EANS/UEMS European examination in neurosurgery

Variants of questions with answers (compilation - Vyacheslav S. Botev, Department of Neurosurgery, M.Gorky Donetsk National Medical University)

MEDICAL STATISTICS AND EPIDEMIOLOGY

Q 1-2

1. A physician is deciding whether to use a new test to screen for disease X in his practice. The prevalence of disease X is 5%. The sensitivity of the test is 85%, and the specificity is 75%. In a population of 1000, how many patients will have the diagnosis of disease X missed by this test?

A. 50
B. 42
C. 8
D. 4

2. How many patients will be erroneously told they have diagnosis X on the basis of the results of this test?

A. 713
B. 505
C. 237
D. 42

Q 3-4

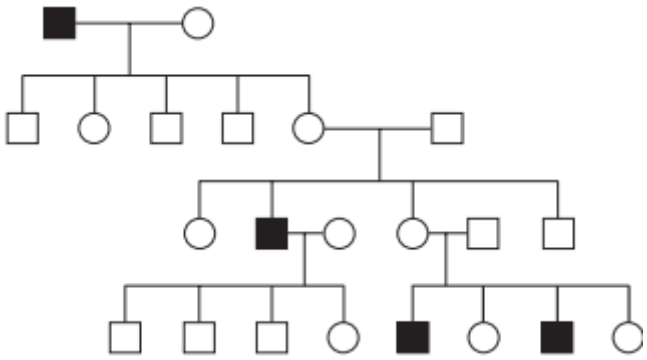
3. Drug X is investigated in a meta-analysis for its effect on mortality after stroke. It is found that mortality drops from 10 to 2% when this drug is administered. What is the absolute risk reduction conferred by drug X?

A. 2%
B. 8%
C. 20%
D. 200%
E. None of the above

4. How many patients will have to be treated with drug X to prevent one death?

A. 2
B. 8
C. 12.5
D. 50
E. 93

5. The following pedigree is an example of what pattern of inheritance?



Solid figure = Affected individuals
Open figure = Unaffected individuals

A. X-linked recessive inheritance
B. X-linked dominant inheritance
C. Autosomal recessive inheritance
D. Autosomal dominant inheritance
E. Cannot be determined by the limited information provided in this pedigree

6. In a study of 500 subjects with a GBM below 50, a new serological marker for glioblastoma was assessed against the gold standard test of GBM biopsy. The following results were obtained:

	Test positive	Test negative
Biopsy positive	40	10
Biopsy negative	60	840

What is the sensitivity of this test?

A. 40%
B. 55%
C. 66%
D. 80%
E. 93%

7. In a study of 1000 subjects with brain tumors, a new serological marker for astrocytoma was assessed against formal histology. The following results were obtained:

	Test positive	Test negative
Histology positive	40	10
Histology negative	50	900

To what does the specificity approximate?

A. 50%
B. 60%
C. 70%
D. 80%
E. 90%

8. A study was performed to assess the usefulness of a new autoantibody test for the detection of suspected Parkinson disease. The test was undertaken in 1000 subjects who complained of tremor and all test results were compared with FNA biopsy results which provided a gold standard for the diagnosis of Parkinson disease. The following table lists the results:

	Antibody +ve	Antibody –ve	Total
Parkinson disease confirmed at FNA	35	15	50
No evidence of disease at FNA	30	920	950

Approximately, what is the sensitivity of the antibody test for the detection of Parkinson disease?

A. 50%
B. 60%
C. 70%
D. 80%
E. 90%

9. In a study of 1000 patients with brain tumors, a new serological test for the disease was assessed against diagnostic brain biopsy. The following results were obtained:

	Test positive	Test negative
Histology positive	80	20
Histology negative	100	800

To what does the sensitivity of the new test approximate?
A. 50%
B. 60%
C. 70%
D. 80%
E. 90%

10. An experienced group of surgeons report on a randomized placebo-controlled trial comparing a particular carotid surgery technique as compared to a sham operation. Their study concludes that “using this advanced surgical technique reduces the risk of stroke from 4.3% to 3.8% ($p < 0.05$)”.

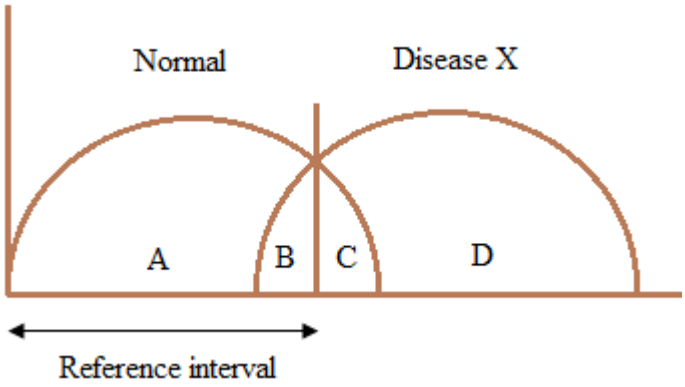
What has this study proved about the surgical procedure?

A. Acceptability
B. Effectiveness
C. Efficacy
D. Safety
E. Usefulness

11. A researchers compared the mean scores for nausea on a rating scale between standard therapy and a new drug in the treatment of chemotherapy induced nausea. Which one of the following is the most appropriate statistical test?

A. Chi-square test
B. Paired T-test
C. Life table analysis (log rank test)
D. Pearson correlation
E. Unpaired T-test

12. Study the following schematic involving a control group and disease X.



Which of the following correctly describes test results in the space occupied by each of the lettered groups?

A. Group A: true negatives + false negatives
B. Group B: true negatives + false positives
C. Group C: true positives + false positives
D. Group D: true positives + false negatives

13. If you have ordered two tests on a patient, what is the chance of one of those two tests having a false positive test result?

A. 0 %
B. 2 %
C. 5 %
D. 10 %
E. 20 %

14. In a trial of an antiplatelet therapy in secondary prevention of stroke, the drug was shown to reduce mortality from stroke, from 8% to 4% over 10 years. What is the number needed to treat to prevent a death over 10 years?

A. 4
B. 5
C. 10
D. 25
E. 100

15. The frequency of attendance of a 100 medical students at lectures were recorded by an observer over a 3 month period. The students were then assessed at the end with a multiple choice exam with a test score marked out of a

hundred. Which of these statistical methods is best used to analyse the effectiveness of frequency of attendance on higher test scores?

A. Mann-Whitney test
B. Spearmann correlation
C. Chi square test
D. Fisher's exact test
E. Student's T test

16. A researcher is trying to design a study to find out the cause (or causes) of a rare disease, about which very little is known. What study design is most likely to be appropriate?

A. Geographical
B. Cross-sectional
C. Cohort
D. Intervention
E. Case control

17. A new test is developed for the diagnosis of HIV. Blood from 10,000 patients were analysed by the gold standard technique and by the new method. There were 100 positive results with the gold standard technique but there were 150 positive results using the new technique. Approximately which of the following values reflects the positive predictive value of the new technique?
A. 33%
B. 50%
C. 66%
D. 75%
E. 90%

18. In a primary prevention study of stroke comparing a new antihypertensive with conventional antihypertensive therapy, the number of patients who had a stroke over the study period was 200 in group 1 with the new therapy (n=5200) versus 250 with conventional therapy (n=4750). Which of the following is the approximate odds ratio for the new therapy?
A. 0.25
B. 0.5
C. 0.75
D. 1
E. 1.5

19. In a trial of statin therapy in the secondary prevention of ischemic stroke, therapy is shown to reduce mortality from 12% to 8% over the 5 years duration of the study. In comparison with standard therapy, what is the number of patients that need to be treated to prevent one death over five years?

A. 5
B. 10
C. 20
D. 25
E. 50

20. A large multi-centre secondary prevention study reports a reduction in the annual incidence of recurrent subarachnoid hemorrhage from 10% in a medically treated group versus 6% in the group treated with medical therapy plus radiological intervention ($p<0.005$). The cost of the new treatment is 7,000 $ per patient.

In the first year of treatment, what would be the predicted additional cost of preventing a single recurrent subarachnoid hemorrhage?

A. 7,000
B. 72,000
C. 70,000
D. 75,000
E. 70,000

Use the data from Table 1 for questions 21 to 26.

Relationship between test A and disease B (Table 1)

	Disease B present	Disease B absent
Test A result positive	30	50
Test A result negative	10	80

21. What is the sensitivity of test A for disease B?
A. 25%
B. 37.5%
C. 75%
D. 62.5%
E. 11%

22. What is the specificity of test A for disease B?
A. 25%
B. 37.5%
C. 75%
D. 62.5%
E. 11%

23. What is the positive predictive value (PPV) of test A in the diagnosis of disease B?
A. 37.5%
B. 25%
C. 75%
D. 61.5%
E. 11%

24. What is the negative predictive value (NPV) of test A in the diagnosis of disease B?
A. 37%
B. 89%
C. 25%
D. 75%
E. 61.5%

25. What is the likelihood ratio for test A in disease B?
A. 0.39
B. 1.95
C. 3.80
D. 0.79
E. 1.51

26. What is the prevalence of disease A in this population?
A. 15.5%
B. 23.5%
C. 40%
D. 10.5%
E. 18.4%

Consider the following experimental data: A population of heavy smokers (men smoking more than 50 cigarettes per day) are divided into two groups and observed for a period of 10 years.
Use the data from Table 2 to answer question 27.

10-year mortality data (Table 2)

Group	Description	Diagnosed with GBM	Average survival time from diagnosis
Group 1 (experimental group)	490 individuals with annual MRI	37	14 months
Group 2 (control group)	510 individuals with no annual MRI	39	8 months

27. Regarding these results, which of the following statements is true?

A. These results prove that MRI improve survival time in GBM
B. These results prove that MRI should be considered for all smokers
C. These results are most likely a result of lead-time bias
D. These results are most likely an example of length-time bias
E. These results do not make any sense; the experiment should be repeated

Consider the data in Table 3 illustrating the prevalence of disease X in various populations.

Prevalence of disease X in certain populations (Table 3)

Setting	Prevalence (cases/100,000)
General population	50
Women, ≥ 50 years	500
Women, ≥ 65 years, with a suspicious finding on clinical examination	40,000

On the basis of this information about disease prevalence and assuming the sensitivity of test A for disease X is 80% and the specificity of test A for disease X is 90%, answer questions 28 to 31.

28. What is the PPV of test A in the diagnosis of disease X in the general population?
A. 0.4%
B. 1.3%
C. 5.4%
D. 15.7%

E. 39.6%

29. What is the PPV of test A in disease X in women aged 50 years or older?
A. 0.4%
B. 3.9%
C. 10.7%
D. 23.6%
E. 52.7%

30. What is the PPV of test A in disease X in women older than 65 years with a suspicious finding on clinical examination?
A. 0.4%
B. 5.6%
C. 34.7%
D. 84.2%
E. 93.0%

31. If the PPV of a test for a given disease in a given population is 4%, how many true positive test results are there in a sample of 100 positive test results?
A. 4
B. 10
C. 40
D. 96
E. none of the above

Answers

1. The answer is C. 8

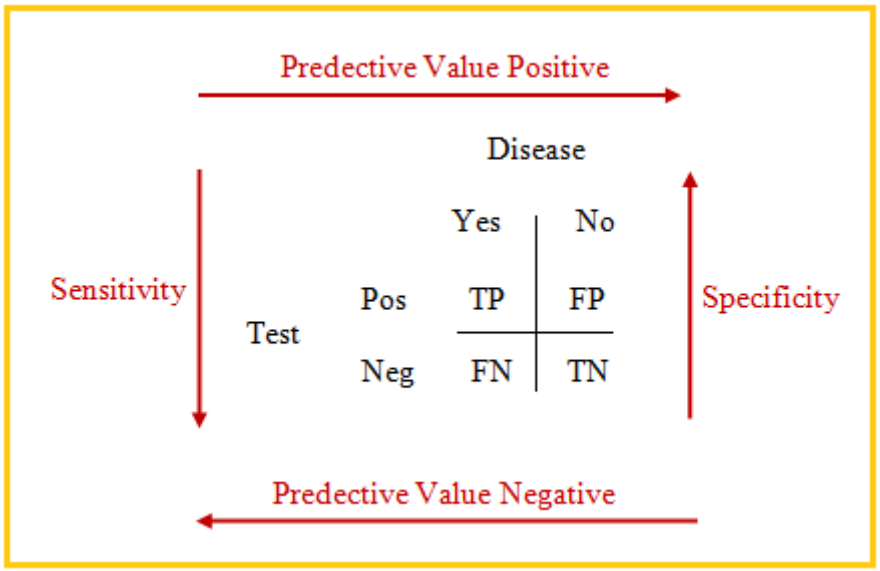
2. The answer is C. 237

In evaluating the usefulness of a test, it is imperative to understand the clinical implications of the sensitivity and specificity of that test. By obtaining information about the prevalence of the disease in the population—the specificity and sensitivity—one can generate a two-by-two table, as shown below. This table is used to generate the total number of patients in each group of the population:

	Disease status	
Test result	Present	Absent
Positive	True-positive	False-positive
Negative	False-negative	True-negative
	Total number of patients with disease	Total number of patients without disease

The sensitivity of the test is TP/(TP + FN). The specificity is TN/(TN + FP). In this case the table is filled in as follows:

	Disease status	
Test result	Present	Absent
Positive	42	237
Negative	8	713
	Total number of patients with disease = 50	Total number of patients without disease = 950



3. The answer is B. 8%

4. The answer is C. 12.5

The goal of a meta-analysis is to summarize the treatment benefit conferred by an intervention. Risk reduction is frequently expressed by relative risk or odds ratios; however, clinicians also find it useful to be familiar with the absolute risk reduction (ARR). This is the difference in mortality (or another endpoint) between the treatment and the placebo arms. In this case, the absolute risk reduction is 10% – 2% = 8%. From this number, one can calculate the number needed to treat (NNT), which is 1/ARR. The NNT is the number of patients who must receive the intervention to prevent one death (or another outcome assessed in the study). In this case the NNT is 1/8% = 12.5 patients.

5. The answer is A. X-linked recessive inheritance.

The information provided in the pedigree is adequate to determine the mode of a single-gene inheritance pattern. The example provided is typical of patients with hemophilia A or Duchenne's muscular dystrophy. Other examples exist. X-linked recessive inheritance is marked by the fact that the incidence of the trait is much higher in males than in females. The genetic trait is passed from an affected male through all his daughters to, on average, half their sons. The trait is never transmitted directly from father to son. The trait may be transmitted through a series of carrier females; if that occurs, the affected males are related to each other through the female, as in this case.

6. The answer is D. 80%

Sensitivity relates to the probability that the person with a disease will be correctly identified with the disease. Therefore, in this study, 50 subjects have the disease, of whom 40 are correctly identified with the disease giving a sensitivity of 80%. The specificity is the probability that a person without the disease will be correctly identified by the test. In this case, there are 900 subjects without the disease of whom 840 were identified by the test – giving a specificity of 93%.

7. The answer is E. 90%

Sensitivity relates to the probability that the person with a disease will be correctly identified with the disease. Therefore, in this study, 50 subjects have astrocytoma, of whom 40 are correctly identified with the disease giving a sensitivity of 80%. The specificity is the probability that a person without the disease will be correctly identified by the test. In this case, there are 950 subjects without astrocytoma, of whom 900 were identified by the test – giving a specificity of ≈ 95%.

8. The answer is C. 70%

The Sensitivity of a test is the ability of a test to identify those with the condition. In this example, 50 individuals had Parkinson disease according to the Gold standard test of biopsy, with 35 of these being identified by the antibody test.
35 / 50 × 100 = 70%.

9. The answer is E. 90%

Sensitivity relates to the probability that the person with a disease will be correctly identified with the disease. Therefore, in this study, 100 subjects have autoimmune hepatitis, of whom 80 are correctly identified with the new test giving a sensitivity of 80%. The specificity is the probability that a person without the disease will be correctly identified by the test. In this case, there are 900 subjects without autoimmune hepatitis of whom 800 were identified by the test – giving a specificity of ≈89%.

10. The answer is C. Efficacy.

This is an experienced group of vascular surgeons working in ideal conditions. Similar studies have been reported for carotid surgery but it has been difficult to prove their usefulness outside areas of expertise. It is often difficult to generalize the findings in a study group to everyday practice. Efficacy = the effect of something under ideal or laboratory conditions, Effectiveness = the effect of something in the real world.

11. The answer is E. Unpaired T-test.

The two-sample unpaired T-test is used to test the null hypothesis that the two populations corresponding to the two random samples are equal. For a paired T-

test, the data is dependent, i.e., there is a one-to-one correspondence between the values in the two samples. For example, the same subject measured before and after a process change, or the same subject measured at different times.

12. The answer is C. Group C: true positives + false positives.

13. The answer is D. 10 %.

There is a 5% chance of a FP test result per test, hence there is a 10% chance for 1 of 2 tests to be a FP.

14. The answer is D. 25.

The drug reduced the risk of death post stroke by 4% over 10 years. Therefore if 100 people were treated we could expect the prevention of 4 deaths. Therefore the number needed to treat would be 25 to prevent 1 death.

15. The answer is B. Spearmann correlation.

Spearmann's correlation is the best method to determine two variables which do not follow a normal distribution.

16. The answer is E. Case control.

Geographical studies, also called ecological studies, are good at generating hypothesis, but not very helpful in testing them.

Cross-sectional studies, also called prevalence studies, look at the number of cases of a disease at a particular point in time. They are not useful for investigating rare diseases or exposures.

In cohort studies, one group with an exposure of interest is selected and compared over time with another cohort without that exposure. If the control group is well selected, then cohort studies are good for examining the effects of rare exposures, but they are not suited to investigating the cause(s) of a rare disease.

An intervention study cannot be used to look for the cause(s) of a disease.

17. The answer is C. 66%

The positive predictive value is Number of true positive / (Number of true positive + Number of false positive). In the new technique there were 100 true positives and 50 false positives. Thus the positive predictive value is 66%.

18. The answer is C. 0.75

An odds ratio is calculated by dividing the odds in the treated or exposed by the odds in the control group. Studies generally try to identify factors that cause harm – those with odds ratios greater than one. The new therapy odds of an event is 200/5000 (patients without an event 5200-200)=0.04. Group 2's odds event rate if 250/4500 (4750-250)=0.055. The odds ratio is therefore: 0.04/0.055=0.73.

19. The answer is D. 25

The drug has reduced the risk of death post ischemic stroke by 4% over 5 years. Therefore if 100 people were treated we could expect the prevention of 4 deaths. Therefore in order to prevent 1 death, 25 individuals would need to be treated.

20. The answer is D. 75,000 $

This study shows that annual rate of recurrent subarachnoid hemorrhage is reduced from 10% to 6%. Therefore, if you treated 100 patients for one year you would expect 10 patients with subarachnoid hemorrhage in the medically treated group vs 6 patients in the medical plus radiological intervention group – a reduction of 4 patients per hundred. Therefore, you would need to treat 25 patients (4/100) to expect one less case of subarachnoid hemorrhage. Thus the extra cost of this would be
25×3,000=75,000.

21. The answer is C. 75%

Sensitivity is defined as the proportion of people with the disease who have a positive test result. A sensitive test rarely will miss patients who have the disease. In Table 4, sensitivity is defined as the number of true positives (TPs) divided by the number of true positives plus the number of false negatives (FNs). That is,

	Disease X present	Disease X absent
Test A result positive	30 (a) TP	50 (b) FP
Test A result negative	10 (c) FN	80 (d) TN

FN, false negative; FP, false positive; TN, true negative; TP, true positive.
Table 4 illustrates the answers to questions 21 to 26.

Sensitivity = TP / (TP + FN)
Sensitivity = a / (a + c) = 30 / 40 = 75%

A sensitive test (one that is usually positive in the presence of disease) should be selected when there is an important penalty for missing the disease. This would be the case if you had reason to suspect a serious but treatable condition, for example, obtaining a chest radiograph in a patient with suspected tuberculosis or Hodgkin disease. In addition, sensitive tests are useful in the early stages of a diagnostic workup of disease, when several possibilities are being considered, to reduce the number of possibilities. Thus, in situations such as this, diagnostic tests are used to rule out diseases.

22. The answer is D. 62.5%

Specificity is defined as the proportion of people without the disease who have a negative test result. A specific test rarely incorrectly classifies people without the disease as having the disease. In Table 4, specificity is defined as the number of true negatives (TNs) divided by the number of true negatives plus false positives (FPs). That is,

Specificity = TN / (TN + FP)
Specificity = d / (d + b) = 80 /130 = 61.5%

A specific test is useful to confirm, or rule in, a diagnosis that has been suggested by other tests or data. Thus, a specific test is rarely positive in the absence of disease, that is, it gives few false-positive test results. Tests with high specificity are needed when false-positive results can harm the patient physically, emotionally, or financially. Thus, a specific test is most helpful when the test result is positive. There is always a trade-off between sensitivity and specificity. In general, if a disease has a low prevalence, choose a more specific test; if a disease has a high prevalence, choose a more sensitive test.

23. The answer is A. 37.5%

Positive predictive value (PPV) is defined as the probability of disease in a patient with a positive (abnormal) test result. In Table 4, the PPV is as follows:

PPV = a / (a + b) = 30/ 80 = 37.5%

24. The answer is B. 89%

Negative predictive value (NPV) is defined as the probability of not having the disease when the test result is negative. In Table 4, the NPV is as follows:
NPV = d / (c + d) = 80/ 90 = 89%

25. The answer is B. 1.95

The likelihood ratio of a positive test result is the probability of that test result in the presence of disease divided by the probability of the test result in the absence of disease. In Table 4, the likelihood ratio is as follows:

Likelihood ratio (+) test results a / (a + c) divided by
b / (b + d) or 30 / (30 + 10) divided by 50 / (50 + 80) = 1.95

26. The answer is B. 23.5%

The prevalence of a disease in the population at risk is the fraction or proportion of a group with a clinical condition at a given point in time. Prevalence is measured by surveying a defined population containing people with and without the condition of interest (at a given point in time). Prevalence can be equated with pretest probability. In Table 4, prevalence is defined as follows:

Prevalence = (a+c) / (a+b+c+d)
That is, (a+c) divided by ((a+b+c+d) = (30+10) / (30+10+50+80) = 23.5

As prevalence decreases, PPV must decrease along with it and NPV must increase.

27. The answer is C. This is an example of lead-time bias.

Lead-time is the period between the detection of a medical condition by screening and when it ordinarily would have been diagnosed as a result of

symptoms. For GBM, there is absolutely no evidence that MRI have any influence on mortality. However, if, as in this case, the experimental group had MRI done, their GBM would have been diagnosed at an earlier time and it would appear that they were longer survivors. The control group most likely would have had their GBM diagnosed when they developed symptoms. In fact, however, the survival time would have been exactly the same; the only difference would have been that men in the experimental group would have known that they had GBM for a longer period.

28. The answer is A. 0.4%

Answers 28 and 29 are explained in answer 30, including Table 5.

Calculations involved in a general 2 × 2 (Table 5)

	Target disorder	
	Present	**Absent**
Test result positive	Cell a = (sensitivity) (a+c)	Cell b = (b+d) – d
Test result negative	Cell c = (a+c) – a	Cell d = (specificity) (b+d)
Column sums	a+c	Total - (a+c)
Total = a+b+c+d		

29. The answer is B. 3.9% See answer 30.

30. The answer is D. 84.2%

The respective PPVs for test A in the diagnosis of disease X in the general population, in women older than 50 years, and in women older than 65 years with a suspicious finding on clinical examination are 0.4%, 3.9%, and 84.2%, respectively. To perform the calculations necessary to obtain these answers, the following steps are recommended:

Step 1: Identify the sensitivity of the sign, symptom, or diagnostic test that you plan to use. Many of these are published. If you are not certain, consider asking a consultant with expertise in the area.

Step 2: Using a 2 × 2 table, set your total equal to an even number (consider, for example, 1000 as a good choice). Therefore,

Step 3: Using whatever information you have about the patient before you apply this diagnostic test, estimate his or her pretest probability (prevalence) of the disease in question. Next, put appropriate column summation numbers at the bottom of the columns (a + c) and (b + d). The easiest way to do this is to express your pretest probability (or prevalence) as a decimal three places to the right. This result is (a + c), and 1000 minus this result is (b + d).

Step 4: Start to fill in the cells of the 2 × 2 table.
Multiply sensitivity (expressed as a decimal) by (a + c) and put the result in cell a. You can the calculate cell c by simple subtraction.

Step 5: Similarly, multiply specificity (expressed as a decimal) by (b + d) and put the result in cell d. Calculate cell b by subtraction.

Step 6: You now can calculate PPVs and NPVs for the test with the prevalence (pretest probability) used. For example, to calculate the PPV for test A in the diagnosis of disease in women older than 65 years with a suspicious finding on clinical examination, use the following equation:
Prevalence = 40,000 cases /100,000 = 400 /1000

Setting the total number equal to 1000,
(a+c) / (a+b+c+d) = 400/1000
Therefore, (a+c) = 400 and (b+d) = 600
Thus,
Cell a = sensitivity × 400 = 0.8 × 400 = 320
Cell b = 400 – 320 = 80
Similarly,
Cell d = Specificity × 600 = 0.9 × 600 = 540
Cell b = 600 – 540 = 60
Calculate the positive predictive value as follows:
PPV = a / (a+b) = 320 / (320+60) = 84.2%

Similar calculations can be made for the general population (prevalence = 50 /100,000) and for women older than 50 years (prevalence = 500 /100,000).

31. The answer is A. 4

If the PPV of a test for a given disease is 4%, then only 4 of 100 positive test results will be true positives; the remainder will be false positives. Further testing (often invasive) and anxiety will be inflicted on the 96% of the

population with a positive test result but without the disease. Thus, careful consideration should be given to the PPV of any test for any disease in a given population before ordering it.

References

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