

Relative Risk, Odds, and Fisher's exact test

I) Relative Risk

A) Simply, relative risk is the ratio of \hat{p}_1/\hat{p}_2 . For instance, suppose we wanted to take another look at our Seat belt safety data from Florida:

Safety equipment in use	Injury		Total
	Fatal	Non-fatal	
None	1,601	165,527	167,128
Seat belt	510	412,368	412,878

Previously, we established that the proportion of fatalities wearing seat belts is $510/412,878 = \hat{p}_2 = .001235$, and the proportion of fatalities for not wearing a seat belt is $1,601/165,128 = \hat{p}_1 = .00958$.

So, this means that our relative risk is $.009672/.001235 = 7.83$. In other words, the risk of dying is 7.8 times higher if one is not wearing a seatbelt than if one is wearing a seatbelt. This makes it sound pretty good for wearing a seatbelt!

Often, when one hears reports in the news that a particular risk is x times something else, they are talking "relative risk". It is important to realize that often the overall chance of something happening is very small. The chance of dying in a car accident, regardless of seatbelt use is quite small.

B) Another example (from text, p. 436, [445], 4th and 5th edition have removed this example - but see example {10.9.1, p. 401} {10.9.7, p. 427} for a similar example.

Birthweight	Smoking Status	
	Smoker	Nonsmoker
Low	237	197
Normal	3,489	5,870
TOTAL	3,726	6,067

(note that the table is arranged the other way from the one above)

$$\hat{p}_1 = 237/3,726 = .064 \qquad \hat{p}_2 = 197/6,067 = .032$$

So our relative risk is $.064/.032 = 2$, indicating that the risk for low birthweight in babies is twice as high for smokers as for non-smokers.

(Incidentally - what do we need to know before we can really conclude this? Chi-square = 52.8, , and $p < .001$, so there is a significant difference here.)

II. Odds ratio

A) This time, one develops the "odds" of something happening. The odds ratio is defined as follows:

$$\theta = \frac{\frac{p_1}{1-p_1}}{\frac{p_2}{1-p_2}}$$

where theta is the odds ratio. As you might guess, we estimate this using theta-hat and the appropriate p-hat:

$$\hat{\theta} = \frac{\frac{\hat{p}_1}{1-\hat{p}_1}}{\frac{\hat{p}_2}{1-\hat{p}_2}}$$

B) For example, using the seat-belt data above, we have:

$$\hat{\theta} = \frac{\frac{0.00958}{1-0.00958}}{\frac{0.001235}{1-0.001235}} = 7.822$$

which is very similar to the relative risk given above.

C) Relative Risk and Odds ratio.

1) As it turns out, when \hat{p}_1 and \hat{p}_2 are both very small, the Relative Risk and the Odds ratio are very close. This is easy to see from the equation above for $\hat{\theta}$. If \hat{p}_1 and \hat{p}_2 are small, then you wind up dividing \hat{p}_1 and \hat{p}_2 by 1, which is essentially the Relative Risk.

2) However, if \hat{p}_1 and \hat{p}_2 are not both small, you can get quite different results (your book is quite wrong when it says this happens only rarely - lets use an example from the book p. 396, [p. 404], (not in the 4th or 5th editions, but you should be able to follow this fairly easily) looking at the treatment of angina patients):

	Treatment	
	Timolol	Placebo
Angina-free	44	19
Not angina-free	116	128
TOTAL	160	147

a) Note that what we're really interested in here is the relative risk of having an angina if one takes a placebo as opposed to Timolol. We really should re-arrange the table a bit, but it's not necessary. What we want is \hat{p}_1 = proportion of people taking placebo who have angina = $128/147 = .871$, and \hat{p}_2 = proportion of people taking timolol who have angina = $116/160 = .725$.

b) So now our Relative Risk = $.871/.725 = 1.20$

c) But what happens to our Odds Ratio?

Odds Ratio = $.871/(1-.871)/.725/(1-.725) = 2.55$

d) So here we have two different bits of information:

i) The risk of having an angina attack if taking a placebo rather than timolol is 1.2.

ii) But the odds of having an angina attack are actually 2.6 if one is taking a placebo rather than timolol.

3) A little confusing, no??

Remember:

Relative Risk measures the risk of a nasty outcome compared to some “treatment”.

Odds Ratio just compares the odds of one outcome happening over another.

(odds ratio often makes more sense than relative risk: “the relative risk of having dark eyes if one has dark hair.....???)

4) To finish off this topic (and to confuse things a bit more!!):

a) When can one use RR and OR?

i) OR one can use anytime

ii) RR can only be used in certain circumstances

b) For example, if one goes out and samples 10,000 smokers and 10,000 non-smokers to see if they died of lung cancer, what happens? (The proportions are real data based on a study in Britain, but the numbers in the table are made up).

Death from lung cancer	Disease	
	Smoker	Non-smoker
Yes	14	1
No	9,986	9,999
TOTAL	10,000	10,000

c) Relative risk of smoker dying from lung cancer as opposed to a non-smoker dying of lung cancer is $14/1 = 14$ (technically $(14/10,000) / (1/10,000) = 14$).

d) Does it make sense to calculate the relative risk of dying from lung cancer if you're a smoker as opposed to dying from something else and if you're a smoker?

the math would be: $14/15 = .933$
 $9986/19985 = .500$

and the relative risk would be $.933/500 = 1.87$

But it doesn't make any sense!!!

NO - For two reasons:

i) it doesn't really make much sense (think about it)

ii) you can't do it mathematically:

- you selected the number of smokers and non-smokers!! The number of smokers in your study is no longer random, so you can't estimate anything having to do with the number of smokers, at least not directly.

- for example, suppose you picked 5,000 smokers and 10,000 non-smokers. Using the same proportions, our relative risk would now be:

$$7/8 = .875$$
$$4993/14992 = .333$$

and the RR would be: $.875/.333 = 2.627$

- notice that it's changed completely! In other words, it depends on our sample sizes, and it SHOULD NOT! But it does, so it's totally useless.

e) But what about the Odds ratio? The Odds ratio is:

$$\text{Odds ratio} = \frac{14 \times 9,999}{1 \times 9,986} = 14$$

(this is a shortcut formula, only usable in 2x2 tables:

$$\hat{\theta} = \frac{n_{11} \times n_{22}}{n_{12} \times n_{21}}$$

where n_{11} is the upper left, n_{12} the upper right, etc.)

almost the same (it is the same if you round it like here). But now a little mathematical fact:

\hat{p}_1 = proportion of people who died of lung cancer who smoke

\hat{p}_1^* = proportion of people who smoke if they died of lung cancer

\hat{p}_2 = proportion of people who died of lung cancer who didn't smoke

\hat{p}_2^* = proportion of people who smoke if they did not die of lung cancer

As it turns out, the Odds ratio is the same if one uses \hat{p}_1 and \hat{p}_2 or \hat{p}_1^* and \hat{p}_2^* .

So suppose we had the following data (were we select 10,000 people who died of lung cancer and 10,000 people who didn't die of lung cancer):

Death from lung cancer	Disease		
	Smoker	Non-smoker	
Yes	9,333	667	10,000
No	4,997	5,003	10,000

Now we can't calculate the Relative Risk of dying from lung cancer if you're a smoker vs. a non-smoker.

But the Odds ratio still works, and we can easily calculate it:

$$\frac{9,333 \times 5,003}{4,997 \times 667} = 14 \text{ (I used the same proportions as above, just made the samples bigger)}$$

So now we can say that the odds of a smoker dying of lung cancer are 14 times that of a non-smoker dying of lung cancer. It still works!

This is why the Odds ratio is used a lot in medicine and epidemiology - it can be used even when the study wasn't designed to find certain relationships.

III. Fisher's exact test

A) This example doesn't come from biology, but a little history of statistics doesn't hurt (this is a famous example from statistics).

1) Way back when, Fisher came across a lady who claimed to be able to tell if tea or milk were poured into a cup first (the British like to drink milk with their tea). So he put her to the test with eight cups, four of which had milk added first, the other four tea first. He got the following results:

	Lady's guess		
	Milk	Tea	Total
Poured first			
Milk	3	1	4
Tea	1	3	4
Total	4	4	8

2) Looking at the results, one can see that the lady seems to have done a little better than “random guessing”, but is this result explainable by chance?

3) Can we use a chi-squared statistic? NO! (all categories have expected values < 5)

4) But we can generate exact probabilities!

But before we do:

H_0 : The lady can not tell the difference between pouring tea or milk first.

H_1 : The lady can tell if milk or tea is poured first (note that this is actually a directional hypothesis)

$$\alpha = .05$$

a) what we do is calculate the probability of having gotten that result or “worse” if our null hypothesis is that the lady can't tell the difference. Our marginal totals are fixed for this test (more later).

i) What is “worse”?

$$\begin{array}{cc} 4 & 0 \\ 0 & 4 \end{array}$$

(the lady did perfectly)

ii) So now we just need to calculate the probability of getting this and the result we got.

iii) This uses something called a “hypergeometric distribution”, which is kind of similar to the binomial. Here's how you make it work:

The number of ways the lady could guess milk first in 3 out of 4 cups with milk poured first is:

$$\binom{4}{3} = \frac{4!}{3!1!} = 4$$

The number of ways the lady could guess milk first in 1 out of 4 cups with tea poured first is:

$$\binom{4}{1} = \frac{4!}{1!3!} = 4$$

And the number of ways she can guess milk first in four out of 8 cups:

$$\binom{8}{4} = \frac{8!}{4!4!} = 70$$

Notice that what we're doing is calculating the probability of getting the result she got and then dividing by the total number of possible outcomes one can get.

So now we just multiply the first two quantities and divide by the last:

$$4 \times 4 = 16 \quad 16/70 = 0.229$$

$$\Pr\{\text{of getting the above result}\} = 0.229$$

Now we repeat all this for the table with the "worse result":

$$\Pr\{\text{of getting even worse result}\} = .014$$

add these up and we get $0.229 + 0.014 = 0.243$.

iv) So the probability of the lady guessing is .243, or a little less than $\frac{1}{4}$. We conclude that we do not have any evidence that she can tell the difference.

B) Some more details:

1) Here's a formula (for 2 x 2 tables):

$$\frac{\begin{array}{l} \# \text{ of ways of} \\ \text{getting result} \\ \text{in first cell} \end{array} \times \begin{array}{l} \# \text{ of ways of} \\ \text{getting result} \\ \text{in second cell (row wise)} \end{array}}{\begin{array}{l} \text{Probability of getting result in} \\ \text{column 1 total} \end{array}}$$

where: # of ways of getting result in first cell = Binom (row 1 total, first cell count)

of ways of getting result in second cell = Binom (row 2 total, second cell count)

of ways of getting result in column totals = Binom (grand total, column 1 totals)

(you're basically going row by row, using the first column and the total column to get your binomial coefficients).

- 2) As you can see, this gets messy real fast. Not only do you have to calculate the probability of getting the table you got (the above formula), but also the probability of getting each worse table.
- 3) Fisher's exact test is almost always done on a computer, particularly for 3 x 3 tables and higher (the formula above will need to be modified).
- 4) You should know how to do a very simple test, sort of like the Tea-drinker example.
- 5) Your text has another nice example in section 10.4 and goes through this again. READ IT!
- 6) As presented, Fisher's test is actually directional. One can use Fisher's test in a non-directional setting, but then we'd have to calculate all the tables in the "opposite direction" of our result or worse. For our tea drinker, we'd have to include tables:

$$\begin{array}{cc} 1 & 3 & \text{and} & 0 & 4 \\ 3 & 1 & & 4 & 0 \end{array}$$

(add up the probabilities of these to our total)

See the example on page 418, [426], ~~{384}~~ ~~{405}~~ in your text.

- 7) Not all statistical packages will not perform Fisher's exact test (but many other packages (e.g. R) do). Incidentally, any problems you get will be very simple.

C) One more example (since this is sort of confusing):

- 1) Exercise 10.35, [10.40], ~~{10.4.1}~~ ~~{10.4.1}~~ (fictional data):

		Treatment		Total
		A	B	
Outcome	Die	4	2	6
	Live	10	14	24
Total		14	16	

- 2) H_0 : Treatment A and B are the same
 H_1 : Treatment B is better (directional)

$$\alpha = .05$$

- 3) Which tables are worse than our result? First, remember that our marginal totals are fixed. Why? because we picked 14 people for treatment A and 16 people for group B. Also, our H_0 implies that the proportions in column a and b are the same, so that our row totals can't change (if there is no effect, then the probability of dying is the same regardless of column, and we can use the row total to estimate that - but that also means the row total does not change).

So here are the tables that would be worse than what we got.

5	1	6	0
9	15	8	16

4) So now all we have to do (ha, ha) is figure out the probability of getting these three tables and add these probabilities up.

5) Probability of getting the result we got:

$$\frac{\binom{6}{4}\binom{24}{10}}{\binom{30}{14}} = 0.20229$$

(we could stop here - why??)

6) Probability of getting the two worse tables:

$$\frac{\binom{6}{5}\binom{24}{9}}{\binom{30}{14}} = 0.0539 \quad \text{and} \quad \frac{\binom{6}{6}\binom{24}{8}}{\binom{30}{14}} = 0.00506$$

7) Adding up all these probabilities, we get:

$$.20229 + .0539 + .00506 = .26129$$

8) Since our p -value is $> \alpha$, we conclude that we have no evidence that treatment B is better than treatment A and the observed result is due to chance.