**Section 1.2.4 – Relative risks**

Frequently, the news media will report the results of a study and say something like “the researchers showed that an individual was <number> times more likely to get <disease> if they did <one behavior choice> than <second behavior choice>. IF the reporter understands basic statistics, they are reporting about a numerical measure called the *relative risk*.

One problem with basing inference on π1 – π2 is that it measures a quantity with a meaning that changes depending on the sizes of π1 – π2. For example, consider the following two scenarios:

|  |  |  |  |
| --- | --- | --- | --- |
|  | Adverse reactions | |  |
|  | Yes | No | Total |
| Drug | π1 = 0.510 | 1 – π1 = 0.490 | 1 |
| Placebo | π2 = 0.501 | 1 – π2 = 0.499 | 1 |

π1 – π2 = 0.510 – 0.501 = 0.009

|  |  |  |  |
| --- | --- | --- | --- |
|  | Adverse reactions | |  |
|  | Yes | No | Total |
| Drug | π1 = 0.010 | 1 – π1 = 0.990 | 1 |
| Placebo | π2 = 0.001 | 1 – π2 = 0.999 | 1 |

π1 – π2 = 0.010 – 0.001 = 0.009

In the first scenario, an increase of 0.009 is rather small **relative** to the already sizable probabilities given for the two groups. On the other hand, the second scenario has a much larger adverse reaction probability for the drug group **relative** to the placebo group.

We need to be able to convey the relative magnitudes of these changes better than differences allow. The relative risk allows us to make these comparisons by taking the ratio of the two success probabilities:



For scenario #2, the relative risk is RR = 0.010/0.001 = 10. The interpretation for this case is:

An adverse reaction is 10 *times as likely* for those individuals taking the drug than those individuals taking the placebo.

or

The probability of an adverse reaction is 10 *times as large* for those individuals taking the drug than those individuals taking the placebo.

where “likely” and “probability” are synonymous. Alternatively, we could also say,

An adverse reaction is 9 *times* *more* *likely* for individuals taking the drug than those individuals taking the placebo.

or

The probability of an adverse reaction is 9 *times* *larger* for individuals taking the drug than those individuals taking the placebo.

Why does one interpretation have 10 (RR) and another have 9 (RR – 1)? It can be helpful to look at some examples.

* “3 times as likely” and “2 times more likely” are equivalent to π1/π2 = 0.75/0.25 = 3.

“3 times as likely”: To get π1 = 0.75, one needs to take π2 + π2 + π2 = 0.25 + 0.25 + 0.25

“2 times more likely”: To get π1 = 0.75, one starts with 0.25 and take π2 + π2 = 0.25 + 0.25

* π1/π2 = 0.6/0.4 = 1.5 means that a success is 50% more likely for group 1 than for group 2. Alternatively, a success is 1.5 times as likely for group 1 than for group 2.
* “2 times as likely” is equivalent to π1/π2 = 0.6667/0.3333 = 2. In other words, π1 is twice the size of π2, π1 = 2×π2.
* “1 times as likely” and “0 times more likely” is equivalent to π1/π2 = 0.5/0.5 = 1. In other words, π1 and π2 are equal.

Other interpretations are possible depending on the context of the application. Please see the upcoming example for a specific case.

Questions:

* What does a relative risk of 1 mean?
* What is the numerical range of the relative risk?

The MLE of RR can be found by substituting MLEs of π1 and π2 into the equation for RR:



As with other maximum likelihood estimators, we could use a normal approximation with the statistic here and form a Wald confidence interval. However, the large sample normal approximation can be improved upon by working with the natural log transformation of the relative risk first. Thus, a Wald confidence interval for  is



where



is derived through using a delta method approximation (see Appendix B).

Of course, we are still interested in RR itself, so we can apply the exponential function to find the Wald confidence interval for RR:



What if w1 or w2 is equal to 0? You will have difficulty calculating the variance used in the interval! An ad-hoc solution is to add a small constant, either to wj and its corresponding nj count or to all cells of the contingency table even if some are not 0.

Example: COVID-19 vaccine clinical trial (COVID19vaccine.R)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Positive | Negative |  |
| Vaccine | 8 | 17,403 | 17,411 |
| Placebo | 162 | 17,349 | 17,511 |
|  | 170 | 34,752 | 34,922 |

> c.table <- array(data = c(8, 162, 17403, 17349), dim = c(2,2), dimnames = list(Treatment = c("Vaccine", "Placebo"), Outcome = c("Positive", "Negative")))

> c.table

Outcome

Treatment Positive Negative

Vaccine 8 17403

Placebo 162 17349

> pi.hat.table <- c.table/rowSums(c.table)

> pi.hat.table

Outcome

Treatment Positive Negative

Vaccine 0.0004594796 0.9995405

Placebo 0.0092513277 0.9907487

> pi.hat1 <- pi.hat.table[1,1]

> pi.hat2 <- pi.hat.table[2,1]

> round(pi.hat1/pi.hat2, 4)

[1] 0.0497

> round(1/(pi.hat1/pi.hat2), 4) # inverted

[1] 20.1344

> alpha <-0.05

> n1 <- sum(c.table[1,])

> n2 <- sum(c.table[2,])

> # Wald confidence interval

> var.log.RR <- 1/c.table[1,1] - 1/sum(c.table[1,]) + 1/c.table[2,1] - 1/sum(c.table[2,])

> RR.ci <- exp(log(pi.hat1/pi.hat2) + qnorm(p = c(alpha/2, 1-alpha/2)) \* sqrt(var.log.RR))

> round(RR.ci, 4)

[1] 0.0244 0.1010

> rev(round(1/RR.ci, 4)) # inverted

[1] 9.9034 40.9345

Defining index 1 to represent the vaccine group and 2 the placebo group, we find  = 0.0497. The **estimated** probability of infection is 0.05 times as large for those individuals receiving the vaccine than those receiving the placebo.

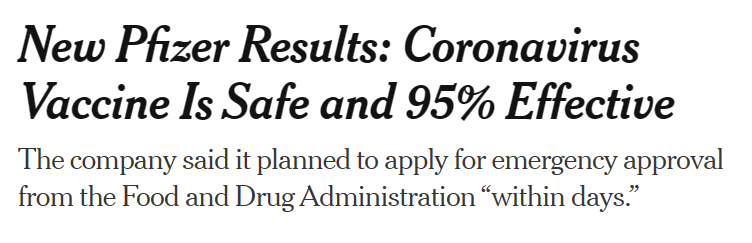
The 95% confidence interval is 0.0244 < RR < 0.1010. Therefore, with 95% confidence, probability of infection is between 0.02 and 0.10 times as large for those individuals receiving the vaccine than those receiving the placebo.

Comments:

* For cases like this, we are interested in “risk reduction” provided by one of the groups, so it is natural to interpret the relative risk in this manner. For example, we could say the vaccine reduces the risk of infection by an estimated 95%, and

with 95% confidence, the vaccine reduces the risk of infection by 90% to 98%.

Risk reduction for vaccine clinical trials corresponds to the measure known as vaccine efficacy: VE = 1 – RR. A headline from *The New York Times* in 2020 highlighted this measure when the results from the clinical trial for the Pfizer-BioNTech COVID-19 vaccine were released:



* In other situations, we will want to invert the relative risk so that we are always interpreting a quantity greater than 1. For example, the estimated probability of infection is 20 times as large for the placebo group than the vaccine group. This interpretation is probably not as desirable for this example.
* Notice that “estimated” is not used for the confidence interval interpretation because it is stated for a particular parameter not the statistic (estimate).
* Would you rather be in the placebo or vaccine group? Why?

Example: Larry Bird (Bird.R)

Examining the relative risk may not be as important for this problem, but we can still calculate it.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Second | |  |
|  |  | Made | Missed | Total |
| First | Made | = 0.8807 | = 0.1193 | 1 |
| Missed | = 0.9057 | = 0.0943 | 1 |

Code and output from earlier:

> c.table <- array(data = c(251, 48, 34, 5), dim = c(2,2), dimnames = list(First = c("made", "missed"), Second =

c("made", "missed")))

> pi.hat.table <- c.table/rowSums(c.table)

> pi.hat1 <- pi.hat.table[1,1]

> pi.hat2 <- pi.hat.table[2,1]

New code and output:

> round(pi.hat1/pi.hat2, 4)

[1] 0.9724

> alpha <- 0.05

> n1 <- sum(c.table[1,])

> n2 <- sum(c.table[2,])

> ci <- exp(log(pi.hat1/pi.hat2) + qnorm(p = c(alpha/2, 1-

alpha/2)) \* sqrt((1-pi.hat1)/(n1\*pi.hat1) + (1-

pi.hat2)/(n2\*pi.hat2)))

> round(ci, 4)

[1] 0.8827 1.0713

> rev(round(1/ci, 4)) #inverted

[1] 0.9334 1.1329

/ = 0.8807/0.9057 = 0.9724

If the relative risk is inverted: / = 0.9057/0.8807 = 1.0284. Thus, a successful second free throw is estimated to be 2.84% times more likely to occur when the first free throw is missed rather than made. Alternatively, a successful second free throw attempt is estimated to be 1.0284 times as likely when the first free throw is missed rather than made.

With 95% confidence, a second free throw success is between 0.9334 and 1.1329 times as likely when the first free throw is missed rather than made.

Questions:

1. What else could be said here if one wanted to do a hypothesis of H0: π1/π2 = 1 vs. Ha: π1/π2 ≠ 1.
2. What if the interval was 2 < π1/π2 < 4?

Perhaps it may be more of interest for this example to examine a relative risk with respect to a missed second free throw attempt:

> (1-pi.hat1)/(1-pi.hat2)

[1] 1.264561

> exp(log((1-pi.hat1)/(1-pi.hat2)) + qnorm(p = c(alpha/2,

1-alpha/2)) \* sqrt((pi.hat1)/(n1\*(1-pi.hat1)) +

(pi.hat2)/(n2\*(1-pi.hat2))))

[1] 0.5183628 3.0849352

A missed second free throw is estimated to be 26.5% times more likely to occur when the first free throw is made than when it is missed. While this may sound to be an important finding, notice the confidence interval contains 1.

Other confidence intervals have been proposed. In particular a score interval can be calculated using the riskscoreci() function of the PropCIs package.