\( \chi^2 \) test of Association – Onset of Deep Vein Thrombosis versus Drug Treatment Group

Use the information in the following setting to answer questions 1 - 4

Patients with acute medical conditions such as congestive heart failure, respiratory failure, infection etc. often require prolonged hospital stays where their mobility is severely restricted. In this environment a blood clot in a leg or pelvis vein can develop. This condition is called deep vein thrombosis (DVT). In a product information document Pfizer Pharmaceuticals details the results of a double blind, multinational clinical trial on the drug Fragmin. Of interest was the number of patients in each group that suffered a complication such as pulmonary embolism, DVT or sudden death. Table 1 below summarizes these results.

Table 1: Complication occurrence versus treatment group for the Fragmin study.

<table>
<thead>
<tr>
<th></th>
<th>Treatment Outcome</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complication</td>
<td>No Complication</td>
<td></td>
</tr>
<tr>
<td>Fragmin</td>
<td>( 42 = O_{11} )</td>
<td>( E_{11} = \frac{(O_{11})(O_{1})}{2a_{1}a_{1}} = 1518.155 )</td>
<td>1476</td>
</tr>
<tr>
<td></td>
<td>( 42 = O_{11} )</td>
<td>( E_{11} = \frac{(O_{11})(O_{1})}{2a_{1}a_{1}} = 1518.155 )</td>
<td>1476</td>
</tr>
<tr>
<td></td>
<td>( x^2_{11} = 4.59 )</td>
<td>( \chi^2 = 58.37 )</td>
<td></td>
</tr>
<tr>
<td></td>
<td>( x^2_{11} = 4.59 )</td>
<td>( \chi^2 = 58.37 )</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>( 73 = O_{21} )</td>
<td>( E_{21} = O_{21} = 56.63 )</td>
<td>1400</td>
</tr>
<tr>
<td></td>
<td>( 73 = O_{21} )</td>
<td>( E_{21} = O_{21} = 56.63 )</td>
<td>1400</td>
</tr>
<tr>
<td></td>
<td>( x^2_{21} = 4.73 )</td>
<td>( \chi^2 = 18.92 )</td>
<td></td>
</tr>
<tr>
<td></td>
<td>( x^2_{21} = 4.73 )</td>
<td>( \chi^2 = 18.92 )</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>115</td>
<td>2876</td>
<td>2991</td>
</tr>
</tbody>
</table>

1) For this study, identify the response and explanatory variables

response - Treatment Outcome

explanatory - treatment

2) Investigators would like to determine whether or not an association exists, i.e. treatment outcome and treatment group are not independent, between experiencing complications and treatment group

A) A statistical technique that could be used to test whether or not experiencing complications and treatment group are independent is: \( \chi^2 \) test of association

B) Compute and enter the expected frequencies for each cell

C) Compute and enter the corresponding \( \chi^2 \) contribution for each cell

D) The number of degrees of freedom associated with this study is: \( (r-1)(c-1) \)
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E) Perform the hypothesis test at the 0.05 level,

Step 1

\( H_0: \) Treatment outcome and treatment group are not associated

\( H_a: \) Treatment outcome and treatment group are associated

Step 2

\( \alpha = 0.05 \) level

Step 3

\( E_{ij} \geq 5 \) for all \( i, j \)

random sample

Continue with the rest of the hypothesis test even if the assumptions do not hold.

Step 4

\[ \chi^2 = 4.5910 + 4.7321 + 0.1836 + 0.1892 \]

\[ = 9.6959 \]

Step 5

\( p\)-value = \( P(\chi^2 \geq 9.6959) < 0.005 \)

(critical value = 3.841)

Step 6

\( p\)-value < 0.005 < 0.05 = \( \alpha \)

\[ \Rightarrow \) Reject

Step 7

We have enough evidence at the 0.05 level to conclude that there is an association between treatment and outcome. (ie They're not independent.)
The Confidence Interval for the difference between two proportions:

3) When the study design results in a 2 x 2 table there is only 1 possible comparison of interest. In this case, investigators would like to estimate the true difference between the proportion of the placebo group that had complications and that of the Fragmin group that had complications. Assume that each sample group is a good representative for its respective population.

A) The point estimates for the true proportion of Fragmin users and non-Fragmin users respectively are:

\[ P_F = \frac{42}{1518} \times 0.0277 \quad \text{and} \quad P_p = \frac{73}{1473} \times 0.0496 \]

B) Choose one of the point estimates computed above and provide an English interpretation for it.

about 2.77% of all people with acute medical conditions who take Fragmin suffer complications.

C) The point estimate for the true difference between the proportion of Fragmin users and non-Fragmin users is:

\[ P_p - P_F = \left( \frac{73}{1473} \right) - \left( \frac{42}{1518} \right) = 0.02189 \]

D) Interpret the point estimate for the difference between the proportion of Fragmin users and non-Fragmin users:

the probability of experiencing complications is about 0.222 greater for those taking a placebo than those on Fragmin

E) Construct a 90% CI for the true difference between the proportion of Fragmin users and non-Fragmin users

i) \( z_{0.05} = Z^* = 1.645 \)

ii) 90% bound = ME.

\[ 1.645 \sqrt{\frac{0.0277(1-0.0277)}{1518} + \frac{0.0496(1-0.0496)}{1473}} = 0.01597 \]

iii) Based on E.i and E.ii compute the interval and draw the corresponding CI diagram

\[ CI = 0.02189 \pm 0.01597 \]

\[ = (0.010293, 0.033487) \]

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iv) Provide an English interpretation for the interval constructed above.

We are 90% confident that the true difference in proportion of those on the placebo suffering complications versus those on Fragmin suffering complications is between .0103 and .0335.

v) Invert the CI and conduct the corresponding hypothesis test for no difference between the rates of complications in the two populations.

reject $H_0: \pi_F = \pi_P$ at $\alpha = .10$ level since our entire 90% CI is greater than .0.

The directional hypothesis test for the difference between two proportions

4) Let’s say that, from the outset of the study, the investigators believed that the Fragmin treatment can be used as an effective prophylactic for reducing the rate of DVT for patients whose mobility is severely restricted. Let $\alpha = 0.01$.

Step 1

$H_0: \pi_F \geq \pi_P$

$H_a: \pi_F < \pi_P$

Step 2

$\alpha = .01$

Step 3

$n_1 p_1 \geq 10$

$n_2 (1-p_2) \geq 10$

$n_1 (1-p_1) \geq 10$

$n_2 p_2 \geq 10$

Continue with the rest of the hypothesis test even if the assumptions do not hold.

Step 4

*use pooled proportion

$\bar{p} = \frac{115}{2991}$

$Z_{test} = \frac{-0.2189}{\sqrt{\frac{115}{2991} (1 - \frac{115}{2991}) + \frac{115}{2991} (1 - \frac{115}{2991})} \sqrt{1518 / 1473}} = -3.127$
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**Step 5**

\[ p\text{-value} = P(Z < -3.11) = .0009 \]

**Step 6**

\[ p\text{-value} < \alpha \implies \text{Reject } H_0 \]

**Step 7**

interpret!

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**Output 1:** \( \chi^2 \) results for the Fragmin study

**Chi-Square Test: Complications, No Complications**

<table>
<thead>
<tr>
<th></th>
<th>Complications</th>
<th>No Complications</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fragmin</td>
<td>42</td>
<td>1518</td>
<td></td>
</tr>
<tr>
<td></td>
<td>58.37</td>
<td>1459.63</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.589</td>
<td>0.183</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>73</td>
<td>1473</td>
<td></td>
</tr>
<tr>
<td></td>
<td>56.63</td>
<td>1416.37</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.729</td>
<td>0.189</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>115</td>
<td>2991</td>
<td></td>
</tr>
</tbody>
</table>

Chi-Sq = 9.690, DF = 1, P-Value = 0.002

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**Output 2:** 2-Sample CI and hypothesis test results for the Fragmin study

**Test and CI for Two Proportions**

<table>
<thead>
<tr>
<th>Sample</th>
<th>X</th>
<th>N</th>
<th>Sample p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73</td>
<td>1473</td>
<td>0.049559</td>
</tr>
<tr>
<td>2</td>
<td>42</td>
<td>1518</td>
<td>0.027668</td>
</tr>
</tbody>
</table>

Difference = p (1) - p (2)

Estimate for difference: 0.0218907

90% CI for difference: (0.0102949, 0.0334866)

Test for difference = 0 (vs > 0): Z = 3.11 P-Value = 0.001