Inference for independent binomial data. Consider a clinical trial comparing two treatments A and B.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cured</th>
<th>N</th>
<th>Prop</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>58</td>
<td>150</td>
<td>.387</td>
</tr>
<tr>
<td>B</td>
<td>63</td>
<td>200</td>
<td>.315</td>
</tr>
</tbody>
</table>

Is there a difference between the cure rates of two treatments?

\[ X = \# \text{ of cures for trt A } \sim \text{Bin}(150, p_1) \]
\[ Y = \# \text{ of cures for trt B } \sim \text{Bin}(200, p_2) \]

\[ H_0 : p_1 = p_2 \text{ versus } H_1 : p_1 \neq p_2 \]
The test statistic

\[ TS = \frac{\hat{p}_1 - \hat{p}_2}{SE} \]

Will be normally distributed when both sample sizes are large.

\[ SE = Var(\hat{p}_1 - \hat{p}_2) = Var(\hat{p}_1) + Var(\hat{p}_2) \]

Therefore

\[ SE = \frac{p_1(1-p_1)}{n_1} + \frac{p_2(1-p_2)}{n_2} \]

Under the null hypothesis

\[ SE = \frac{p(1-p)}{n_1} + \frac{p(1-p)}{n_2} \]
To calculate SE under the null hypothesis we use:

\[ \hat{p} = \frac{X + Y}{n_1 + n_2} \]

The associated confidence interval is

\[ (\hat{p}_1 - \hat{p}_2) \pm Z_{1-\alpha/2} \sqrt{\frac{\hat{p}_1(1-\hat{p}_1)}{n_1}} \]

The coverage of this interval can be poor. A simple fix is to use:

\[ \tilde{p}_1 = \frac{X + 1}{n_1 + 2} \quad \tilde{p}_2 = \frac{Y + 1}{n_2 + 2} \]

instead.
Example
Interval estimation for the relative risk. The relative risk is defined as $p_1 / p_2$.

The logical estimate of the RR is

$$\hat{RR} = \frac{\hat{p}_1}{\hat{p}_2} = \frac{X/n_1}{Y/n_2}$$

The standard error of the log of the RR is

$$SE = \left( \frac{(1-p_1)}{p_1 n_1} + \frac{(1-p_2)}{p_2 n_2} \right)^{1/2}$$

Therefore, the interval for the log RR is

$$\log RR \pm Z_{1-\alpha/2}$$

Exponentiate to get an interval for the RR.
Confidence intervals for the log odds ratio. The odds ratio is defined as:

$$\text{Odds A} / \text{Odds B} = \frac{\frac{p_1}{1-p_1}}{\frac{p_2}{1-p_2}} = \frac{p_1(1-p_2)}{p_2(1-p_1)}$$

The estimate of the odds ratio plugs in the estimates for $p_1$ and $p_2$. If the data are organized into a two by two table:

<table>
<thead>
<tr>
<th></th>
<th>Successes</th>
<th>Failures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment A</td>
<td>$n_{11}$</td>
<td>$n_{12}$</td>
</tr>
<tr>
<td>Treatment B</td>
<td>$n_{21}$</td>
<td>$n_{22}$</td>
</tr>
</tbody>
</table>

Then the odds ratio estimate is

$$\hat{\theta} = \frac{n_{11} n_{22}}{n_{12} n_{21}}$$
The standard error for the *log odds ratio* is

\[
SE = \left( \frac{1}{n_{11}} + \frac{1}{n_{12}} + \frac{1}{n_{21}} + \frac{1}{n_{22}} \right)^{1/2}
\]

Notice that the log odds ratio and its standard error do not change if we transpose the rows and the columns. The interval for the log odds ratio is then:

\[
\log \hat{\theta} \pm Z_{1-\alpha/2} \cdot SE
\]

Exponentiating the endpoints yields an interval for the odds ratio. Taking logs first helps with the convergence to normality. You can not use this formula if any of the counts are 0.
Example:
Some final thoughts on the two sample binomial intervals presented.

• There are alternatives to the Wald intervals presented (score, likelihood ratio).
• Coverage of the intervals can be poor for small sample sizes.
• Independence of the groups is assumed.