**Biostatistics and Epidemiology**

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1. You have diagnosed five children with acute myeloid leukemia and hyperleukocytosis since beginning your fellowship. Their ages at diagnosis were 2, 2, 5, 7, and 19 years of age. What is the median age of your cohort?

A. 19

B. 5

C. 14

D. 2

E. 7

**Explanation**

The median value is the middle one when placed in order (ie, the 50th percentile). If there are five values, then the median value is the third value, which is 5 in this case.

2. You have performed a double-blind randomized controlled trial to compare a drug versus placebo to reduce clinically documented central line–associated thrombosis in children with newly diagnosed acute lymphoblastic leukemia. These are the results:

|  |  |  |
| --- | --- | --- |
|  | **Thrombosis** | **No thrombosis** |
| Drug | 2 | 98 |
| Placebo | 10 | 90 |

What is the odds ratio of thrombosis associated with drug therapy?

A. (2/100)/(10/100) = 0.02/0.10 = 0.20

B. (2 × 90)/(10 × 98) = 0.18

C. 2/100 = 0.02

D. 98/188 = 0.52

E. 1 – 0.20 = 0.80

**Explanation**

The odds ratio is the ratio of the odds of thrombosis associated with the drug to the odds of thrombosis with placebo. In this case, it is (2/98)/(10/90). This can be rewritten as (2 × 90)/(10 × 98) = 0.18. This is different from the risk ratio that is found by computing the ratio of the proportions of thrombosis for the drug group (2/100) and the placebo group (10/100), which would be (2/100)/(10/100) = 0.02/0.10 = 0.20 in this case.

3. You have performed a double-blind randomized controlled trial to compare a drug with placebo to reduce clinically documented central line–associated thrombosis in children with newly diagnosed acute lymphoblastic leukemia. These are the results:

|  |  |  |
| --- | --- | --- |
|  | **Thrombosis** | **No thrombosis** |
| Drug | 2 | 98 |
| Placebo | 10 | 90 |

What is the absolute risk reduction associated with treatment?

A. 0.1 – 0.02 = 0.08, or 8%

B. (0.1 – 0.02)/0.1 = 0.8, or 80%

C. 2/100

D. 98/188

E. 1 – 0.08 = 0.92

**Explanation**

The absolute risk reduction is the difference in risk associated with placebo compared with drug. In this case, it is 0.1 – 0.02 = 0.08, or 8%.

4. You are evaluating a new test to predict invasive fungal disease in children undergoing chemotherapy for acute myeloid leukemia. You have enrolled 1,000 patients over 7 years. Here are the results:

|  |  |  |
| --- | --- | --- |
|  | **Invasive fungal disease: yes** | **Invasive fungal disease: no** |
| Test positive | 100 | 300 |
| Test negative | 200 | 400 |

What is the sensitivity of the test?

A. 33.3%

B. 57.1%

C. 25%

D. 66.7%

E. 75%

**Explanation**

The sensitivity of the test is the proportion of those with the disease who test positive. In this case, it is 100/300 = 33.3%. A helpful approach here is to create a table of the given information with the screening or diagnostic test results as the rows and the pathological findings as the columns, such as the one below:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Disease positive** | **Disease negative** | **Total** |
| Screening test positive | TP | FP | TP + FP |
| Screening test negative | FN | TN | FN + TN |
| Total | TP + FN | FP + TN |  |

Here, TP = true positive; TN = true negative; FP = false positive; and FN = false negative. With the table constructed in this manner, it is straightforward to compute sensitivity, specificity, positive predictive value, and negative predictive value.

Sensitivity is the probability of obtaining a positive test result when the subject has the disease. The only portion of the table relevant to this quantity is the first column, representing the disease-positive subjects. TP tells us how many positive test results were obtained among subjects who truly had the disease, and TP + FN tells us how many subjects truly had the disease. Thus the sensitivity can be computed as TP/(TP + FN).

5. You are evaluating a new test to predict invasive fungal disease in children undergoing chemotherapy for acute myeloid leukemia. You have enrolled 1,000 patients over 7 years. Here are the results:

|  |  |  |
| --- | --- | --- |
|  | **Invasive fungal disease: yes** | **Invasive fungal disease: no** |
| Test positive | 100 | 300 |
| Test negative | 200 | 400 |

What is the specificity of the test?

A. 75%

B. 25%

C. 66.7%

D. 57.1%

E. 33.3%

**Explanation**

The specificity of the test is the proportion of those without the disease who test negative. In this case, it is 400/700 = 57.1%. A helpful approach here is to create a table of the given information with the screening or diagnostic test results as the rows and the pathological findings as the columns, such as the one below:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Disease positive** | **Disease negative** | **Total** |
| Screening test positive | TP | FP | TP + FP |
| Screening test negative | FN | TN | FN + TN |
| Total | TP + FN | FP + TN |  |

Here, TP = true positive; TN = true negative; FP = false positive; and FN = false negative. With the table constructed in this manner, it is straightforward to compute sensitivity, specificity, positive predictive value, and negative predictive value.

Specificity is the probability of obtaining a negative test result when the subject does *not* have the disease. The only portion of the table relevant to this quantity is the second column, representing the disease-negative subjects. TN tells us how many negative test results were obtained among subjects who truly did not have the disease, and FP + TN tells us how many subjects truly did not have the disease. Thus, the specificity can be computed as TN/(FP + TN).

6. You are evaluating a new test to predict invasive fungal disease in children undergoing chemotherapy for acute myeloid leukemia. You have enrolled 1,000 patients over 7 years. Here are the results:

|  |  |  |
| --- | --- | --- |
|  | **Invasive fungal disease: yes** | **Invasive fungal disease: no** |
| Test positive | 100 | 300 |
| Test negative | 200 | 400 |

What is the positive predictive value of the test?

A. 66.7%

B. 57.1%

C. 33.3%

D. 75%

E. 25%

**Explanation**

The positive predictive value is the proportion of those who test positive who actually have the disease. In this case, it is 100/400 = 25%. A helpful approach here is to create a table of the given information with the screening or diagnostic test results as the rows and the pathological findings as the columns, such as the one below:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Disease positive** | **Disease negative** | **Total** |
| Screening test positive | TP | FP | TP + FP |
| Screening test negative | FN | TN | FN + TN |
| Total | TP + FN | FP + TN |  |

Here, TP = true positive; TN = true negative; FP = false positive; and FN = false negative. With the table constructed in this manner, it is straightforward to compute sensitivity, specificity, positive predictive value, and negative predictive value.

Positive predictive value is the probability a subject has the disease, given a positive test result. The only portion of the table relevant to this quantity is the first row, representing the screening test positive subjects. TP tells us how many subjects truly had the disease among all of the positive screening test results, and TP + FP tells us how many subjects yielded a positive screening test. With some simplifying assumptions about the prevalence of the disease, the positive predictive value can be computed as TP/(TP + FP).

7. You are evaluating a new test to predict invasive fungal disease in children undergoing chemotherapy for acute myeloid leukemia. You have enrolled 1,000 patients over 7 years. Here are the results:

|  |  |  |
| --- | --- | --- |
|  | **Invasive fungal disease: yes** | **Invasive fungal disease: no** |
| Test positive | 100 | 300 |
| Test negative | 200 | 400 |

What is the negative predictive value of the test?

A. 25%

B. 57.1%

C. 66.7%

D. 33.3%

E. 75%

**Explanation**

The negative predictive value is the proportion of those who test negative who do not have the disease. In this case, it is 400/600 = 66.7%. A helpful approach here is to create a table of the given information with the screening or diagnostic test results as the rows and the pathological findings as the columns, such as the one below:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Disease positive** | **Disease negative** | **Total** |
| Screening test positive | TP | FP | TP + FP |
| Screening test negative | FN | TN | FN + TN |
| Total | TP + FN | FP + TN |  |

Here, TP = true positive; TN = true negative; FP = false positive; and FN = false negative. With the table constructed in this manner, it is straightforward to compute sensitivity, specificity, positive predictive value, and negative predictive value.

Negative predictive value is the probability a subject does not have the disease, given a negative test result. The only portion of the table relevant to this quantity is the second row, representing the screening test negative subjects. TN tells us how many subjects truly did not have the disease among all the negative screening test results, and FN + TN tells us how many subjects yielded a negative screening test. With some simplifying assumptions about the prevalence of the disease, the negative predictive value can be computed as TN/(FN + TN).

8. A new biomarker is developed to make an early diagnosis of bacteremia. The sensitivity of the test is 60%, and the specificity is 90%. What is the likelihood ratio positive?

A. 0.6

B. 0.9 – 0.6 = 0.3

C. (0.9 – 0.6)/0.3 = 1

D. 0.6/(1 – 0.9) = 6

E. (1 – 0.6)/0.9 = 0.44

**Explanation**

The likelihood ratio positive is given by the following formula:

LR+ = sensitivity/(1 – specificity)

In this case, it is 0.6/1 – 0.9 = 0.6/0.1 = 6.

The likelihood ratio negative is given by the following formula:

LR– = (1 – sensitivity)/specificity

9. Which of the following study designs is most likely to yield valid information about the prognosis of a condition?

A. Randomized controlled trial

B. Case series

C. Case control study

D. Cohort study

E. Crossover study

**Explanation**

A cohort study is the best study design to obtain valid information about the prognosis of a condition. The best design to determine the benefits or harms of an intervention is a randomized controlled trial. The best design to evaluate a diagnostic test is a cross-sectional study, and a case control study is best for identifying risk factors for a rare outcome.

10. What is the best study design to evaluate a diagnostic test?

A. Randomized controlled trial

B. Case series

C. Case control study

D. Cohort study

E. Cross-sectional study

**Explanation**

A cohort study is the best study design to obtain valid information about the prognosis of a condition. The best design to determine the benefits or harms of an intervention is a randomized controlled trial. The best design to evaluate a diagnostic test is a cross-sectional study, and a case control study is best for identifying risk factors for a rare outcome.

11. A double-blind randomized controlled trial was conducted to compare a drug with placebo to reduce clinically documented central line–associated thrombosis in children with newly diagnosed acute lymphoblastic leukemia. The 95% confidence interval for the difference in proportions (drug group – placebo group) of subjects with thrombosis was (–16.2, 2.5).

Based on these results, what is the best conclusion about the proportion of thrombosis for patients treated with the drug?

A. The proportion of thrombosis is significantly lower in subjects treated with the drug.

B. The proportion of thrombosis is significantly higher in subjects treated with the drug.

C. The proportion of thrombosis is lower, but not significantly lower, in subjects treated with the drug.

D. The proportion of thrombosis is higher, but not significantly higher, in subjects treated with the drug.

E. Not enough information is given to answer this question.

**Explanation**

The proportions of subjects with thrombosis in each group will be significantly different if the 95% confidence interval for the difference does not contain 0. The 95% confidence interval for the difference contains 0, implying that there is potentially no difference between the proportions of thrombosis for those treated with the drug and those given the placebo. Most of the values of the 95% confidence interval are negative, implying that the proportion of subjects with thrombosis in the drug group is smaller than that of the placebo group. Therefore, the proportion of thrombosis is lower in the drug group but not significantly lower.

12. A randomized clinical trial assessed the effectiveness of the standard antinausea treatment plus a new antinausea drug compared with the standard antinausea treatment plus a placebo to reduce emesis among patients undergoing chemotherapy. The proportion of subjects in the placebo group experiencing emesis was 60%, and the proportion of subjects in the treatment group experiencing emesis was 50%.

What is the number needed to treat to prevent one episode of emesis?

A. 10

B. 50

C. 40

D. 5

E. 15

**Explanation**

Recall that if *p*placebo and *p*trt represent the proportion of bad outcomes for the placebo and treatment groups, respectively, then the absolute risk reduction (ARR) is (*p*placebo – *p*trt), and the number needed to treat (NNT) is 1/(*p*placebo – *p*trt). The proportion of subjects experiencing emesis in the placebo group is 60%, and it is 50% in the treatment group. Thus, the ARR is

$$ARR = .6 – .5 = .1$$

And the NNT is

$$NNT=\frac{1}{ARR}=\frac{1}{.6-.5}=\frac{1}{.1}=10$$

This means for every 10 subjects given the additional antinausea drug, one additional subject receiving chemotherapy will avoid emesis.

13. A double-blind randomized controlled trial was conducted to compare a drug with placebo to reduce clinically documented central line–associated thrombosis in children with newly diagnosed acute lymphoblastic leukemia. The 95% confidence interval for the odds ratio of thrombosis for subjects treated with the drug and those receiving the placebo is 0.23 (0.10, 0.31).

Based on these results, what is the best conclusion about the odds of thrombosis for patients treated with the drug?

A. The odds of thrombosis are significantly lower in subjects treated with the drug.

B. The odds of thrombosis are significantly higher in subjects treated with the drug.

C. The odds of thrombosis are lower, but not significantly lower, in subjects treated with the drug.

D. The odds of thrombosis are higher, but not significantly higher, in subjects treated with the drug.

E. Not enough information is given to answer this question.

**Explanation**

The odds of thrombosis between the two groups will be significantly different if the 95% confidence interval does not contain 1. The odds ratio comparing the risk of thrombosis in subjects treated with the drug with that of the placebo group is 0.23. Thus, there is reduced odds of thrombosis in the drug group (odds of numerator). If the decrease is *not* significant, the 95% confidence interval for the odds ratio will contain 1, meaning the odds of thrombosis in both groups are the same. Here the 95% confidence interval does not contain 1, so we can conclude that the odds are significantly lower.

14. A randomized clinical trial assessed the effectiveness of the standard antinausea treatment plus a new antinausea drug versus the standard antinausea treatment plus a placebo to reduce emesis among patients undergoing chemotherapy. The study concluded there was not a significant difference in the proportion of subjects experiencing emesis between the two groups.

Based on these results, what error could the researchers be making relative to the hypotheses being tested?

A. Type I error because the null hypothesis is rejected

B. Type II error because the null hypothesis is rejected

C. Type I error because the study fails to reject the null hypothesis

D. Type II error because the study fails to reject the null hypothesis

E. No error because the findings are not significant

**Explanation**

In this study the null hypothesis is that there is no difference in the proportion of subjects experiencing emesis between the two groups. The researcher’s alternative hypothesis is that there is a significant difference in the proportion of subjects experiencing emesis between the two groups. The study concluded there was no significant difference in the proportion of subjects experiencing emesis between the two groups, so the study fails to reject the null hypothesis. A type II error is defined as failing to reject the null hypothesis when it is in fact false. Hence a type II error is possible with this conclusion. In contrast, a type I error is defined as rejecting the null hypothesis when it is true. This would be a possibility only if the researchers rejected the null hypothesis, which is not the case here.

15. In a randomized clinical trial, children aged 3 to 16 treated with photon therapy for medulloblastoma were randomly assigned to the standard neurocognitive therapy group or to a game-based “enhanced” neurocognitive therapy group. The study’s aim was to determine whether the enhanced neurocognitive therapy group had improved processing time scores. The study concluded the mean processing time for the enhanced neurocognitive therapy group was significantly higher than that of the standard therapy group.

Based on these results, what error could the researchers be making relative to the hypotheses being tested?

A. Type I error because the null hypothesis is rejected

B. Type II error because the null hypothesis is rejected

C. Type I error because the study fails to reject the null hypothesis

D. Type II error because the study fails to reject the null hypothesis

E. No error because the findings are significant

**Explanation**

In this study the null hypothesis is that the mean processing time is the same for both the standard and enhanced neurocognitive therapies. The researcher’s alternative hypothesis is that the mean neurocognitive score in the enhanced neurocognitive therapy group is significantly higher than that of the standard therapy group. The study concluded the mean processing score of the enhanced neurocognitive therapy group was significantly higher than that of the standard neurocognitive therapy group, so the study rejects the null hypothesis. A type I error is defined as rejecting the null hypothesis when it is true. Hence a type I error is possible with this conclusion. In contrast, a type II error is defined as failing to reject the null hypothesis when it is false. This would be a possibility only if the researchers failed to reject the null hypothesis, which is not the case here.