Hepatitis E Vaccine

From the study ‘Safety and Efficacy of a Recombinant Hepatitis E Vaccine’ by Shrestha et al. in the New England Journal of Medicine in March 2007 (Vol. 356 No. 9), the results were

<table>
<thead>
<tr>
<th></th>
<th>Hepatitis E</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine</td>
<td>3</td>
<td>898</td>
</tr>
<tr>
<td>Placebo</td>
<td>66</td>
<td>896</td>
</tr>
</tbody>
</table>

The vaccine efficacy, as reported in the article, was 95.5% with a 95% confidence interval of (85.6%, 98.6%). How?
Risk Ratio

Consider

<table>
<thead>
<tr>
<th>Disease</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>a</td>
<td>a + b</td>
</tr>
<tr>
<td>No</td>
<td>b</td>
<td>c + d</td>
</tr>
</tbody>
</table>

where Exposure = Exposure to treatment (i.e., Vaccine in this example).

The risk ratio (or relative risk) is

\[ RR = \frac{P(\text{Disease}|\text{Exposure})}{P(\text{Disease}|\text{No Exposure})} = \frac{\frac{a}{a+b}}{\frac{c}{c+d}} \]

and the efficacy of the exposure is \((1 - \text{risk ratio})\) if \(\text{risk ratio} \leq 1\).

Hepatitis E Vaccine Example, continued

\[ RR = \frac{\frac{3}{66}}{\frac{66}{696}} = 0.045 \text{ or } 4.5\% \]

That is, getting the vaccine reduces your risk to only 4.5% of the original. The efficacy of the vaccine is 95.5% \(= 100\% - 4.5\%\)
Calculating a 95% Confidence Interval for risk ratio

1. Calculate a 95% confidence interval for ln(RR):
   - calculate ln(RR)
   - calculate
     \[
     \text{SE of ln(RR)} = \sqrt{\frac{1}{a} + \frac{1}{c} - \frac{1}{a+b} - \frac{1}{c+d}}
     \]
   - calculate 95% confidence interval for ln(RR):
     \[
     (\ln(RR) - 1.96\text{SE}, \ln(RR) + 1.96\text{SE})
     \]

2. A 95% confidence interval for RR is
   \[
   \left( e^{\ln(RR) - 1.96\text{SE}}, e^{\ln(RR) + 1.96\text{SE}} \right)
   \]
   and the RR is statistically significant if the interval excludes 1.

Hepatits E Vaccine Example, continued

1. 95% c.i. for ln(RR)
   - ln(RR) = ln(0.045) = -3.101
   - \[
   \text{SE(ln(RR))} = \sqrt{\frac{1}{3} + \frac{1}{66} - \frac{1}{898} - \frac{1}{896}} = \sqrt{.3462} = .5884
   \]
   - a 95% c.i. for ln(RR) is
     \[
     (-3.101 - [1.96 \times .5884], -3.101 + [1.96 \times .5884]) = (-4.254, -1.948)
     \]

2. a 95% c.i. for RR is
   \[
   (e^{-4.254}, e^{-1.948}) = (.014, .143)
   \]
   That is, with 95% confidence, the relative risk of getting hepatitis with the vaccine is only 1.4% to 14.3% of placebo. In other words, the vaccine reduces your risk by as low as 85.7% (= 100% - 14.3%) or as high as 98.6% (= 100% - 1.4%).
iClicker Question 14.1

In an observational study, a sample of 10000 smokers was taken, 50 were found to have lung cancer. Another sample of 10000 non-smokers was taken, only 2 have lung cancer. What is the relative risk of having lung cancer for smokers versus non-smokers?

A. 50
B. 2
C. 25
D. 100
E. cannot determine

iClicker Question 14.2

In an observational study, a sample of 10000 smokers was taken, 50 were found to have lung cancer. Another sample of 10000 non-smokers was taken, only 2 have lung cancer. A 95% confidence interval for the relative risk of having lung cancer for smokers versus smokers is (6.1, 102.5). Which of the following is true?

A. The proportion of smokers having lung cancer is significantly different than that of non-smokers.
B. There is no difference between the two proportions.
C. cannot determine