BIOS:4120 – Introduction to Biostatistics
Unit 5: Probability (Screening Tests)

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Learning Objectives

At the end of this session, you should be able to:

- Explain the purpose of screening/diagnostic tests.
- Explain and calculate the following probabilities from a screening test: sensitivity; specificity; false positive; false negative; positive predictive value; negative predictive value; and prevalence.
- Define the law of total probability, and use it in appropriate situations.
- Define Bayes' theorem, and use it in appropriate situations.
- Calculate the relative risk and odds ratio.

Overview

- Screening Tests: Representative Data
- Bayes' Theorem
- Screening Tests: Case Partitioned
- Relative Risk and Odds Ratio

Screening Tests

- A *Screening Test* is used to determine whether an individual is likely, or unlikely to have, a particular disease or condition.
- Often, those who test positive on a screening test are then subjected to further testing to confirm or deny the diagnosis.
- Examples:
  Home pregnancy tests, Pap smears, HIV screening tests.

Screening Tests

- What would be characteristics of a good test?
- What use are screening tests? Why would we want them?

Screening Tests (Representative Data)

- Consider an individual selected at *random* from a defined population. Suppose that a screening test is administered to this individual.

- We define the following events:

$$
\begin{aligned}
D &= \text{the individual has the disease} \\
D^C &= \text{the individual does not have the disease} \\
T^+ &= \text{the individual has a positive test result} \\
T^- &= \text{the individual has a negative test result}
\end{aligned}
$$

Screening Tests (Representative Data)

- From a *random* sample of a defined population, we obtain the following data in regard to a diabetes screening test.
- What questions might we wish to ask about the test?

	True State of Disease		
	Diabetic	Not Diabetic	
Test Result	D	D^C	Total
Positive (T^+)	56	49	105
Negative (T^-)	14	461	475
Total	70	510	580

Screening Tests (Representative Data)

Test Result	True State of Disease: Diabetic D	Not Diabetic D^C	Total
Positive (T^+)	56	49	105
Negative (T^-)	14	461	475
Total	70	510	580

- If I have the disease what is the probability I will test positive?
- If I am disease free what is the probability I will test positive?
- If I test positive what is the probability that I have the disease?
- If I test negative what is the probability that I am disease free?

Sensitivity and Specificity

To assess how well a screening test performs, we consider the following probabilities:

- *Sensitivity*: The probability of obtaining a positive test result, given that the individual has the disease.

$$\text{Sensitivity} = P(T^+ \mid D).$$

- *Specificity*: The probability of obtaining a negative test result, given that the individual does not have the disease.

$$\text{Specificity} = P(T^- \mid D^C).$$

Sensitivity and Specificity

- Sensitivity and specificity each measure the probability of the test making the **correct** classification, **given** the disease status.
- The complements of these measures are called *False Negatives* and *False Positives*.

False Negative and False Positive

- A *False Negative* occurs when a negative test result is obtained for an individual who has the disease.

- The probability of a false negative is given by

$$P(T^- \mid D) = 1 - P(T^+ \mid D) = 1 - \text{sensitivity}.$$

- A *False Positive* occurs when a positive test result is obtained for an individual who does not have the disease.

- The probability of a false positive is given by

$$P(T^+ \mid D^C) = 1 - P(T^- \mid D^C) = 1 - \text{specificity}.$$

Screening Tests (Representative Data)

	True State of Disease		
Test Result	Diabetic D	Not Diabetic D^C	Total
Positive (T^+)	56	49	105
Negative (T^-)	14	461	475
Total	70	510	580

For our data:

- What is the sensitivity of the test?
- What is the specificity of the test?
- What is the false negative rate?
- What is the false positive rate?

Screening Tests

- So far we have only answered the first two of the four questions we posed earlier.
- Screening tests are also designed to address the other two very important diagnostic questions:
  1) Given that the test is positive, what is the probability the individual has the disease?
  2) Given that the test is negative, what is the probability the individual does not have the disease?

Positive and Negative Predictive Value

- The *Positive Predictive Value* (PV^+), is the probability that the individual has the disease, **given** that he/she has a positive test result, i.e.,

$$PV^+ = P(D \mid T^+).$$

- The *Negative Predictive Value* (PV^-), is the probability that the individual does not have the disease, **given** that he/she has a negative test result, i.e.,

$$PV^- = P(D^C \mid T^-).$$

Screening Tests (Representative Data)

	True State of Disease		
Test Result	Diabetic D	Not Diabetic D^C	Total
Positive (T^+)	56	49	105
Negative (T^-)	14	461	475
Total	70	510	580

For our data:

- What is the positive predictive value of the test?
- What is the negative predictive value of the test?

Recommendation

- Many texts will present formulas for the calculation of sensitivity, specificity, and so on, with reference to a labeled cell count notation – a, b, c, d.
- My recommendation to you is to not rote learn those formulas, but to understand the concept behind each term and use that knowledge to make the necessary calculations.

Example: Saliva Test (Case Partitioned)

- King et al. (1995) studied the accuracy of a saliva collection and testing protocol for the determination of HIV antibody status.
- The 1,256 study participants included:
  1. HIV-positive individuals attending an HIV/AIDS treatment clinic ($n = 331$),
  2. HIV-positive clients of an outpatient hemophilia clinic ($n = 16$),
  3. self-referred clients of an outpatient AIDS testing clinic ($n = 478$),
  4. individuals contacted by a street-based outreach program ($n = 431$).
- Standard serum testing methods were used as the 'gold standard' to verify actual HIV status.

Example: Saliva Test (Case Partitioned)

- The results were as shown in the table below.

	HIV Antibody Status		
Saliva Test	Positive (D)	Negative (D^C)	Total
Positive (+)	358	2	360
Negative (−)	10	886	896
Total	368	888	1,256

Example: Saliva Test (Case Partitioned)

a) Estimate the sensitivity of the test.

b) Estimate the specificity of the test.

c) Can the positive predictive value and negative predictive value be estimated directly from these data? Why or why not?

Example: Saliva Test (Case Partitioned)

For these data we are able to calculate the:

- Sensitivity (and false positive rate)
- Specificity (and false negative rate)

We are unable to calculate the:

- Positive predictive value
- Negative predictive value
- Prevalence of disease

Example: Saliva Test (Case Partitioned)

In order to be able to calculate the positive and negative predictive values we will need to:

- know the disease prevalence in the population of interest
- do some probability calculations

Bayes' Theorem

- Consider two events A and B.
- Suppose we know the following probabilities:

$$P(B|A), P(B|A^C), P(A), P(A^C).$$

- Can we use these probabilities to find $P(B)$?
- Can we use these probabilities to find $P(A|B)$?
- Result:

$$P(B) = P(B|A)\,P(A) + P(B|A^C)\,P(A^C).$$

- The preceding is often called the *Law of Total Probability*.

Bayes' Theorem

- Justification: Consider representing the event B as the union of two mutually exclusive parts, $A \cap B$ and $A^C \cap B$.

- The rule now follows by application of the additive rule (for mutually exclusive events) and the multiplicative rule.

Bayes' Theorem

- Result:

$$P(A|B) = \frac{P(B|A)P(A)}{P(B|A)P(A) + P(B|A^C)P(A^C)}$$

- The preceding is called *Bayes' Theorem* or *Rule*.

Bayes' Theorem

- Justification:

$$P(A|B) = \frac{P(A \cap B)}{P(B)}$$

- Now use the multiplicative rule for the numerator and the law of total probability for the denominator:

$$\begin{aligned} P(A \cap B) &= P(B|A)\,P(A), \\ P(B) &= P(B|A)\,P(A) + P(B|A^C)\,P(A^C). \end{aligned}$$

- And hence,

$$P(A|B) = \frac{P(A \cap B)}{P(B)} = \frac{P(B|A)P(A)}{P(B|A)P(A) + P(B|A^C)P(A^C)}.$$

Application of Bayes' Theorem

Positive Predictive Value

- Referring to the notation in the Bayes' Theorem section, let the event A correspond to D and let B correspond to T^+,

$$P(D|T^+) = \frac{P(T^+|D)P(D)}{P(T^+|D)P(D) + P(T^+|D^C)P(D^C)}.$$

- We have seen all of these quantities and could rewrite as

$$P(D|T^+) = \frac{\text{sens} \times \text{prev}}{\text{sens} \times \text{prev} + (1 - \text{spec}) \times (1 - \text{prev})}.$$

Application of Bayes' Theorem

Negative Predictive Value

- Referring to the notation in the Bayes' Theorem section, let the event A correspond to D^C and let B correspond to T^-,

$$P(D^C|T^-) = \frac{P(T^-|D^C)P(D^C)}{P(T^-|D^C)P(D^C) + P(T^-|D)P(D)}.$$

- Again, rewriting in different terms

$$P(D^C|T^-) = \frac{\text{spec} \times (1 - \text{prev})}{\text{spec} \times (1 - \text{prev}) + (1 - \text{sens}) \times \text{prev}}.$$

Application of Bayes' Theorem

- Given the sensitivity and the specificity of a screening test, along with the prevalence, then the positive predictive value and/or the negative predictive value can be found using Bayes' Rule.

Example: Saliva Test (Case Partitioned)

- Going back to our problem from before ...

Saliva Test	HIV Antibody Status Positive (D)	Negative (D^C)	Total
Positive (+)	358	2	360
Negative (−)	10	886	896
Total	368	888	1,256

Example: Saliva Test (Case Partitioned)

d) Suppose for our population of interest, the estimated prevalence of HIV was 320 per 100,000 $= 0.0032$.

Estimate the positive predictive value for the test.

Example: ELISA (Case Partitioned)

- The ELISA test is a blood test used to screen for HIV. The test checks for the presence of an antibody produced when an individual is exposed to HIV.
- When the antibody is present, ELISA is positive with probability 0.997; when the antibody is absent, ELISA is negative with probability 0.985 (Sloand et al., 1991). (These probabilities may vary depending on the expertise of the laboratory performing the test.)
- Suppose that in a certain population, the proportion of individuals who carry the HIV antibody in their blood is 0.004. Assume that an individual is randomly selected from this population, and that an ELISA test is performed on a blood sample taken from the individual.

Example: ELISA (Case Partitioned)

a) What is the probability of a false positive test result?

b) What is the probability of a false negative test result?

Example: ELISA (Case Partitioned)

c) Given that the individual has a positive test result, what is the probability he/she is an HIV carrier?

d) What is the probability of a positive test result?

Relative Risk

- In epidemiology, we often investigate the relationship between the presence of a disease (or condition) and exposure to a certain factor.
- Examples:
  - exposure to asbestos and lung cancer,
  - cigarette smoking and lung cancer,
  - chewing tobacco and oral cancer,
  - antibiotic use and dental fluorosis.

Relative Risk

- Consider an individual selected at random from a certain population.
- Define the following events:

$$\begin{aligned} D &= \text{the individual has the disease} \\ D^C &= \text{the individual does not have the disease} \\ E &= \text{the individual has been exposed} \\ E^C &= \text{the individual has not been exposed} \end{aligned}$$

- The *Relative Risk*, denoted RR, is defined by the following ratio:

$$\text{RR} = \frac{P(D|E)}{P(D|E^C)}.$$

Relative Risk: Example

- Based on a study based in the United States, the probability that a male over the age of 35 dies of lung cancer is 0.002679 if he is a smoker and 0.000154 if he is a nonsmoker (Garfinkel & Silverberg, 1991).
- The relative risk for smokers versus nonsmokers is as follows.

$$\begin{aligned} P(D|E) &= 0.002679, \\ P(D|E^C) &= 0.000154 \\ \text{RR} &= \frac{P(D|E)}{P(D|E^C)} = \frac{0.002679}{0.000154} = 17.4. \end{aligned}$$

Relative Risk: Example

- Note that the relative risk is more meaningful than the difference in probabilities, which is quite small and thereby obscures the elevated risk of smoking:

$$
\begin{aligned}
P(D|E) - P(D|E^C) &= 0.002679 - 0.000154 \\
&= 0.002525.
\end{aligned}
$$

Odds

- Let p denote the probability of an event.
- The *Odds* in favor of the event are defined as $p/(1-p)$.
- The odds are often read as '$p/(1-p)$ to 1.'
- If the odds of an event are quoted as 'a to b,' then the probability of the event is $a/(a+b)$.
- The probability of an event reflects the likelihood of occurrence on a scale of 0 to 1, whereas the odds reflects the likelihood on a scale of 0 to $+\infty$.

Odds

- For an exposed individual, the odds of the disease is given by

$$\frac{P(D|E)}{1 - P(D|E)} = \frac{P(D|E)}{P(D^C|E)}.$$

- For unexposed individuals, the odds of the disease is given by

$$\frac{P(D|E^C)}{1 - P(D|E^C)} = \frac{P(D|E^C)}{P(D^C|E^C)}.$$

Odds Ratio

- The *Odds Ratio*, denoted OR, is defined by the ratio of the odds of disease for an exposed individual to the odds of disease for an unexposed individual:

$$\mathrm{OR} = \frac{P(D|E)/P(D^C|E)}{P(D|E^C)/P(D^C|E^C)}.$$

Properties of the Odds Ratio

- The odds ratio has many desirable statistical properties, although it is less intuitive than the relative risk.
- Assuming all conditional probabilities in the definition of the odds ratio are strictly between 0 and 1, then $0 < \text{OR} < +\infty$.
- $\text{OR} = 1$ if and only if D and E are independent.
- OR is between 0 and 1 when exposure reduces the likelihood of the disease.
- OR exceeds 1 when exposure increases the likelihood of the disease.
- When the prevalence of the disease is low (i.e., $P(D) \approx 0$), the odds ratio and the relative risk are approximately equal (i.e., $\text{OR} \approx \text{RR}$).

Odds: Example

- In the previous smoking/lung cancer example, we had

$$\begin{aligned} P(D|E) &= 0.002679, \\ P(D|E^C) &= 0.000154, \\ \text{RR} &= 17.4. \end{aligned}$$

- The odds ratio for smokers versus nonsmokers can be found as follows, first calculate:

$$\begin{aligned} P(D^C|E) &= 1 - P(D|E) &= 1 - 0.002679 = 0.997321 \\ P(D^C|E^C) &= 1 - P(D|E^C) &= 1 - 0.000154 = 0.999846 \end{aligned}$$

Odds: Example

- Odds of death from lung cancer for smokers:

$$P(D|E)/P(D^C|E) = 0.002679/0.997321 = 0.002686$$

- Odds of death from lung cancer for non-smokers:

$$P(D|E^C)/P(D^C|E^C) = 0.000154/0.999846 = 0.000154$$

- Thus the odds ratio is

$$\text{OR} = \frac{P(D|E)/P(D^C|E)}{P(D|E^C)/P(D^C|E^C)} = \frac{0.002686}{0.000154} = 17.4.$$

- Note that this is the same value we obtained for the relative risk.

Odds: Polio Example

- Polio is an acute infectious disease characterized by motor paralysis and atrophy of skeletal muscles. As a public health threat, polio was largely eradicated by the Salk vaccine, introduced by Jonas Salk and investigated in a nationwide clinical trial in the 1950's.
- The following table classifies 141 child polio victims by paralytic status (yes, no) and vaccination status (yes, no). The data was collected in a study conducted in Des Moines, Iowa, in 1961.

Odds: Polio Example

Vaccination Status	Paralytic Status		Total
	Yes	No	
Yes	32	47	79
No	45	17	62
Total	77	64	141

Odds: Polio Example

a) Estimate the probability of paralytic status in both the vaccinated and the non-vaccinated group.

b) Estimate the relative risk.

Odds: Polio Example

c) Estimate the odds of paralytic status in the vaccinated group.

d) Estimate the odds of paralytic status in the non-vaccinated group.

e) Estimate the odds ratio.

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- Explain and calculate the following probabilities from a screening test: sensitivity; specificity; false positive; false negative; positive predictive value; negative predictive value; and prevalence.
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- Define Bayes' theorem, and use it in appropriate situations.
- Calculate the relative risk and odds ratio.