

Review of the odds ratio *Credit: chapter 10 from Rosner and notes from C. Kendzioriski*

If an event takes place with probability p , the odds in favor of the event are $\frac{p}{1-p}$ to 1. $p = \frac{1}{2}$ implies 1 to 1 odds; $p = \frac{2}{3}$ implies 2 to 1 odds.

In this class, the **odds ratio** (OR) is the odds of disease among exposed individuals divided by the odds of disease among unexposed.

Note that the OR is sometimes defined alternatively as

$$OR_{alt} = \frac{P(exposure|disease)/(1 - P(exposure|disease))}{P(exposure|nondiseased)/(1 - P(exposure|nondiseased))}$$

Note that these definitions are equivalent.

	Exposure		
Disease	(Yes)	(No)	total
(Yes)	a	b	a+b
(No)	c	d	c+d
total	a+c	b+d	n

We also showed that the odds ratio (if table above was obtained from n independent observations) could be estimated by $\frac{ad}{bc}$ ($\hat{OR} = \frac{ad}{bc}$).

Back to the C-section example...

	Monitored		
C section	(Yes)	(No)	total
(Yes)	358	229	587
(No)	2492	2745	5237
total	2850	2974	5824

The odds ratio here is estimated to be $\frac{(358)(2745)}{(229)(2492)} = 1.72$

The odds of being delivered by C-section are 1.72 times greater for fetuses that are being monitored.

Question: Is 1.72 significantly different than 1, i.e. is there an association?

For the 2 x 2 table:

	Exposed	Not Exposed	Total
Disease	a	b	a+b
No Disease	c	d	c+d
Total	a+c	b+d	n

The odds ratio OR is estimated by $\hat{OR} = \frac{ad}{bc}$

The estimated standard error of the natural logarithm (\ln) of this estimate is given by

$$\hat{se}(\ln(\hat{OR})) = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$$

An approximate 95 % confidence interval for $\ln(\hat{OR})$ is

$$\left(\ln(\hat{OR}) - 1.96\hat{se}[\ln(\hat{OR})], \ln(\hat{OR}) + 1.96\hat{se}[\ln(\hat{OR})] \right)$$

An approximate 95 % confidence interval for \hat{OR} is

$$\left(e^{\ln(\hat{OR}) - 1.96\hat{se}[\ln(\hat{OR})]}, e^{\ln(\hat{OR}) + 1.96\hat{se}[\ln(\hat{OR})]} \right)$$

For the C-section data:

	Monitored		
C section	(Yes)	(No)	total
(Yes)	358	229	587
(No)	2492	2745	5237
total	2850	2974	5824

The odds ratio OR is estimated by $\hat{OR} = \frac{ad}{bc} = 1.72$
 and $ln(\hat{OR}) = ln(1.72) = 0.542$

The estimated standard error of the natural logarithm (ln) of this estimate is given by

$$\begin{aligned}
 \hat{se}(ln(\hat{OR})) &= \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}} \\
 &= \sqrt{\frac{1}{358} + \frac{1}{229} + \frac{1}{2492} + \frac{1}{2745}} \\
 &= 0.089
 \end{aligned}$$

An approximate 95 % confidence interval for $\ln(\hat{OR})$ is

$$(\ln(\hat{OR}) - 1.96\hat{se}[\ln(\hat{OR})], \ln(\hat{OR}) + 1.96\hat{se}[\ln(\hat{OR})])$$

which is

$$(0.542 - 1.96(0.089), 0.542 + 1.96(0.089)) = (0.368, 0.716)$$

An approximate 95 % confidence interval for \hat{OR} is

$$(e^{0.368}, e^{0.716}) = (1.44, 2.05)$$

The odds ratio is useful to measure the strength of association between two dichotomous variables. However, when drawing conclusions based on calculations of the odds ratio (or other quantity for that matter), care must be taken. For example, a sample from one hospital might not provide information about the population at large. When sampling from a restricted population (one hospital), one can often show relationships between variables that do not in fact exist in the general population. This is an illustration of *Berkson's fallacy*.

Suppose for example that you obtain information on 257 hospitalized patients concerning respiratory and circulatory disease. Using this information, you record the following:

	Respiratory Disease		
Circulatory Disease	(Yes)	(No)	total
(Yes)	7	29	36
(No)	13	208	221
total	20	237	257

You could perform a chi-square test and if you did, you would reject the null and conclude (for $\alpha = 0.05$) that there is an association between respiratory and circulatory disease.

If you instead sampled from the population at large and recorded the same information to obtain

Circulatory Disease	Respiratory Disease		total
	(Yes)	(No)	
(Yes)	22	171	193
(No)	202	2389	2591
total	224	2560	2784

you would not reject the null using a chi-square test with $\alpha = 0.05$. The difference occurs because the rates of case prevalence are different in the two populations.

McNemar's test

Motivational example: Study the association between heart attacks and diabetes in the US Navajo population.

Data: 144 Navajos that had suffered heart attacks were identified and a number of characteristics were recorded (age, gender, smoking status, etc.). For each subject (case) a matching control subject (who did not experience a heart attack) was identified. Thus, 144 pairs of matching case and control subjects was identified. Each pair shared the same characteristics except for heart attack status. These pairs were then evaluated for the presence of diabetes (exposure variable).

	No Heart Attack		
Heart Attack	(Db+)	(Db-)	total
(Db+)	9	37	46
(Db-)	16	82	98
total	25	119	144

We want to test the null hypothesis that diabetes is not associated with having a heart attack. Alternative: diabetes is associated with an increased risk of heart attack. We need a test that allows us to determine whether diabetes can be observed (significantly) more often in heart attack patient than in control subjects (without heart attack).

For McNemar's test only discordant pairs, where one person is diabetic and the other is not, are informative.

Concordant pairs: pairs in which the exposure (diabetes status) is the same, e.g. pairs where both subjects are diabetics.

Discordant pairs: one subject is diabetic and the other is not.

	No Heart Attack		
Heart Attack	(Db+)	(Db-)	total
(Db+)	9	37	46
(Db-)	16	82	98
total	25	119	144

Consider only discordant pairs (where one person is diabetic and the other is not). Let $r = 37$ represent the number of discordant pairs in which the heart attack case has diabetes and $s = 16$ represent the number of discordant pairs in which the non heart attack control subject is the diabetic. If the null is true, r and s should be approximately equal.

Under the null,

$$X^2 = \frac{(|r - s| - 1)^2}{r + s}$$

is approximately chi-square (χ^2) distributed with 1 degree of freedom.

	No Heart Attack		
Heart Attack	(Db+)	(Db-)	total
(Db+)	9	37	46
(Db-)	16	82	98
total	25	119	144

For this example,

$$\begin{aligned}
 X^2 &= \frac{(|37 - 16| - 1)^2}{37 + 16} \\
 &= 7.55
 \end{aligned}$$

p-value=0.0060

Odds ratio for McNemar's test is $r/s = 37/16 = 2.31$, not $(ad)/(bc)$. Confidence intervals can also be obtained (Book).

The previous example was an illustration of McNemar's test. McNemar's test should only be used for paired (matched) data. In contrast, use a proportion test, a chi-square test or Fisher's exact test to compare proportions from **2 independent samples** (e.g. prospective cohort study or retrospective case control study)..

New example involving matched pairs (McNemar's test)

Suppose we want to compare two different chemotherapy protocols for breast cancer after mastectomy. The two treatment groups should be as comparable as possible on other prognostic factors. To accomplish this, we set up a matched study. 621 breast cancer patients are paired. A random member of each pair is assigned to treatment A; the other to treatment B. Survival after 5 years is the measured outcome.

	Outcome		
Treatment	(Survived)	(Died)	total
(A)	526	95	621
(B)	515	106	621
total	1041	201	1242

Note that the 5 year survival rate for treatment A is $526/621 = 0.847$ and for treatment B is $515/621 = 0.829$. You can check that the Yates corrected chi-square statistic is 0.59 with 1 degree of freedom, which is NOT significant.

SINCE THE DATA ARE PAIRED, THE CHI-SQUARE TEST IS NOT APPROPRIATE.

Outcome Tr. A patient	Outcome Tr. B patient		total
	(Survived)	(Died)	
(Survived)	510	16	526
(Died)	5	90	95
total	515	106	621

McNemar's test states that under the null

$$X^2 = \frac{(|r - s| - 1)^2}{r + s}$$

is approximately chi-square (χ^2) distributed with 1 degree of freedom.

For this example,

$$\begin{aligned} X^2 &= \frac{(11 - 1)^2}{5 + 16} \\ &= 4.76 \end{aligned}$$