29%.
• Also, negative predictive value tested at disease prevalence of 90% and 10% is equally variable, 62% and 2%.
• The test is good at confirming the suspected disease when the prevalence of the disease is high, and good at excluding the disease when the prevalence is low. How useful is that?
• The most important variable is not the test, its the prevalance!

Remember, at its most basic,
• If the prevalence of a disease is zero, any positive result is a false positive by definition.
Conversely,
• if the prevalence of a disease is 100%, any negative result must be a false negative.

Exercise stress testing

ETT	Disease present 100	Disease absent 900	PPV*
+ve	86	207	29%
-ve	14	693	2%
	Sens 86%	Spec 77%	

* Positive predictive value

Likelihood ratio

- In clinical situations (real life), the test result is known but its significance unclear.
- Consequently, the problem becomes deciding whether a result is a true or false positive, or negative, as the situation requires.
- For a positive result, this can be resolved by calculating the ratio of true positives to false positives.
- The true positive rate of a test is its sensitivity.
- The false positive rate is (1 - its specificity).
- This resolves as sensitivity / 1 - specificity.

This is known as the +ve Likelihood Ratio.

For a negative result, this can be resolved by calculating the ratio of false negatives to true negatives.

- The true negative rate of a test is its specificity
- The false negative rate is (1 - its sensitivity).
- Hence, the ratio of false negatives to true negatives is (1 - Sensitivity) / Specificity

This is known as the -ve Likelihood Ratio.
Why are these important?
Because the prevalence of any disease in primary care is rarely known at the time of service, but the likelihood ratio - a fixed property - can be used to create a post-test odds of a diagnosis being correct.
Naturally, this depends on an odds of the diagnosis being correct being estimated prior to testing

This is a fundamental step in diagnosis.

A Final Why

Sensitivity is often said to be the key property when the goal of a test is to exclude a disease.

WHY?

- Consider the not unusual test characteristics of sensitivity of 93% and specificity of 85% and consider the test result to be negative!
- This gives a true negative rate of 0.85 and a false negative rate of .07
- In other words, true negatives outweigh false negatives by 12:1

Hence the phrase SNNOUT

A sensitive test that is negative rules out the condition tested for.

There is a corresponding acronym for a test with a high specificity, that is useful for ruling in a diagnosis, SPPIN.
That is, A specific test that is positive rules in the diagnosis.

Work out the reasons for yourself using the steps used for the SNNOUT example.