Analysis of Contingency Table

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Analysis of One-Way Table: Chi-square Goodness-Of-Fit Test

Example: Medelian Law of Genetics

1. Mendelian theory of genetics

2. Shape and color of a certain pea be classified into four groups "round and yellow", "round and green", "angular and yellow" and "angular and green"

3. According to the ratio $9/3/3/1$

Example: Medelian Law of Genetics

For an experiment with $n = 556$ peas, the following Table 1 were observed. We are interested in that: is there good agreement between the observed experiment number and the expected ratio $9/3/3/1$?

Table 1: Medelian law of genetics: observed data

Shape and Color	Observed Number $= O_i$	Expected Number $= E_i$	$= n \times \pi_i^0$
Round and yellow	315	312.75	$= 556 \times 9/16$
Round and green	108	104.25	$= 556 \times 3/16$
Angular and yellow	101	104.75	$= 556 \times 3/16$
Angular and green	32	34.75	$= 556 \times 1/16$

Example: Medelian Law of Genetics

Assume that these measurements came from an underlying known discrete probability distribution $9/16, 3/16, 3/16, 1/16$. How can the validity of this assumption be tested?

1. Suppose there are k categories of a discrete random variable.

2. Total n observations

3. O_i: observed numbers of the i^{th} category

4. E_i: expected numbers of the i^{th} category based on the null hypothesis probability distribution with proportion π_i^0 in i^{th} category, for $i = 1, 2, \ldots, k$.

Notation

$$E_i = n \times \pi_i^0 \; ; \tag{1}$$

$$\sum_{i=1}^{k} \pi_i^0 = 1; \quad i = 1, 2, \ldots k. \tag{2}$$

The null hypothesis and alternative hypothesis are

$$H_0 : \pi_i = \pi_i^0; \; i = 1, 2 \ldots, k \tag{3}$$

versus $H_A : \pi_i \neq \pi_i^0$ for at least one of i, $i = 1, 2, \ldots, k$. (4)

Chi-square Goodness-Of-Fit Test for One-Way Table

1. The observed sample statistic, X^2, is

$$X^2_{GOF} = \sum_{i=1}^{k} \frac{(O_i - E_i)^2}{E_i} \overset{\text{asym}}{\sim} \boldsymbol{\chi}^2_{k-1}. \tag{5}$$

2. X^2_{GOF} asymptotically follows chi-squared distribution with $k-1$ degree of freedom.

3. The approximated p-value is

$$p - \text{value} = P(\boldsymbol{\chi}^2_{k-1} \geq X^2_{GOF}). \tag{6}$$

4. The test is usually used only if $n \times \pi_i^0 \geq 5$, for $i = 1, 2, \ldots, k$.

Example: Medelian Law of Genetics

1. The observed sample statistics X^2_{GOF} is

$$X^2_{GOF} = \frac{(315-312.75)^2}{312.75} + \frac{(108-104.25)^2}{104.25} + \frac{(101-104.25)^2}{104.25} + \frac{(32-34.75)^2}{34.75} = 0.470. \quad (7)$$

2. The observed $X^2_{GOF} = 0.47$ is $\boldsymbol{\chi}^2$ distributed with $4-1=3$ degree of freedom.

3. p-value is 0.9254. (A "huge" p-value!)

4. There is good agreement with the null hypothesis; that is a good fit of the data to the null hypothesis probability distribution.

Example: Medelian Law of Genetics with R

```
> obs.i<-c(315,108,101,32)
> p.null<-c(9,3,3,1)
> chisq.test(obs.i,p=p.null,rescale.p=TRUE)

        Chi-squared test for given probabilities

data:  obs.i
X-squared = 0.47, df = 3, p-value = 0.9254
```

Example: Medelian Law of Genetics with SAS

```
data medgen ;
    input type n @@ ;
cards;
    1 315
    2 108
    3 101
    4 32
run;
```

Example: Medelian Law of Genetics with SAS

```
title1 "FREQ: One-Way Chi-Square Goodness of Fit Test";
title2 "Mendelian genetics data: use
    TESTP=(0.5625 0.1875 0.0625)" ;
    proc freq data=medgen order=data ;
    tables type /
    TESTP=(0.5625 0.1875 0.1875 0.0625) chisq ;
    weight n ;
run;
```

Example: Medelian Law of Genetics with SAS

```
title1 "FREQ: One-Way Chi-Square Goodness of Fit Test";
title2 "Mendelian genetics data: use
    TESTF=(312.75 104.25 104.25 34.75)" ;
proc freq data=medgen order=data ;
    tables type /
    TESTF=(312.75 104.25 104.25 34.75) chisq ;
    weight n ;
run;
```

DM-TKA Example

1. In DM-TKR Data, he medications for DM are oral hypoglycemic agent (OHA), insulin injection (Insulin) and diet control. The population proportion for these three medication are 50% , 30% and 20% respectively.

2. We are interested in that: is there good agreement between the observed sample number and the expected ratio $5/3/2$?

DM-TKA Example

1. The observed sample statistics is $X^2 = 37.45$, with p-value =0.0001.

2. So we reject the null hypothesis, there is no good agreement with the null hypothesis; that is not a good fit of the data to the null hypothesis probability distribution.

DM-TKA Example with R

```
> setwd("C://temp//Rdata")
> DMTKRcsv<-read.csv("DMTKRcsv.csv", header=TRUE, sep=",", dec=".")
> attch(DMTKRcsv)
> (obs.i<-table(Med))
Med
 0  1  2
66  8  4
> p.null<-c(0.5,0.3,0.2)
> chisq.test(obs.i,p=p.null,rescale.p=FALSE)

        Chi-squared test for given probabilities

data:  obs.i
X-squared = 37.453, df = 2, p-value = 7.365e-09
```

DM-TKA Example with SAS

```
title1 "FREQ: One-Way Chi-Square
    Goodness of Fit Test";
title2 "DM-TKA Medication Examples";
proc sort data=dmtkanew ;
by med ;
run;
proc freq data=dmtkanew order=data ;
    tables med /
        TESTP=(0.5 0.3 0.2) chisq ;
run;
```

Introduction to Contingency Tables

DM-TKA Example

1. In DM-TKR Data, investigators are interested in the difference of proportion of infection between two groups: adding antibiotics and non-adding antibiotics.

2. Table 2, shows 0 infective patient of 41 patients in adding antibiotics group and 5 infective patients of 37 patients in non-adding antibiotics group.

DM-TKA Example

Table 2: Summary of antibiotics groups and infection

Antibiotics	Infection	Number
No	Yes	5
No	No	32
Yes	Yes	0
Yes	No	41

DM-TKA Example

Investigators can also summarize the result in different way as so called 2×2 **Contingency Table** as in Table 3.

Table 3: Summary of antibiotics groups and infection as 2×2 table

	Infection		
Antibiotics	No	Yes	Total
No	32	5	37
Yes	41	0	41
Total	73	5	78

DM-TKA Example

1. For another example, investigators are also interested in the difference of proportion of male and female between two groups to evaluate the randomization of subjects.

2. And there are 28 male patients of 41 patients in adding antibiotics group and 25 of 37 patients in non-adding antibiotics group.

3. Investigators can present the result as in Table 4:

DM-TKA Example

Table 4: Summary of Sex and Antibiotics Groups

Sex	Antibiotics	Number
Male	No	25
Female	No	12
Male	Yes	28
Female	Yes	13

DM-TKA Example

Investigator can also summarize the result in different way as so called 2×2 **Contingency Table** as in Table 5.

Table 5: Summary of antibiotics groups and sex as 2×2 table

	Antibiotics		
Sex	No	Yes	Total
Female	12	13	25
Male	25	28	53
Total	37	41	78

Design and Measures of 2×2 Table for Categorical Data

2×2 **Table**

1. A 2×2 **contingency table** is a table composed of two rows cross-classified by two columns.

2. An appropriate way to display data that can be classified by two different variables, say X and Y, each of which has only two possible outcomes.

3. One variable is arbitrarily assigned to the rows.

4. The other to the columns.

5. Each of the four cells represents the number of units, with a specific value for each of the two variables.

2×2 Table

1. The cell are sometimes referred to by number, as in Table 6 and 7.
2. (1, 1) cell being the cell in the first row and first column,
3. (1, 2) cell being the cell in the second row and first column,
4. (2, 1) cell being the cell in the second row and first column,
5. (2, 2) cell being the cell in the second row and second column.
6. The observed (expected) number of units in the four cells are likewise referred to as $O_{11}, O_{12}, O_{21}, O_{22}$, and $E_{11}, E_{12}, E_{21}, E_{22}$ respectively.

2×2 **Table**

Table 6: Summary of observed numbers as 2×2 table

	Variable Y		
Variable X	level 1	level 2	Total
level 1	$O_{11} = a$	$O_{12} = b$	$a + b = n_{1.}$ (row 1 margin)
level 2	$O_{21} = c$	$O_{22} = d$	$c + d = n_{2.}$ (row 2 margin)
Total	$a + c = n_{.1}$	$b + d = n_{.2}$	$a + b + c + d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

2×2 **Table**

Table 7: Summary of expected numbers as 2×2 table

	Variable Y		
Variable X	level 1	level 2	Total
level 1	E_{11}	E_{12}	$a + b = n_{1.}$ (row 1 margin)
level 2	E_{21}	E_{22}	$c + d = n_{2.}$ (row 2 margin)
Total	$a + c = n_{.1}$	$b + d = n_{.2}$	$a + b + c + d = n_{..}$
	column 1 margin	column 2 margin	(grand total)

Note: Computation of expected values for 2×2 contingency table as

$$E_{ij} = \frac{n_{i.}\, n_{.j}}{n_{..}}$$

2×2 **Table**

1. The number of units in each row and display them in the right margins, which are called **row marginal totals** or **row margins**.

2. The number of units in each column and display them in the bottom margins, which are called **column marginal totals** or **column margins**.

3. The total number of units in the four cells, which is displayed into lower right-hand corner of the table and is called the **grand total**.

2×2 **Table**

1. Two different sampling designs, **prospective** or **retrospective**, lend themselves to a contingency-table framework.

2. In both instances, we want to test whether or not the **proportions** are the same in the **two independent samples**.

3. This test is referred to as a **test for homogeneity** of binomial proportions.

Prospective Study

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine

1. Investigators conducted a one-year prospective study to evaluate the re-injury probability of knee sport injury.

2. Students of the department of physical education in a university who have a sport injury after the beg inning of the study are included in the study.

3. These student are followed up at least one year or till the occurrence of re-injury during participating sport activities.

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine

4. Investigators would like to know whether the first time sport injury is knee injury will have higher chance of re-injury. The result is shown in the Table 12.

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine

Table 8: Prospective study: re-injury of knee sports injury

	Re-injury		
Knee injury	Yes	No	Total
Yes	27	42	69
No	72	218	290
Total	99	260	359

Prospective Study

1. A group of disease-free individuals are identified at one point in time

2. Followed over a period of tie until some of them develop of the disease

3. The development of disease over time is then related to other variables (i.e., risk exposure) measured at baseline.

Prospective Study: Initial State

At the initial stage of a prospective study we have the counts or frequencies of a 2×2 contingency table as in Table 9.

Prospective Study: Initial State

Table 9: Summary of the initial stage of a prospective study as a 2×2 table

	Disease will develop	Disease will not develop	Total
Risk factor present (Exposure: Yes +)	unknown	unknown	a+b
Risk factor absent (Exposure: No -)	unknown	unknown	c+d
Total	unknown	unknown	a+b+c+d

Prospective Study: Final Stage

At the final stage of a prospective study, we have complete the 2×2 table as in Table 10.

Prospective Study: Final Stage

Table 10: Summary of the final stage of a prospective study as a 2×2 table

	Disease will develop	disease will not develop	Total
Risk factor present (Exposure: Yes +)	a	b	a+b=$n_{1.}$
Risk factor absent (Exposure: No -)	c	d	c+d=$n_{2.}$
Total	a+c=$n_{.1}$	b+d=$n_{.2}$	a+b+c+d=$n_{..}$

Notation

1. π_1: probability of developing disease for risk-factor-present (exposure $+$) individuals

2. π_2: probability of developing disease for risk-factor-absent (exposure -) individuals

$$\pi_1 = P[\text{ disease} \mid \text{risk factor present }] \tag{8}$$

$$\pi_2 = P[\text{ disease} \mid \text{risk factor absent }] \tag{9}$$

Point Estimators of π_1 and π_2

Table 11: Point Estimation of a Prosiective 2×2 Table

	Disease will develop	disease will not develop	Total
Exposure: Yes +	a	b	a+b=$n_{1.}$
Exposure: No -	c	d	c+d=$n_{2.}$
Total	a+c=$n_{.1}$	b+d=$n_{.2}$	a+b+c+d=$n_{..}$

The point estimates of π_1 and π_2 are

$$\hat{\pi}_1 = \frac{a}{a+b} = \frac{a}{n_{1.}} \tag{10}$$

$$\hat{\pi}_2 = \frac{c}{c+d} = \frac{c}{n_{2.}} \tag{11}$$

Point Estimation of Risk Difference

The point estimate of **risk difference (RD)** is given as

$$\widehat{RD} = \widehat{\textbf{Risk Difference}} = \hat{\pi}_1 - \hat{\pi}_2 \tag{12}$$

Testing Hypothesis

$$
\begin{aligned}
& H_0: && \pi_1 = \pi_2 = \pi \\
\text{versus} \quad & H_A: && \pi_1 \neq \pi_2
\end{aligned}
\tag{13}
$$

Approximate Z Test Statistic

Approximated Z test based on the normal distribution

$$H_0 : \pi_1 = \pi_2 = \pi \tag{14}$$

$$\text{under } H_0 : \quad \hat{\pi} = \frac{n_{1.}\hat{\pi}_1 + n_{2.}\hat{\pi}_2}{n_{1.} + n_{2.}} = \frac{a+c}{n_{..}}; \tag{15}$$

Approximate Z Test Statistic

Approximated Z statistic

$$\mathbf{Z} = \frac{(\hat{\pi}_1 - \hat{\pi}_2)}{\sqrt{\hat{\pi}(1-\hat{\pi})\left(\frac{1}{n_{1.}} + \frac{1}{n_{2.}}\right)}}. \tag{16}$$

We can also use the binomial continuity correction as

$$\mathbf{Z}^c = \frac{|\ \hat{\pi}_1 - \hat{\pi}_2\ | - \left(\frac{1}{2n_{1.}} + \frac{1}{2n_{2.}}\right)}{\sqrt{\hat{\pi}(1-\hat{\pi})\left(\frac{1}{n_{1.}} + \frac{1}{n_{2.}}\right)}}. \tag{17}$$

Approximate Z Test Statistic Sampling Distribution

1. Under H_0,

$$\mathbf{Z}(\text{or } \mathbf{Z}^c) \quad \overset{\text{asym}}{\sim} \quad N(0,1); \tag{18}$$

$\mathbf{Z}$ (or $\mathbf{Z}'$) follows approximated standard normal distribution.

2. The p-value is calculated as

$$p\text{-value} \quad = \quad 2\left[1 - \Phi(|\mathbf{Z}|)\right]. \tag{19}$$

Approximate Z Test Statistic

The observed sample statistic z is

$$z = \frac{\frac{a}{a+b} - \frac{c}{c+d}}{\sqrt{\frac{(a+c)(b+d)}{(a+b+c+d)^2}\left[\frac{1}{a+b} + \frac{1}{c+d}\right]}} \tag{20}$$

$$z^2 = \frac{(a+b+c+d)(|ad-bc|)^2}{\left[(a+b)(c+d)(a+c)(b+d)\right]} \tag{21}$$

Confidence Interval of Risk Difference

When we reject the null hypothesis $H_0 : \pi_1 = \pi_2 = \pi$, we can calculate the $(1-\alpha) \times 100\%$ confidence interval. The variance of estimated risk difference

$$\mathbf{Var}(\hat{\pi}_1 - \hat{\pi}_2) = \frac{\hat{\pi}_1(1-\hat{\pi}_1)}{n_{1.}} + \frac{\hat{\pi}_2(1-\hat{\pi}_2)}{n_{2.}} \tag{22}$$

$(1-\alpha) \times 100\%$ C.I. : of risk difference

$$\hat{\pi}_1 - \hat{\pi}_2 \pm Z_{1-\alpha/2}\sqrt{\frac{\hat{\pi}_1(1-\hat{\pi}_1)}{n_{1.}} + \frac{\hat{\pi}_2(1-\hat{\pi}_2)}{n_{2.}}} \tag{23}$$

Note:

use this statistic and C.I. only if $n_1\hat{\pi}(1-\hat{\pi}) \geq 5$ and $n_2\hat{\pi}(1-\hat{\pi}) \geq 5$ (under H_0).

Point Estimation of Risk Ratio

The **risk ratio** or **relative risk (RR)** is defined as

$$RR = \frac{\pi_1}{\pi_2}. \tag{24}$$

The point estimator is given as

$$RR(=\rho) = \frac{Pr[\text{disease} + \mid \text{risk-present (exposure} +)\ ]}{Pr[\text{disease} + \mid \text{risk-absent (exposure -)}\ ]} \tag{25}$$

Confidence Interval of Risk Ratio

1. Risk ratio ranges between $(0, \infty)$

2. Risk ratio is right skewed

3. Apporximate C.I. should consider these two points

Confidence Interval of Risk Ratio

$$\mathbf{Var}(\log \hat{\pi}_1) \approx \frac{1}{\hat{\pi}_1^2}\mathbf{Var}(\hat{\pi}_1) \tag{26}$$

$$= \frac{1}{\hat{\pi}_1^2}\left(\frac{\hat{\pi}_1(1-\hat{\pi}_1)}{n_{1.}}\right) = \frac{(1-\hat{\pi}_1)}{n_{1.}\hat{\pi}_1} \tag{27}$$

$$= \frac{b}{a\ n_{1.}} = \frac{b}{a\ (a+b)} = \frac{1}{a} - \frac{1}{a+b} \tag{28}$$

Confidence Interval of Risk Ratio

$$\mathbf{Var}[\log(\widehat{RR})] = \mathbf{Var}[\log(\hat{\pi}_1)] + \mathbf{Var}[\log(\hat{\pi}_2)] \tag{29}$$

$$\widehat{\mathbf{Var}}[\log(\widehat{RR})] = \frac{1}{a} - \frac{1}{a+b} + \frac{1}{c} - \frac{1}{c+d} \tag{30}$$

$$\text{s.e. } [\log(\widehat{RR})] = \sqrt{\frac{1}{a} - \frac{1}{a+b} + \frac{1}{c} - \frac{1}{c+d}} \tag{31}$$

Confidence Interval of Risk Ratio

The approximated $(1-\alpha)\times 100\%$ C.I. of $\widehat{RR}$:

$$\exp[\ \log(\widehat{RR}) \pm Z_{1-\alpha/2}\ \text{s.e.}(\log(\widehat{RR}))\ ] \tag{32}$$

That is

$$\Big(\exp[\ \log(\widehat{RR}) - Z_{1-\alpha/2}\ \text{s.e.}(\log(\widehat{RR}))\ ],$$
$$\exp[\ \log(\widehat{RR}) + Z_{1-\alpha/2}\ \text{s.e.}(\log(\widehat{RR}))\ ]\Big) \tag{33}$$

Risk Difference and Risk Ratio

There are several restrictions of risk difference and relative risk. For examples

1. If $\pi_1 = 0.001$ and $\pi_2 = 0.005$, then the risk difference $(RD = 0.004)$ is very small.

2. If $\pi_1 = 0.001$ and $\pi_2 = 0.005$, RD is always less than $RR = 1/5 = 0.2$,

3. If $\pi_1 = 0.001$ and $\pi_2 = 0.01$, RD is always less than $RR = 1/10 = 0.1$.

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine

Investigators would like to know whether the first time sport injury is knee injury will have higher chance of re-injury.

Table 12: Prospective study: re-injury of knee sports injury

	Re-injury		
Knee injury	Yes	No	Total
Yes	27	42	69
No	72	218	290
Total	99	260	359

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine

1. Pearson's Chi-Square Test X^2 is 5.70, p-value is 0.0169.

2. Continuity Adjusted Chi-Square Test X^2 is 5.0155 and p-value is 0.0251.

3. Fisher's Exact Test with two-sided p-value is 0.024.

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine

4. Relative Risk (RR) is 1.579, 95% C.I. $(1.10, 2.25)$.

5. When the first time sports injury is knee injury, it has 1.58 times higher of re-injury proportion than the others.

6. Odds Ratio (OR) is 1.94, and 95% Wald C.I. is $(1.07, 3.49)$.

7. Odds ratio is not close to risk ratio, why?

8. The risk difference is 0.14 (s.e. 0.064).

9. When the first time sport injury is knee injury, it has 0.14 higher proportion with 95% Wald C.I. $(0.176, 0.268)$.

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: R

```
> reinj.tab<-matrix(c(27,42,72,218),nrow=2,byrow=T)
> reinj.tab
     [,1] [,2]
[1,]   27   42
[2,]   72  218
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: R

```
> chisq.test(reinj.tab,correct=F)

        Pearson's Chi-squared test

data:  reinj.tab
X-squared = 5.7092, df = 1, p-value = 0.01688
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: R

```
> chisq.test(reinj.tab)

        Pearson's Chi-squared test with Yates' continuity c


data:  reinj.tab
X-squared = 5.0155, df = 1, p-value = 0.02512
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: R

```
> fisher.test(reinj.tab)

        Fisher's Exact Test for Count Data

data:  reinj.tab
p-value = 0.02392
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
 1.070824 3.488594
sample estimates:
odds ratio
  1.942525
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: R

```
relative.risk <- function(a, b, c, d)
{
    cl <- function(x)
    {
     exp(log(rr)
     +c(1, -1)*qnorm(x)*sqrt(b/a/(a+b)+d/c/(c+d)))
    }
    rr <- a*(c+d)/c/(a+b)
    list(rr=rr, Wald.cl95=cl(0.025))
}
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: R

```
> relative.risk(27,42,72,218)
$rr
[1] 1.576087
$Wald.cl95
[1] 1.104046 2.249952
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: R

```
> temp<-prop.test(c(27,72),c(69,290),correct=F)
> temp

        2-sample test for equality of proportions without continuity co

data:  c(27, 72) out of c(69, 290)
X-squared = 5.7092, df = 1, p-value = 0.01688
alternative hypothesis: two.sided
95 percent confidence interval:
 0.01759800 0.26845897
sample estimates:
   prop 1    prop 2
0.3913043 0.2482759
> temp$estimate[[1]]-temp$estimate[[2]]
[1] 0.1430285
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: SAS

```
title "Prospective study: 2x2 Table of Knee Reinjury Data";
data kneereinj ;
     input knee reinj count @@ ;
     cards;
     1 1 27
     1 0 42
     0 1 72
     0 0 218
run;
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: SAS

```
proc freq data=kneereinj order=data page ;
     tables knee*reinj / exact riskdiff relrisk  ;
     weight count;
run;
```

Example: Re-Injury Probability of Initial Knee Injury

knee Frequency| Percent | Row Pct | Col Pct	reinj 1	reinj 0	Total
1	27	42	69
	7.52	11.70	19.22
	39.13	60.87	
	27.27	16.15	
0	72	218	290
	20.06	60.72	80.78
	24.83	75.17	
	72.73	83.85	
Total	99	260	359
	27.58	72.42	100.00

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: SAS

Statistics for Table of knee by reinj

Statistic	DF	Value	Prob
Chi-Square	1	5.7092	0.0169
Likelihood Ratio Chi-Square	1	5.4189	0.0199
Continuity Adj. Chi-Square	1	5.0155	0.0251

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: SAS

```
       Fisher's Exact Test
---------------------------------
Cell (1,1) Frequency (F)       27
Left-sided Pr <= F         0.9935
Right-sided Pr >= F        0.0140
Table Probability (P)      0.0075
Two-sided Pr <= P          0.0239
```

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: SAS

Statistics for Table of knee by reinj

Column 1 Risk Estimates

	Risk	ASE	(Asymptotic) 95% Confidence Limits		(Exact) 95% Confidence Limits	
Row 1	0.3913	0.0588	0.2761	0.5065	0.2760	0.5163
Row 2	0.2483	0.0254	0.1986	0.2980	0.1996	0.3021
Total	0.2758	0.0236	0.2295	0.3220	0.2302	0.3251
Difference	0.1430	0.0640	0.0176	0.2685		

Difference is (Row 1 - Row 2)

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: SAS

Column 2 Risk Estimates

	Risk	ASE	(Asymptotic) 95% Confidence Limits		(Exact) 95% Confidence Limits	
Row 1	0.6087	0.0588	0.4935	0.7239	0.4837	0.7240
Row 2	0.7517	0.0254	0.7020	0.8014	0.6979	0.8004
Total	0.7242	0.0236	0.6780	0.7705	0.6749	0.7698
Difference	-0.1430	0.0640	-0.2685	-0.0176		

Difference is (Row 1 - Row 2)

Example: Re-Injury Probability of Initial Knee Injury in Sports Medicine: SAS

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	1.9464	1.1207	3.3804
Cohort (Col1 Risk)	1.5761	1.1040	2.2500
Cohort (Col2 Risk)	0.8097	0.6627	0.9894

Sample Size = 359

Retrospective Study

Hip Dislocation and Infection in Bipolar Hemiarthroplasty

1. Investogators conduct a retrospective study to assess the outcomes of hip hemiarthroplasty surgery.

2. Hip dislocation after surgery is one of the worest outcomes of hemiarthroplasty.

3. Infection is considered one of important risk factors related to dislocation.

Hip Dislocation and Infection in Bipolar Hemiarthroplasty

1. Subjects who have received hip hemiarthroplasty are included in this retrospective study.

2. There are total 980 subjects, and these subjects are classified into a 2×2 table according to two variables: dislocation and infection.

3. Investigators assessed whether infection would have higher chance of dislocation.

4. The result is shown in the Table 13.

Hip Dislocation and Infection in Bipolar Hemiarthroplasty

Table 13: Retrospective study: dislocation and infection in hip hemiarthroplasty

	Dislocation		
Infection	Yes (cases)	No (controls)	Total
Yes	10	19	29
No	11	940	951
Total	21	959	980

Retrospective Study

1. **Retrospective study** is a study in which two groups of individuals are identified:

   (a) A group that has the disease under study (the cases)

   (b) A group that does not have the disease under study (the controls).

2. An attempt is then made to relate theirs health habits to their current disease status.

Retrospective Study: Initial Stage

At the initial stage of a prospective study, we have the counts or frequencies of a 2×2 contingency table as in Table 14.

Retrospective Study: Initial Stage

Table 14: Summary of the initial stage of a retrospective study as a 2×2 table

	Disease will develop	Disease will not develop	Total
Risk factor present (Exposed Yes +)	unknown	unknown	unknown
Risk factor absent (Exposed No -)	unknown	unknown	unknown
Total	a+c	b+d	a+b+c+d

Retrospective Study: Final Stage

At the final stage of a retrospective study, we have complete the 2×2 table as in Table 15.

Retrospective Study: Final Stage

Table 15: Summary of the final stage of a retrospective study as a 2×2 table

	Disease will develop	Disease will not develop	Total
Risk factor present (Exposure: Yes +)	a	b	a+b=$n_{1.}$
Risk factor absent (Exposure: No -)	c	d	c+d=$n_{2.}$
Total	a+c=$n_{.1}$	b+d=$n_{.2}$	a+b+c+d=$n_{..}$

Odds and Odds Ratio

1. If the probability of a success is π, then

$$\text{the } \textbf{odds} \text{ in favor of success } = \frac{\pi}{1-\pi} \tag{34}$$

2. If the probability of a success for two conditions are π_1 and π_2, then the **odds ratio** in favor of success for condtion 1 relative to condition 2 is

$$\text{Odds Ratio } = \frac{\pi_1/(1-\pi_1)}{\pi_2/(1-\pi_2)} = \frac{\pi_1 \times (1-\pi_2)}{\pi_2 \times (1-\pi_1)} \tag{35}$$

Notatoin

1. π_1 : Probability of developing disease for risk-factor-present (exposure $+$) individuals

2. π_2 : Probability of developing disease for risk-factor-absent (exposure -) individuals

$$\pi_1 = P[\text{ disease} \mid \text{risk factor present }] \tag{36}$$

$$\pi_2 = P[\text{ disease} \mid \text{risk factor absent }] \tag{37}$$

Point Estimation of Odds

The point estimates of odds in favor of risk-factor-present in cases and controls are

1. Odds_{D+} : Odds in favor of risk factor being present (exposure $+$) in cases

2. Odds_{D-} : Odds in favor of risk factor being present (exposure $+$) in controls

Point Estimation of Odds

$$\begin{aligned} \text{Odds}_{D+} &= \frac{P[\text{ risk present} \mid \text{cases (disease present)}\ ]}{P[\text{ risk absent} \mid \text{cases (disease present)}\ ]} \\ \widehat{\text{Odds}}_{D+} &= \frac{a}{c} \end{aligned} \tag{38}$$

$$\begin{aligned} \text{Odds}_{D-} &= \frac{P[\text{ risk present} \mid \text{controls (disease absent)}\ ]}{P[\text{ risk absent} \mid \text{controls (disease absent)}\ ]} \\ \widehat{\text{Odds}}_{D-} &= \frac{b}{d} \end{aligned} \tag{39}$$

Odds Ratio

1. If two proportions π_1, π_2 are considered, the odds in favor of risk present relative to risk absent given cases or controls are computed for each groups, then the **ratio of odds**, or **odds ratio**, becomes a useful measure for relating the two proportions.

2. The **Odds Ratio (OR)** is defined as

$$\frac{P[\text{disease} + \mid \text{risk-present (exposure} +)] \,/\, P[\text{disease} - \mid \text{risk-present (exposure} +)]}{P[\text{disease} + \mid \text{risk-absent (exposure} -)] \,/\, P[\text{disease} - \mid \text{risk-absent (exposure} -)]}$$

Odds Ratio: Point Estimation

$$OR = \frac{\pi_1/(1-\pi_1)}{\pi_2/(1-\pi_2)} = \frac{\pi_1(1-\pi_2)}{\pi_2(1-\pi_1)} \tag{40}$$

$$\widehat{OR} = \frac{\hat{\pi}_1(1-\hat{\pi}_2)}{\hat{\pi}_2(1-\hat{\pi}_1)} = \frac{[a/(a+b)] \times [d/(c+d)]}{[c/(c+d)] \times [b/(a+b)]} \tag{41}$$

$$\widehat{OR} = \frac{ad}{bc} \tag{42}$$

Odds Ratio: Confidence

$$\mathbf{Var}[\log(\widehat{OR})] \approx \frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d} \tag{43}$$

The approximated $(1-\alpha)\times 100\%$ C.I.:

$$\exp[\ \log(\widehat{OR}) \pm Z_{1-\alpha/2}\text{s.e.}(\log(\widehat{OR}))\ ] \tag{44}$$

That is

$$\Big(\exp[\ \log(\widehat{OR}) - Z_{1-\alpha/2}\text{s.e.}(\log(\widehat{OR}))\ ] \quad \exp[\ \log(\widehat{OR}) + Z_{1-\alpha/2}\text{s.e.}(\log(\widehat{OR}))\ ]\Big). \tag{45}$$

Variance of log Odds Ratio

$$
\begin{aligned}
& \mathbf{Var}[\log(\widehat{OR})] \\
\approx\ & \mathbf{Var}\left[\log[(\frac{\hat{\pi}_1}{(1-\hat{\pi}_1)})/(\frac{\hat{\pi}_2}{(1-\hat{\pi}_2)})]\right] && (46) \\
\approx\ & \mathbf{Var}\left[\log(\frac{\hat{\pi}_1}{(1-\hat{\pi}_1)}) - \log(\frac{\hat{\pi}_2}{(1-\hat{\pi}_2)})\right] && (47) \\
\approx\ & \mathbf{Var}\left[\log(\frac{\hat{\pi}_1}{(1-\hat{\pi}_1)})\right] + \mathbf{Var}\left[\log(\frac{\hat{\pi}_2}{(1-\hat{\pi}_2)})\right] && (48)
\end{aligned}
$$

Variance of log(Odds Ratio)

$$\mathbf{Var}\left[\log\left(\frac{\hat{\pi}_1}{(1-\hat{\pi}_1)}\right)\right] \approx \frac{1}{[\hat{\pi}_1(1-\hat{\pi}_1)]^2}\mathbf{Var}(\hat{\pi}_1) \tag{49}$$

$$\approx \frac{1}{[\hat{\pi}_1(1-\hat{\pi}_1)]^2}\left[\frac{\hat{\pi}_1(1-\hat{\pi}_1)}{n_{1.}}\right] \tag{50}$$

$$\approx \frac{1}{\hat{\pi}_1(1-\hat{\pi}_1)}\frac{1}{n_{1.}} = \frac{a+b}{ab} \tag{51}$$

$$= \frac{1}{a}+\frac{1}{b} \tag{52}$$

$$\mathbf{Var}\left[\log\frac{\hat{\pi}_2}{(1-\hat{\pi}_2)}\right] \approx \frac{1}{c}+\frac{1}{d} \tag{53}$$

Disease Odds Ratio

Disease Odds Ratio is the odds in favor of disease for the risk-present group divided by odds in favor of disease for the risk-absent group.

$$\widehat{\text{Disease Odds Ratio}} = \frac{a/b}{c/d} \tag{54}$$

Risk-present Odds Ratio (Exposure Odds Ratio)

Risk-Present Odds Ratio (Exposure Odds Ratio) is the odds in favor of being risk-present for disease (cases) subjects divided by odds in favor of being risk-present for non-disease (controls) subjects.

$$\widehat{\text{Risk-Present Odds Ratio}} = \frac{a/c}{b/d} \tag{55}$$

Disease odds ratio and Exposure Odds Ratio

$$\widehat{\text{Disease Odds Ratio}} = \frac{a/b}{c/d}$$

$$\widehat{\text{Risk-Present Odds Ratio}} = \frac{a/c}{b/d} \tag{56}$$

Actually, **risk-present odds ratio is equal to disease odds ratio**.

$$\widehat{\text{Disease Odds Ratio}} = \widehat{\text{Risk-Present Odds Ratio}} \tag{57}$$

Odds Ratio and Risk Ratio

1. If the disease is rare, $P[\text{ disease }] \longrightarrow 0$
2. And if $\pi_1 \longrightarrow 0, \pi_2 \longrightarrow 0$
3. Then a will be small relative to b and. similarly, c will be small compared to d.
4. $b/(a+b) \longrightarrow 1$ and $c/(c+d) \longrightarrow 1$.

Odds Ratio and Risk Ratio

So $a+b$ can be replaced by b and $c+d$ can be replaced by d in the expression for risk ratio (relative risk), and the result is that the **odds ratio** is approximate to **risk ratio (relative risk)**.

$$OR = \frac{\pi_1/\pi_1}{\pi_2/\pi_2} = \frac{\pi_1/(1-\pi_1)}{\pi_2/(1-\pi_2)} \approx \frac{\pi_1}{\pi_2} = RR \tag{58}$$

$$\widehat{OR} = \frac{\hat{\pi}_1(1-\hat{\pi}_2)}{\hat{\pi}_2(1-\hat{\pi}_1)} = \frac{[a/(a+b)] \times [d/(c+d)]}{[c/(c+d)] \times [b/(a+b)]} \approx \frac{[a/(a+b)]}{[c/(c+d)]} = \widehat{RR} \tag{59}$$

Notes: Odds Ratio and Risk Ratio

1. The odds ratio is often used as an approximation to the relative risk for rare disease.

2. General Rule of Thumb: OR is a good approximation as long as the probability of the outcome in the unexposed is less than 10%.

Notes: Odds Ratio and Risk Ratio

1. If the probability of disease is the same for exposed and unexposed subjects, then $\widehat{OR} = 1$.

2. Conversely, odds ratios greater than 1 indicate a greater likelihood of disease among the exposed than among the unexposed, whereas odds ratios less than 1 indicate a greater likelihood of disease among the unexposed than among the exposed.

3. There is no restriction on the odds ratio as there was for the risk ratio. Specifically, as the probability of disease among the exposed π_1 approaches 0, OR approaches 0, whereas as π_1 approaches 1, OR approaches ∞, regardless of value of the probability of disease among the unexposed π_2.

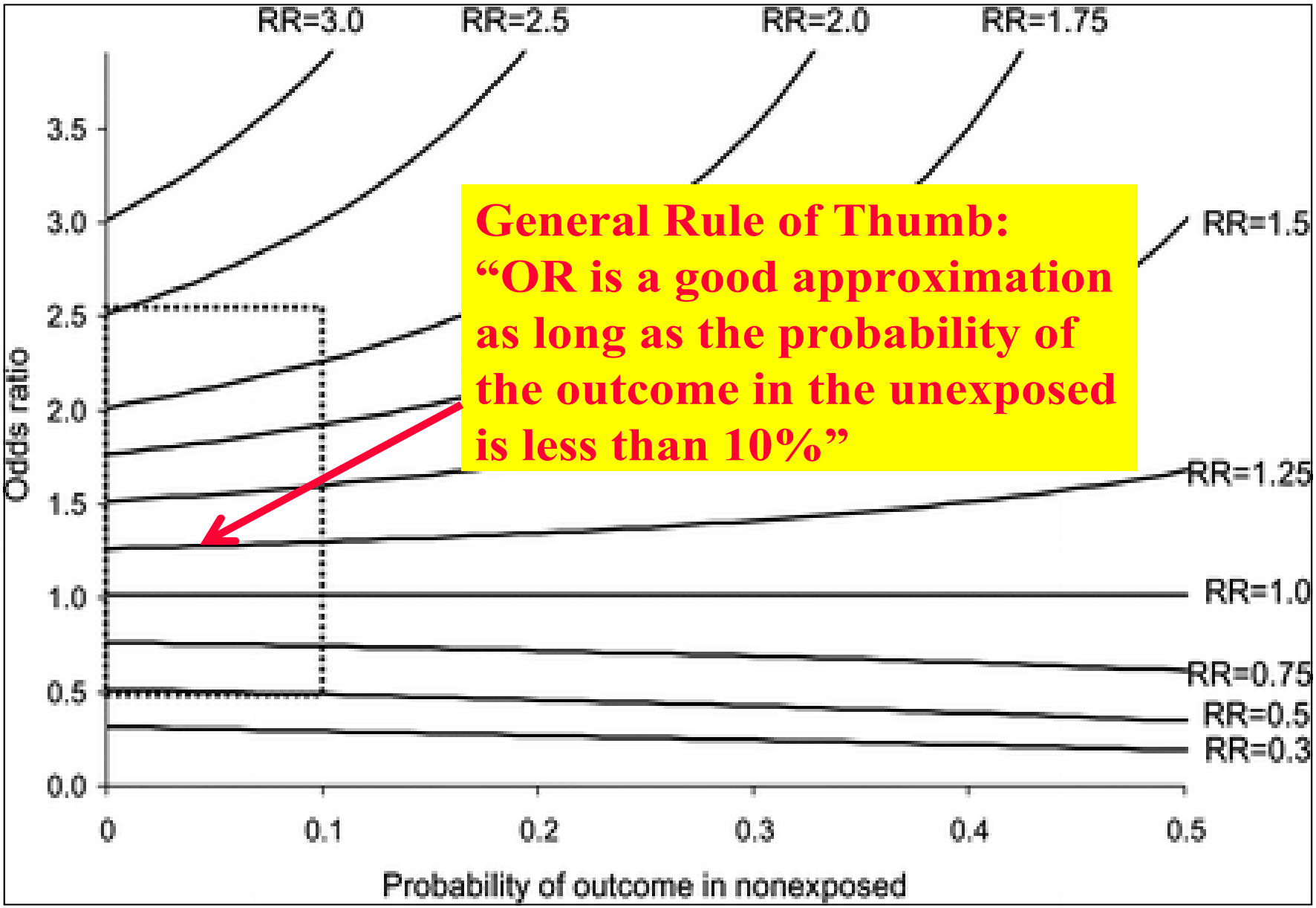

Figure 1: When is the OR is a good approximation of the RR?

Hip Dislocation and Infection in Bipolar Hemiarthroplasty

Table 16: Retrospective study: dislocation and infection in hip hemiarthroplasty

	Dislocation		
Infection	Yes (cases)	No (controls)	Total
Yes	10	19	29
No	11	940	951
Total	21	959	980

Hip Dislocation and Infection

1. Pearson's Chi-Square Test X^2 is 149.05, p-value is less than 0.0001.

2. Continuity Adjusted Chi-Square Test X^2 is 133.58, p-value is less than 0.0001.

3. Fisher's Exact Test two-sided p-value is 2.69×10^{-11}.

Hip Dislocation and Infection

4. Odds Ratio (OR) is 44.97, with 95% C.I. $(17.06, 118.56)$.

5. The odds for dislocation in infection subjects is 44.9 times higher than that of others,

6. That is the risk for dislocation in infection subjects is approximated 44.9 times higher than those without infection.

Hip Dislocation and Infection

```
> hip.dis.tab<-matrix(c(10,19,11,940),nrow=2,byrow=T)
> hip.dis.tab
     [,1] [,2]
[1,]   10   19
[2,]   11  940
```

Hip Dislocation and Infection

```
> chisq.test(hip.dis.tab,correct=F)

        Pearson's Chi-squared test

data:  hip.dis.tab
X-squared = 149.0511, df = 1, p-value < 2.2e-16

Warning message:
Chi-squared approximation may be incorrect in:
    chisq.test(hip.dis.tab, correct = F)
```

Hip Dislocation and Infection

```
> chisq.test(hip.dis.tab)
Pearson's Chi-squared test with Yates' continuity correction

data:  hip.dis.tab
X-squared = 133.582, df = 1, p-value < 2.2e-16

Warning message:
Chi-squared approximation may be incorrect in:
chisq.test(hip.dis.tab)
```

Hip Dislocation and Infection

```
> fisher.test(hip.dis.tab)

        Fisher's Exact Test for Count Data

data:  hip.dis.tab
p-value = 2.694e-11
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
  14.90394 131.06932
sample estimates:
odds ratio
  44.12354
```

Hip Dislocation and Infection

```
odds.ratio <- function(a, b, c, d, correct=FALSE)
{
    cl <- function(x)
    {
        or*exp(c(1, -1)*qnorm(x)*sqrt(1/a+1/b+1/c+1/d))
    }
    if (correct || a*b*c*d == 0) {
        a <- a+0.5
        b <- b+0.5
        c <- c+0.5
        d <- d+0.5
    }
    or <- a*d/(b*c)
    list(or=or, cl90=cl(0.05), cl95=cl(0.025))
}
```

Hip Dislocation and Infection

```
> odds.ratio(10, 19, 11, 940)
$or
[1] 44.97608

$cl90
[1]  19.93799 101.45692

$cl95
[1]  17.06077 118.56722
```

Hip Dislocation and Infection

```
> odds.ratio(10, 19, 11, 940,correct=TRUE)
$or
[1] 44.03679

$cl90
[1] 19.85456 97.67219

$cl95
[1]  17.04451 113.77499
```

Hip Dislocation and Infection

```
title "Retrospective study: 2 x 2 Table
    of Dislocation and Infection Data";
data disinf ;
     input infection dislocation count @@ ;
     cards;
     1 1 10
     1 0 19
     0 1 11
     0 0 940
run;
```

Hip Dislocation and Infection

```
proc freq data=disinf order=data page ;
     tables infection*dislocation / exact relrisk ;
     weight count;
     run;
```

Hip Dislocation and Infection

infection Frequency / Percent / Row Pct / Col Pct	dislocation 1	dislocation 0	Total
1	10	19	29
	1.02	1.94	2.96
	34.48	65.52	
	47.62	1.98	
0	11	940	951
	1.12	95.92	97.04
	1.16	98.84	
	52.38	98.02	
Total	21	959	980
	2.14	97.86	100.00

Hip Dislocation and Infection

Statistics for Table of infection by dislocation

Statistic	DF	Value	Prob
Chi-Square	1	149.0511	<.0001
Likelihood Ratio Chi-Square	1	45.6074	<.0001
Continuity Adj. Chi-Square	1	133.5820	<.0001
Mantel-Haenszel Chi-Square	1	148.8990	<.0001

WARNING: 25% of the cells have expected counts less than 5. Chi-Square may not be a valid test.

Hip Dislocation and Infection

Fisher's Exact Test	
Cell (1,1) Frequency (F)	10
Left-sided Pr <= F	1.0000
Right-sided Pr >= F	2.694E-11
Table Probability (P)	2.640E-11
Two-sided Pr <= P	2.694E-11

Hip Dislocation and Infection

STATISTICS for Table of infection by dislocation

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	44.9761	17.0608	118.5672
Cohort (Col1 Risk)	29.8119	13.7679	64.5525
Cohort (Col2 Risk)	0.6628	0.5090	0.8632

Sample Size = 980

Pearson's Chi-square Test for Association of 2×2 Table

Pearson's Chi-square Test for 2×2 Table

1. A 2×2 **contingency table** is a table composed of two rows cross-classified by two columns.

2. 2×2 Table displays data that can be classified by two different variables, each of which has only two possible outcomes.

3. One variable is arbitrarily assigned to the rows and the other to the columns.

4. Each of the four cells represents the number of units, with a specific value for each of the two variables.

Pearson's Chi-square Test for 2×2 Table

1. The cell are sometimes referred to by number, as in Table 17, with the (i, j) cell being the cell in the i^{th} row and j^{th} column.

2. The observed (expected) number of units in the four cells are likewise referred to as $O_{11}, O_{12}, O_{21}, O_{22}$, and $E_{11}, E_{12}, E_{21}, E_{22}$ respectively.

Pearson's Chi-square Test for 2×2 Table

Table 17: Pearson's chi-square test: observed 2×2 table

	Variable Y		
Variable X	level 1	level 2	Total
level 1	$O_{11} = a$	$O_{12} = b$	$a + b = n_{1.}$ (row 1 margin)
level 2	$O_{21} = c$	$O_{22} = d$	$c + d = n_{2.}$ (row 2 margin)
Total	$a + c = n_{.1}$	$b + d = n_{.2}$	$a + b + c + d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

Note: Computation of expected values for 2×2 contingency table as

$$E_{ij} = \frac{n_{i.}\, n_{.j}}{n_{..}}$$

Notation

$$\pi_1 = P[Y = 1 \mid X = 1] \tag{60}$$

$$= P[\text{ variable } Y, \text{ level one} \mid \text{variable } X, \text{ level one }] \tag{61}$$

$$\pi_2 = P[Y = 1 \mid X = 2] \tag{62}$$

$$= P[\text{ variable } Y, \text{ level one} \mid \text{variable } X, \text{ level two }] \tag{63}$$

Testing Hypothesis

$$H_0 \ : \ RR = 1 \tag{64}$$

$$\text{or } H_0 \ : \ OR = 1, \tag{65}$$

$$\text{or } H_0 \ : \ \text{4 cells are independent,} \tag{66}$$

$$\text{or } H_0 \ : \ \text{no association of } 2 \times 2 \text{ contingency table,} \tag{67}$$

$$\text{such as } H_0 \ : \ \pi_1 = \pi_2. \tag{68}$$

Point Estimation

$$\hat{\pi}_1 = \frac{a}{a+b} = \frac{a}{n_{1.}} \tag{69}$$

$$\hat{\pi}_2 = \frac{c}{c+d} = \frac{c}{n_{2.}} \tag{70}$$

Pearson's Chi-square Test for 2×2 Table

If the corresponding cells of **observed** and **expected** values in these two (observed and expected) tables are **close**, then H_0 will be approximate. If they are sufficiently different, then H_0 will be rejected.

Pearson's Chi-square Test for 2×2 Table

1. Pearson's chi-square test is

$$X_p^2 = \sum_{i,j} \frac{(O_{ij} - E_{ij})^2}{E_{ij}} \overset{\text{asym}}{\sim} \boldsymbol{\chi}_1^2 \tag{71}$$

2. X^2 asymptotically follows chi-squared distribution with 1 degree of freedom under H_0.

Pearson's Chi-square Test for 2×2 Table

$$X_p^2 = \sum_{i,j} \frac{(O_{ij} - E_{ij})^2}{E_{ij}} \tag{72}$$

1. For a level α test, reject H_0 if $X_p^2 > \boldsymbol{\chi}^2_{1,1-\alpha}$.

2. The p-value is that

$$p\text{-value} = Pr[\boldsymbol{\chi}_1^2 > X_p^2] \tag{73}$$

3. Use this test only if none of the four expected values (or observed ?) is less than 5.

Yates-Corrected (Continuity Adjusted) Chi-Square Test for 2×2 Table

$$X^2_{p,\star} = \sum_{i,j} \frac{\left(\mid O_{ij} - E_{ij} \mid -0.5 \right)^2}{E_{ij}} \tag{74}$$

$$= \frac{n_{..}\left(\mid ad - bc \mid -\frac{n}{2} \right)^2}{\left[(a+b)(c+d)(a+c)(b+d) \right]} \tag{75}$$

$$\text{p-value} = Pr[\boldsymbol{\chi}^2_1 > X^2_{p,\star}] \tag{76}$$

Likelihood-Ratio Statistic for 2×2 Contingency Table

Likelihood-Ratio Statistic for 2×2 Contingency Table

1. An alternative statistic for testing H_0 results from the likelihood-ratio method for significance tests.

2. The test is based on the ratio of the maximized likelihoods,

$$\Lambda = \frac{\text{maximum likelihood when parameters satisfy } H_0}{\text{maximum likelihood when parameters are unstriated}}. \quad (77)$$

3. This ratio cannot exceed 1.

4. If the maximized likelihood has much larger when the parameters are not forced to satisfy H_0, then the ratio Λ is far below 1 and there is strong evidence against H_0.

Likelihood-Ratio Statistic for 2×2 Contingency Table

5. The test statistic for a likelihood ratio test equals $-2\log(\Lambda)$.

6. This value is "nonnegative", and "small" values yields "large" value of $-2\log(\Lambda)$.

7. The reason for the log transform is to yield an approximate chi-squared sampling distribution.

Likelihood-Ratio Statistic for 2×2 Contingency Table

8. For two-way contingency tables, this statistic simplifies to the formula

$$G^2 = 2 \sum n_{ij} \log \left(\frac{n_{ij}}{\mu_{ij}} \right). \tag{78}$$

9. The statistic G^2 is called the likelihood-ratio chi-squared statistic.

10. Like the Pearson statistic, G^2 takes its minimum values of 0 when all $n_{ij} = \mu_{ij}$, and larger values provide stronger evidence against H_0.

Fisher's Exact Test

Fisher's Exact Test

In a 2×2 contingency table, the exact probability of observing a table with cells a, b, c, d in Table 18 is **hypergeometric distribution**.

Table 18: Fisher's exact test: observed 2×2 table

	Variable Y		
Variable X	level 1	level 2	Total
level 1	$O_{11} = a$	$O_{12} = b$	$a + b = n_{1.}$ (row 1 margin)
level 2	$O_{21} = c$	$O_{22} = d$	$c + d = n_{2.}$ (row 2 margin)
Total	$a + c = n_{.1}$	$b + d = n_{.2}$	$a + b + c + d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

Notation

$$\pi_1 = P[Y = 1 \mid X = 1] \tag{79}$$

$$= P[\text{ variable } Y, \text{ level one} \mid \text{variable } X, \text{ level one }] \tag{80}$$

$$\pi_2 = P[Y = 1 \mid X = 2] \tag{81}$$

$$= P[\text{ variable } Y, \text{ level one} \mid \text{variable } X, \text{ level two }] \tag{82}$$

Point Estimation

The point estimates of π_1 and π_2 are

$$\hat{\pi}_1 = \frac{a}{a+b} = \frac{a}{n_{1.}} \tag{83}$$

$$\hat{\pi}_2 = \frac{c}{c+d} = \frac{c}{n_{2.}} \tag{84}$$

Fisher's Exact Test

To test the hypothesis $H_0 : \pi_1 = \pi_2 = \pi$ by using exact probability distribution.

Fisher's Exact Test

The exact probability of observing a table with cells a, b, c, d is hypergeometric distribution as

$$Pr(a,b,c,d) = \frac{\binom{a+b}{a}\binom{c+d}{c}}{\binom{n}{a+c}} = \frac{(a+b)!\,(c+d)!\,(a+c)!\,(b+d)!}{n!\,a!\,b!\,c!\,d!} \tag{85}$$

Fisher's Exact Test

1. Rearrange the row and columns of the observed table

2. the smaller row total is in he first row and the smaller column total is in the first column.

3. Assume the smallest is a.

Fisher's Exact Test

Start with the table 19 with 0 in the (1,1) cell, the other cells in the table are then determined from the row and column margins.

Table 19: Fisher's exact test: assume $(1,1) = 0$ in 2×2 table

1^{st} Table	Variable Y		
Variable X	level 1	level 2	Total
level 1	0	$a+b = n_{1.}$	$a+b$ (row 1 margin)
level 2	$a+c$	$d-a = n_{2.} - (a+c)$	$c+d = n_{2.}$ (row 2 margin)
Total	$a+c = n_{.1}$	$b+d = n_{.2}$	$a+b+c+d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

Fisher's Exact Test

Construct the next table 20 by increasing the (1,1) cell by 1, decreasing the (1,2) and (2,1) cell by 1, and increasing the (2,2) cell by 1.

Table 20: Fisher's exact test: assume $(1,1) = 1$ in 2×2 table

2^{nd} Table	Variable Y		
Variable X	level 1	level 2	Total
level 1	1	$a+b-1 = n_{1.} - 1$	$n_{1.} = a+b$ (row 1 margin)
level 2	$a+c-1$	$d-a+1 = n_{2.} - (a+c-1)$	$c+d = n_{2.}$ (row 2 margin)
Total	$a+c = n_{.1}$	$b+d = n_{.2}$	$a+b+c+d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

Fisher's Exact Test

Table 21: Fisher's exact test: observed 2×2 table

a^{th} Table	Variable Y		
Variable X	level 1	level 2	Total
level 1	$O_{11} = a$	$O_{12} = b$	$a + b = n_{1.}$ (row 1 margin)
level 2	$O_{21} = c$	$O_{22} = d$	$c + d = n_{2.}$ (row 2 margin)
Total	$a + c = n_{.1}$	$b + d = n_{.2}$	$a + b + c + d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

Fisher's Exact Test

Continue increasing and decreasing the cells by 1, $\cdots$, as in table 21, $\cdots$, as in table 22 until one of the cells is 0.

Table 22: Fisher's exact test: assume $(1,1) = k-1$ in 2×2 table

$(k-1)^{th}$ Table	Variable Y		
Variable X	level 1	level 2	Total
level 1	$a+c-1$	$b-c+1 = n_{1.} - (a+c-1)$	$a+b = n_{1.}$ (row 1 margin)
level 2	1	$c+d-1 = n_{2.} - 1$	$c+d = n_{2.}$ (row 2 margin)
Total	$a+c = n_{.1}$	$b+d = n_{.2}$	$a+b+c+d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

Fisher's Exact Test

Table 23: Fisher's exact test: assume $(1,1) = k$ in 2×2 table

k^{th} Table	Variable Y		
Variable X	level 1	level 2	Total
level 1	$a + c$	$b - c = n_{1.} - (a + c)$	$a + b = n_{1.}$ (row 1 margin)
level 2	0	$c + d = n_{2.}$	$c + d = n_{2.}$ (row 2 margin)
Total	$a + c = n_{.1}$	$b + d = n_{.2}$	$a + b + c + d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

Fisher's Exact Test

1. Start with the table 19 with 0 in the (1,1) cell, the other cells in the table are then determined from the row and column margins.

2. Construct the next table 20 by increasing the (1,1) cell by 1, decreasing the (1,2) and (2,1) cell by 1, and increasing the (2,2) cell by 1.

3. Continue increasing and decreasing the cells by 1, $\cdots$, as in table 21, $\cdots$, as in table 22 until one of the cells is 0.

4. Let the total number of tables is k as in table 23.

Fisher's Exact Test

Table 24: Fisher's exact test: observed 2×2 table

a^{th} Table	Variable Y		
Variable X	level 1	level 2	Total
level 1	$O_{11} = a$	$O_{12} = b$	$a + b = n_{1.}$ (row 1 margin)
level 2	$O_{21} = c$	$O_{22} = d$	$c + d = n_{2.}$ (row 2 margin)
Total	$a + c = n_{.1}$	$b + d = n_{.2}$	$a + b + c + d = n_{..} = n$
	column 1 margin	column 2 margin	(grand total)

Fisher's Exact Test

1. Suppose that the observed a^{th} table is Table (24). (The first table enumerated is the 1^{st} table, Table 19, and the last table enumerated is the k^{th} table, Table 23.)

$$\begin{aligned} \pi_1 &= P[Y = 1 \mid X = 1] \\ \pi_2 &= P[Y = 1 \mid X = 2] \end{aligned} \tag{86}$$

2. We wish to test the hypothesis

$$\begin{aligned} & H_0 : \quad \pi_1 = \pi_2 \\ \text{versus} \quad & H_a : \quad \pi_1 \neq \pi_2. \end{aligned} \tag{87}$$

Fisher's Exact Test: p-Value

1. The two-sided p-value is calculated as

$$p - \text{value (two tails)} = \tag{88}$$

$$2 \times \min[Pr(0) + Pr(1) + \cdots + Pr(a),$$

$$Pr(a) + Pr(a+1) + \cdots + Pr(k),$$

$$0.5] \tag{89}$$

Fisher's Exact Test: p-Value

2. Test one-sided alternative hypothesis, $H_a : \pi_1 < \pi_2$

$$p - \text{value (one tail)} = Pr(0) + Pr(1) + \cdots + Pr(a) \tag{90}$$

3. Test another one-sided alternative hypothesis, $H_a : \pi_1 > \pi_2$

$$p - \text{value (one tail)} = Pr(a) + Pr(a+1) + \cdots + Pr(k) \tag{91}$$

Fisher's Exact Test: p-Value

SAS uses the sum of the probability of all tables whose probability is less than or equal to the observed table probability as two-tailed p-value.

$$\text{SAS:} \qquad p - \text{value (two tail)} = \sum_{i:Pr(i)\leq Pr(a)} Pr(i) \tag{92}$$

Note: Fisher's exact test is more conservative, in generally, I use Fisher's exact test in all reports of medical studies.

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

Example 1: Pain relief for arthritis with four treatments

1. Suppose we conducted a study about pain relief for arthritis with four treatments: 1) control, 2) topic medication, 3) oral medication, 4) combined oral and topic medication. The outcome is measured by the pain with four levels as 1) severe 2) moderate 3) mild and 4) none.

2. We can construct a 4×4 table as in Table 25.

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

Table 25: $R \times C$ Table: pain relief and four treatments data

	Pain Level				
Treatment	Severe	Moderate	Mild	None	Total
Control	20	24	80	82	206
Topic	22	38	104	125	289
Oral	13	28	81	113	235
Combined	7	18	54	92	171
Total	62	108	319	412	901

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

1. In general, a categorical variable under study have more than two categories.

2. Methods of analyzing data with 2×2 table can be extend to or than only two categories of each variables.

3. An $R \times C$ **contingency table** is a table with R rows and C columns.

4. It displays the relationship between two variables, where the variable depicted in the rows has R categories and the variable depicted in the column has C categories.

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

1. Let two variables, A with $i = 1, 2, \cdots, R$ categories, and B with $j = 1, 2, \cdots, C$ categories.

2. The observed number of the cell (i, j) is O_{ij}, and the expected number is E_{ij}. Let $\pi_{i.}$ be the marginal probability of i^{th} category of variable A, and $\pi_{.j}$ be the marginal probability of j^{th} category of variable B.

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

3. Let π_{ij} be the joint probability of i^{th} category of variable A and j^{th} category of variable B.

4. Under the null hypothesis, H_0, there is no association of variable A and B, or there is the homogeneity of two variables.

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

5. So the two variables are independent under null hypothesis, then

$$H_0 \ : \ \pi_{ij} = \pi_{i.} \times \pi_{.j}, \ \ i = 1, 2, \cdots, R, \ \ j = 1, 2, \cdots, C,$$

versus H_A : at least one (i, j) cell such that $\pi_{ij} \neq \pi_{i.} \times \pi_{.j}$

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

$$\text{Let } E_{ij} = \frac{n_{i+} \times n_{+j}}{n}, \text{ where } n_{i+} = \sum_j O_{ij}, \; n_{+j} = \sum_i O_{ij}$$

$$X_p^2 = \sum_{ij} \frac{(O_{ij} - E_{ij})^2}{E_{ij}} \overset{\text{asym}}{\sim} \boldsymbol{\chi}^2_{(R-1)(C-1)}. \tag{93}$$

6. That is, X_p^2 asymptotically follows chi-squared distribution with $(R-1)(C-1)$ degrees of freedom.

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

7. The p-value is calculated as

$$p - \text{value} = P(\boldsymbol{\chi}^2_{(R-1)(C-1)} > X^2_p) \tag{94}$$

8. For a level α test, if $X^2_p > \boldsymbol{\chi}^2_{(R-1)(C-1),1-\alpha}$, reject H_0.

9. Use this test only if the following two conditions are satisfied:

   (a) No more than $1/5$ of the cells should have expected values less than 5,

   (b) No cell should have expected value less than 1.

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

For the above example of 4 treatments of arthritis, $X^2 = 11.9886$, p-value is 0.214, we do not reject the hypothesis.

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

```
title "RxC Table: Pain relief of arthritis and four treatments data";
data pain ;
     do treat= "Control", "Topic", "Oral", "Combined";
     do pain= "Severe", "Moderate", "Mild", "None" ;
        input count @@;
        output;
      end;
      end;
  cards;
 20 24 80 82
22 38 104 125
13 28 81 113
7 18 54 92
run;
```

Chi-square Test for Association (Homogeneity) of $R \times C$ Contingency Table

```
proc freq data=pain order=data page;
       tables treat*pain / chisq ;
       weight count;
run;
```

Partitioning Chi-Squared Tests

Partitioning Chi-Squared Tests

1. Let Z denote a standard normal random variable.

2. Z^2 has a chi-squared distribution with df $= 1$.

3. A chi-squared random variable with df $= v$ has representation $Z_1^1 + \cdots + Z_v^2$, where $Z_1, \ldots, Z_v$ are independent standard normal variables.

Partitioning Chi-Squared Tests

4. A chi-squared statistic having df $= v$ has partitionings into independent chi-squared components—for example, into v components each having df $= 1$

5. Conversely, if X_1^2 and X_2^2 are independent chi-squared random variables having degrees of freedom v_1 and v_2, then $X^2 = X_1^2 + X_2^2$ has a chi-squared distribution with df $= v_1 + v_2$.

Partitioning Chi-Squared Tests

1. Another supplement to a chi-squared test partitions its test statistic so that the components represent certain aspects of the effects.

2. A partitioning may show that an association reflects primary differences between certain categories or groupings of categories.

Partitioning Chi-Squared Tests

1. We begin with a partitioning for the test of independence in a $2 \times J$ tables.

2. We partition G^2, which has df $= (J-1)$, into $J-1$ components.

3. The jth component is G^2 for a 2×2 table where the first column combines columns 1

4. through j of the full table and the second column is column $j+1$.

Partitioning Chi-Squared Tests

5. That is, G^2 for testing independence in a $2 \times J$ table equals a statistic that compares the first two columns, plus a statistic that combines the first two columns and compares them to the third column, and so on, up to a statistic that combines the first $J - 1$ columns and compares them to the last column.

6. Each component statistic has df $= 1$.

Partitioning Chi-Squared Tests

1. It might seem more natural to compute G^2 for the $(j-1)$ separate 2×2 tables that pair each column with a particular one, say the last.

2. However, these component statistics are not independent and do not sum G^2 for the full table.

Partitioning Chi-Squared Tests: Lancaster (1949)

1. For an $I \times J$ table, independent chi-squared components result from comparing column 1 and 2 and then combing them and comparing them to column 3, and so on.

2. Each of the $J - 1$ statistics has df $= I - 1$.

3. More refined partitions contain $(I - 1)(J - 1)$ statistics, each having df $= 1$.

4. One such partitioning (Lancaster 1949) applies to the $(I - 1)(J - 1)$ separate 2×2 tables is in Table 26.

Partitioning Chi-Squared Tests: Lancaster (1949)

Table 26: Lancaster (1949) χ^2 Partition

$\sum_{a<i}\sum_{b<j} n_{ab}$	$\sum_{a<i} a_{aj}$
$\sum_{b<j} n_{ib}$	n_{ij}

for $i = 2, \ldots, I$, and $j = 2, \ldots, J$.

Partitioning Chi-Squared Tests

Goodman (1968, 1969a, 1971b) and Lancaster (1949, 1969) gave rules for determining independent components of chi-squared. For forming subtables, aiming the necessary conditions are the following:

1. The df for the subtables must sum to df for the full table.

2. Each cell count in the full table must be a cell count in one and only one subtable.

3. Each marginal total of the full table must be a marginal total for one and only one subtable.

Partitioning Chi-Squared Tests

1. For a certain partitioning, when the subtable df values sum properly but G^2 values do not, the components are not independent.

2. For the G^2 statistic, exact partitioning occur. the Pearson X^2 need not equal the sum of the X^2 values for the subtables.

Partitioning Chi-Squared Tests: Lancaster (1949)

3. It is valid to use X^2 statistics for the separate subtables; they simply need not provide an exact algebraic partitioning of X^2 for the full table.

4. When the null hypothesis all hold, X^2 does have an asymptotic equivalence with G^2, however.

5. In addition, when the table has a small counts, in argue-sample chi-squared tests it is safer to use X^2 to study the subtables.

Limitations of Chi-Squared Tests

1. Chi-squared tests of independence merely indicate the degree of evidence of association.

2. They are rarely adequate for answering all questions about a data set.

3. Rather then relying solely on the results of the tests, investigate the mature of the association:

4. Study residuals, decomposed chi-squared into components, and estimate parameters such as odds ratios that describe the strength of association.

Limitations of Chi-Squared Tests: Residuals

Discuss in later.

Limitations of Chi-Squared Tests

5. The chi-squared tests also have limitations in the types of data to which they apply.

6. For instance, they require large samples.

7. Also, the $\hat{\mu}_{ij} = n_{i+}n_{+j}/n$ used in X^2 and G^2 depend on he marginal totals but not on the order of listing the rows and columns.

8. Thus, X^2 and G^2 do not change value with arbitrary re-orderings of rows or of columns.

Limitations of Chi-Squared Tests

9. This implies that they treat both classifications as nominal .

10. When at least one variable is ordinal, test statistics that utilize the ordinality are usually more appropriate.

Why Consider Independence?

Why Consider Independence?

1. Any idealized structure such as independence is unlikely to hold in any given particular situation.

2. With large samples it is not surprising to obtain a small p-value.

3. Given this and the limitations just mentioned, why even bother to consider independence as a possible representation for a joint distribution?

Why Consider Independence?

1. One reason refers to the benefits of model parsimony.

2. If the independence model approximates the true probabilities well, then unless n is very large, the model-based estimates $\hat{\pi}_{ij} = n_{i+}n_{+j}/n$ of cell probability tend to be better than the sample proportions $p_{ij} = n_{ij}/n$.

3. The independence ML estimates smooth the sample counts, somewhat damping the random sampling fluctuations.

Why Consider Independence?

4. The mean-squared error (MSE) formula

$$\text{MSE} = \text{variance} + (\text{bias})^2$$

   explains why the independence estimators can have smaller MSE.

5. Although they may be biased, they have smaller variance because they are based on estimating fewer parameters π_i and π_{+j} instead of π_{ij}.

6. Hence, MSE can be smaller unless n is so large that the bias term dominates the variance.

Chi-square Test for Trend in $2 \times K$ Table: Cochran-Armitage Trend Test

Chi-square Test for Trend in $2 \times K$ Table: Cochran-Armitage Trend Test

Sometimes we investigate relationship in categorical data when one of the two variables has only two categories, and the second variable can be categorized into K categories that are ordered in some sense.

Cochran-Armitage Trend Test for $2 \times K$ Table

1. For example, a cross-sectioned study was carried out among the elder population with the objective of measuring the association of sport injuries and year of class major in the department of physical education.

2. A total 267 individuals were grouped into 4 year of class group as 1, 2, 3, 4 at the time of interview whether individual had sport injury in class or not.

3. The result are shown as $2 \times K$ table 27.

Cochran-Armitage Trend Test for $2 \times K$ Table

Table 27: $2 \times K$ Table: sports injury and year of class data

	Year of class				
Sport injury	1	2	3	4	Total
Yes	32	41	54	62	189
No	30	23	17	8	78
Total	62	64	71	70	267

Cochran-Armitage Trend Test for $2 \times K$ Table

1. The Pearson chi-square test for the association of two variables is $X^2 = 24.08$ and the p-value is 0.001.

2. We reject the hypothesis and conclude that there exist association between sport injuries and year of class.

Cochran-Armitage Trend Test for $2 \times K$ Table

3. However, this result shows some relationship exists between sport injury and year of class.

4. It does not tell us specifically about the nature of the relationship.

5. We notice an increasing trend in the proportion of sport injury in each succeeding column (year of class).

6. We would like to employ a specific test to detect such trend.

Cochran-Armitage Trend Test for $2 \times K$ Table

1. For this purpose, a score variable S_j is introduced to correspond the j^{th} category, for $j = 1, 2, \cdots, K$.

2. Suppose we wish to test if there is an increasing (or decreasing) trend in the proportion of "success" π_j, the proportion of units in the first row (the first category of two categories of the row variable) of the j^{th} category as j increase.

3. We set up the data in the form of a $2 \times K$ table 28, where success or failure is listed along the rows and the K categories are list along the column.

Cochran-Armitage Trend Test for $2 \times K$ Table

Table 28: Binomial Trend Test: 2×2 table

	Variable B: K categories i^{th} category with score S_i						
Variable A:	1	2	...	j	...	K	Total
2 categories	S_1	S_2	...	S_j	...	S_K	
1	x_1	x_2	...	x_j	...	x_K	x
2	...	...	...	...	...	...	...
Total	n_1	n_2	...	n_j	...	n_K	n

Cochran-Armitage Trend Test for $2 \times K$ Table

1. Let x_j be the number of successes in the j^{th} category, the total number units in the j^{th} group by n_j.

2. Denote total number of success over all k categories by x and the total number by n.

3. Assign score variable S_j to correspond the j^{th} category.

4. This variable will usually either be $1, 2, \cdots, K$ for the K categories or be defined to correspond to some other numerical attribute of the group.

Cochran-Armitage Trend Test for $2 \times K$ Table

$$H_0: \quad \text{there is no trend} \tag{95}$$

$$\text{versus } H_A: \quad \pi_j = \alpha + \beta S_i, \tag{96}$$

$$\text{for some constant } \alpha \text{ and } \beta. \tag{97}$$

$$\text{Then, } \quad \hat{p}_j = \frac{x_j}{n_j}; \tag{98}$$

the proportion of success in j^{th} category

Cochran-Armitage Trend Test for $2 \times K$ Table

$$\bar{p} = \frac{x}{n}; \text{ overall proportion of success} \tag{99}$$

$$\bar{q} = 1 - \bar{p} \tag{100}$$

$$\bar{S} = \frac{\sum_{j=1}^{K} n_j S_j}{n} \tag{101}$$

Cochran-Armitage Trend Test for $2 \times K$ Table

$$\mathbf{A} = \sum_{j=1}^{K} n_j(\hat{p}_j - \bar{p})(S_j - \bar{S}) \tag{102}$$

$$\mathbf{B} = \bar{p}\,\bar{q}\,\left[(\sum_{j=1}^{K} n_j S_j^2) - \frac{(\sum_{j=1}^{K} n_j S_j)^2}{n}\right] \tag{103}$$

$$X^2 = \frac{\mathbf{A}^2}{\mathbf{B}} \quad \text{asym} \quad \sim \quad \boldsymbol{\chi}_1^2. \tag{104}$$

5. That is, X^2 is approximated chi-squared distributed with 1 degree of freedom.

Cochran-Armitage Trend Test for $2 \times K$ Table

6. The p-value is calculated as

$$p - \text{value} \quad = \quad P(\boldsymbol{\chi}_1^2 > X^2) \tag{105}$$

7. For a two sided test with significant level α, we rejected H_0, if $X^2 > \boldsymbol{\chi}^2_{1,1-\alpha}$ then reject H_0.

Cochran-Armitage Trend Test for $2 \times K$ Table

8. The direction of the trend in proportions is indicated by the sign of $\mathbf{A}$.

9. If $\mathbf{A} > 0$, then the proportions increase with increasing score.

10. We use this test only if $n\bar{p}\bar{q} > 5$.

Cochran-Armitage Trend Test for $2 \times K$ Table

1. For most data sets, the choice of scores as little effect on the results.

2. Different choices of monotone scores usually give similar results.

3. This may not happen, however, when the data are very unbalanced, such as when some categories have many more observations than other categories.

Cochran-Armitage Trend Test for $2 \times K$ Table

4. It is usually to better use one's judgement by selecting scores than reflect distances between categories.

5. When uncertain about this choice, perform a sensitivity analysis. Select two or three "sensible" scores and check that results are similar for each.

6. Equally-spaced scores often provide a reasonable compromise when the category labels do not suggest any obvious choices

Cochran-Armitage Trend Test for $2 \times K$ Table

The above example, we choice the equally-spaced scores, $1, 2, 3$, and 4, the test statistic is $X^2 = 24.7$ with p-value 0.0001.

Cochran-Armitage Trend Test for $2 \times K$ Table

```
data trend ;
    do injury=1 to 0 by -1 ;
    do year=1 to 4 ;
       input count @@;
       output;
     end;
     end;
cards;
32 41 54 62
30 23 17 8
run;
```

Cochran-Armitage Trend Test for $2 \times K$ Table

```
proc freq data=trend order=data page;
      tables injury*year / chisq trend ;
      weight count;
run;
```

injury Frequency| Percent | Row Pct | Col Pct |	year 1	2	3	4	Total
1	32	41	54	62	189
	11.99	15.36	20.22	23.22	70.79
	16.93	21.69	28.57	32.80	
	51.61	64.06	76.06	88.57	
0	30	23	17	8	78
	11.24	8.61	6.37	3.00	29.21
	38.46	29.49	21.79	10.26	
	48.39	35.94	23.94	11.43	
Total	62	64	71	70	267
	23.22	23.97	26.59	26.22	100.00

Cochran-Armitage Trend Test for $2 \times K$ Table

Statistics for Table of injury by year

Statistic	DF	Value	Prob
Chi-Square	3	24.0819	<.0001
Likelihood Ratio Chi-Square	3	25.1721	<.0001
Mantel-Haenszel Chi-Square	1	23.9901	<.0001
Phi Coefficient		0.3003	
Contingency Coefficient		0.2876	
Cramer's V		0.3003	

Cochran-Armitage Trend Test for $2 \times K$ Table

```
Cochran-Armitage Trend Test
---------------------------
Statistic (Z)       4.9072
One-sided Pr >  Z   <.0001
Two-sided Pr > |Z|  <.0001

Sample Size = 267
```

USE FOR BIOSTATISTICS

Measures of Impact

1. Measures of association providing information about absolute effects of exposure

2. Two concepts

   (a) Attributable risk among exposed

   (b) Population attributable risk

Attributable Risk (AR)

Quantifies disease burden in exposed group attributable to exposure

Provides answers to

1. What is the risk which can be attributed to the exposure?

2. What is the excess risk due to the exposure?

Calculated as risk difference (RD)

Absolute Measures of Risk

1. Absolute implies that we are interested in the difference between two incidences.

2. There are four types of absolute measures of risk:

   (a) Risk difference (or attributable risk, AR)
   (b) Attributable risk percent (AR%)
   (c) Population attributable risk (PAR)
   (d) Population attributable risk percent (PAR%)

Attributable Risk (AR)

1. Attributable risk is the difference in risk between exposed and unexposed

$$\text{AR} = RR = \pi_1 - \pi_2 = \pi_{\text{Risk}+} - \pi_{\text{Risk-}} \tag{106}$$

$$\widehat{\text{AR}} = \hat{\pi}_1 - \hat{\pi}_2 = \frac{a}{a+b} - \frac{c}{c+d} \tag{107}$$

2. This corresponds to the absolute added risk due to exposure

RR and AR

1. The main use of RR is to guide inferences of cause and effect when an association is observed between exposure and disease

2. The main use of AR is to quantify the potential importance of an association

   (a) Over a given time, how many additional ill or injured persons would there be out of the total number who were exposed?

   (b) Which measure is more useful for an etiologic study? For a health department allocating funds for different prevention measures?

Attributable Risk Percent (AR%)

1. AR expressed as a percentage of risk in exposed Provides answers to What is the proportion of disease among the exposed which
   (a) can be attributed to the exposure?
   (b) could be avoided by eliminating the exposure?

2. Synonyms
   (a) Attributable proportion
   (b) Etiologic fraction (EF)

Attributable Risk Percent (AR%)

$$\text{AR\%} = \frac{\pi_{\text{Risk+}} - \pi_{\text{Risk-}}}{\pi_{\text{Risk+}}} \times 100\% = \frac{RR - 1}{RR} \times 100\% \tag{108}$$

Attributable Risk Percent (AR%)

AR% is often used to determine efficacy of vaccines in prevention trials. The unvaccinated population is the exposed group, and the vaccinated are unexposed.

Example: Attributable Risk Percent (AR%)

1. For the polio vaccine, the cumulative incidence of polio among unvaccinated was 57 per 100,000, while among the vaccinated it was 16 per 100,000.

$$\frac{57-16}{57} = 71.9 \tag{109}$$

2. The vaccine efficacy was 71.9%.

AR and AR% in Case-Control Studies

1. No direct risk estimates in case-control study

2. No calculation of AR (risk difference) and AR% possible

Prevented Fraction (PF)

1. Calculate if relative risk < 1 (Exposure to some "Risk" factor)

2. Proportion of potential new cases which would have occurred if the exposure had been absent

3. Proportion of potential cases prevented by the exposure

$$\text{PF} = \frac{\pi_{\text{Risk-}} - \pi_{\text{Risk+}}}{\pi_{\text{Risk-}}} = 1 - RR \tag{110}$$

Prevented Fraction (PF)

Table 29: Vaccine Efficacy with 2×2 Table

	Disease will develop	Disease will not develop	Total
Vaccinated	150	301,395	301,545
Unvaccinated	515	298,140	298,655
Total	665	602,790	600200

Prevented Fraction (PF)

$$\frac{150}{301545} = 0.0497\% \tag{111}$$

$$\frac{515}{298655} = 0.0172\% \tag{112}$$

$$\mathsf{RR} = 0.28 \tag{113}$$

$$\mathsf{PF} = \frac{0.0172 - 0.049}{0.0172} = 1 - 0.28 = 0.72 \tag{114}$$

Prevented Fraction (PF)

1. Expected number of cases among vaccinated if unvaccinated

$$301545 \times 0.0172\% = 519 \tag{115}$$

2. Observed number of cases: 150

3. Estimated number of cases prevented: 369

$$\frac{519 - 150}{519} = 71\% \tag{116}$$

Population Attributable Risk (PAR)

1. Excess risk of disease in total population attributable to exposure

2. Reduction in risk which would be achieved if population entirely unexposed

3. Helps determining which exposures relevant to public health in community

$$\text{PAR} = \pi_{\text{Polulation}} - \pi_{\text{Risk-}} = \text{AR} \times Pr(\text{Risk-}) \tag{117}$$

Population Attributable Risk Percent (PAR%)

PAR expressed as a precentage of total risk in population

$$\text{PAR} = \frac{\pi_{\text{Polulation}} - \pi_{\text{Risk-}}}{\pi_{\text{Polulation}}} \times 100\% \tag{118}$$

Measures of Population Impact and Infectiousness

1. Population attributable risk (PAR): is the absolute difference between the risk in the whole population and the risk in the unexposed group.

2. If π_0 is the risk in the total study population and π_2 is the risk in the unexposed group then

$$\text{PAR} = \pi_0 - \pi_2 \tag{119}$$

Measures of Population Impact and Infectiousness

3. Alternatively, if π_1 is the risk in the exposed and π_2 is the risk in the unexposed and the proportion of exposed in the population is P

$$\text{PAR} = P \times (\pi_1 - \pi_2) \tag{120}$$

Measures of Population Impact and Infectiousness

4. Population attributable risk fraction (PAF): The proportion of all cases in the whole study population (exposed and unexposed) that may be attributable to the exposure, on the assumption of a causal association.

$$\text{PAF} = \frac{\text{PAR}}{\pi_0} = \frac{\pi_0 - \pi_2}{\pi_0} \tag{121}$$

Notes on PAR and PAR%

1. PAR is very useful for allocating resources for prevention.

2. Efforts can be made to prevent or modify exposures that have a large burden of disease (i.e. smoking vs. cosmic rays from air travel)

3. PAR% can be used to identify the primary exposure that causes a given disease, and allocate resources towards it.

Issues in the Use of Measures of Impact

In interpreting the results of measures of impact several assumptions are made

1. All of the association between the risk factor and the disease is causal (complete control of confounding has been achieved).

2. Both the risk factor and frequency of outcome were accurately measured

3. Removal of the risk factor actually removes the risk

4. The risk factor is actually removable

Measures of Impact and Public Health

1. Measures of impact are important in public health as they assist health planners to prioritize policy decisions

2. If the primary prevention focus is on the whole population then measures of impact allow us to evaluate the intervention's effects at the level of the (general) population

3. If the strategy is to focus on high-risk individuals then measures of effect allow us to evaluate the program

Stratified Categorical Data: The (Cochran) Mantel-Haenszel Test

Example: Coronary Artery Disease

Table 30 are based on a study on coronary artery disease (Koch, Imrery et al. 1985). The sample is one of convenience since the patients studied were people who came to clinic and requested an evaluation.

Example: Coronary Artery Disease

Table 30: Retrospective study: gender, ECG and disease

Gender	ECG Condition	Disease (Cases)	No Disease (Controls)	Total
Female	> 0.1 ST depression	8	10	18
Female	≤ 0.1 ST depression	4	11	15
Male	> 0.1 ST depression	21	6	27
Male	≤ 0.1 ST depression	9	9	18
Total		42	36	78

Example: Coronary Artery Disease: ECG vs. Gender

Table 31: Retrospective study: EKG and Gender

	Gender		
ECG Condition	Female	Male	Total
> 0.1 ST depression	18	27	45
≤ 0.1 ST depression	15	18	33
Total	33	45	78

Example: ECG and Gender

```
> # EKG vs. Gender
> EKG.Gender<-matrix(c(18,27,15,18),nrow=2,byrow=T)
> fisher.test(EKG.Gender)

        Fisher's Exact Test for Count Data
data:  EKG.Gender
p-value = 0.6502
alternative hypothesis: true odds ratio is not equal to 1

95 percent confidence interval:
 0.2932842 2.1906132
sample estimates:
odds ratio
 0.8023104
```

Example: ECG Condition and Coronary Artery Disease

Investigators were interested in whether (electrocardiogram) ECG measurement was associated with disease status.

Table 32: Retrospective study: ECG and coronary heart disease

	Coronary Artery Disease		
ECG Condition	Yes (cases)	No (controls)	Total
> 0.1 ST depression	29	16	45
≤ 0.1 ST depression	13	20	33
Total	42	36	78

Example: ECG and Coronary Artery Disease

```
> EKG.CAD<-matrix(c(29,16,13,20),nrow=2,byrow=T)
> fisher.test(EKG.CAD)

    Fisher's Exact Test for Count Data
data:  EKG.CAD
p-value = 0.03894
alternative hypothesis: true odds ratio is not equal to 1

95 percent confidence interval:
 1.003021 7.828855
sample estimates:
odds ratio
  2.750314
```

Example: Gender and Coronary Artery Disease

Investigators were interested in whether gender was associated with disease status.

Table 33: Retrospective study: gender and coronary heart disease

	Coronary Artery Disease		
Gender	Yes (cases)	No (controls)	Total
Female	12	21	33
Male	30	15	45
Total	42	36	78

Example: Gender and Coronary Artery Disease

```
> gender.CAD<-matrix(c(12,21,30,15),nrow=2,byrow=T)
> fisher.test(gender.CAD)

        Fisher's Exact Test for Count Data
data:  gender.CAD
p-value = 0.01142
alternative hypothesis: true odds ratio is not equal to 1

95 percent confidence interval:
 0.09986503 0.80674974
sample estimates:
odds ratio
  0.290676
```

Example: Coronary Artery Disease: Stratification

Gender was though to be associated with disease status, so investigators stratified the data into female and male groups.

Example: Coronary Artery Disease: Female

Table 34: Retrospective study: ECG and coronary heart disease for female

Female	Coronary Artery Disease		
ECG Condition	Yes (cases)	No (controls)	Total
>0.1 ST depression	8	10	18
≤ 0.1 ST depression	4	11	15
Total	12	21	33

Example: Female and Coronary Artery Disease

```
> Female.CAD<-matrix(c(8,10,4,11),nrow=2,byrow=T)
> fisher.test(Female.CAD)

        Fisher's Exact Test for Count Data
data:  Female.CAD
p-value = 0.4688
alternative hypothesis: true odds ratio is not equal to 1

95 percent confidence interval:
  0.4113675 12.9927377
sample estimates:
odds ratio
  2.147678
```

Example: Coronary Artery Disease: Male

Table 35: Retrospective study: ECG and coronary heart disease for male

Male	Coronary Artery Disease		
ECG Condition	Yes (cases)	No (controls)	Total
> 0.1 ST depression	21	6	27
≤ 0.1 ST depression	9	9	18
Total	30	15	45

Example: Male and Coronary Artery Disease

```
> Male.CAD<-matrix(c(21,6,9,9),nrow=2,byrow=T)
> fisher.test(Male.CAD)

        Fisher's Exact Test for Count Data
data:  Male.CAD
p-value = 0.1049
alternative hypothesis: true odds ratio is not equal to 1

95 percent confidence interval:
  0.8034904 15.6456384
sample estimates:
odds ratio
  3.395449
```

Example: Coronary Artery Disease: Male

1. What's Wrong?

2. Is ECG associated with CAD?

3. Is Gender associated with CAD?

4. Do female and male have the **same** odds ratio?

5. Wha't the "**common odds ratio**"?

Stratified Categorical Data: The (Cochran) Mantel-Haenszel Test

Confounding Variable

1. A **confounding variable** is a variable that is associated with both the disease and the exposure variable.

2. Such a variable must usually be controlled for before disease-exposure relationship.

Confounding Variables and stratification

1. The analysis of disease-exposure relationships in separate **sub-groups** of the data, where the sub-groups are defined by one or more potential confounders, referred to as **stratification**.

2. The sub-groups themselves are referred to as **strata**.

3. In general the data will be stratified into k sub-groups according to one or more confounding variables to make the units within a stratum as **homogeneous** as possible.

4. The data for each stratum consist of a 2×2 contingency table, as in Table 36, relating exposure to disease.

Confounding Variables and Stratification

Stratified 2×2 Table

Table 36: 2×2 Table of disease and exposure in the ith stratum, $i = 1, 2, \ldots, k$.

	Disease will develop	Disease will not develop	Total
Risk factor present (Exposure: Yes +)	$O_i = a_i$	b_i	$a_i + b_i = n_{1.i}$
Risk factor absent (Exposure: No -)	c_i	d_i	$c_i + d_i = n_{2.i}$
Total	$a_i + c_i = n_{.1i}$	$b_i + d_i = n_{.2i}$	$a_i + b_i + c_i + d_i = n_i$

Stratified 2×2 Table

1. Based on Fisher's exact test within each stratum, the distribution of a_i follows a **hypergeometric distribution**.

2. The test procedure will be based on a comparison of the observed number of units in the $(1,1)$ cell of each stratum (denoted by $O_i = a_i$) with the expected number of units in that cell (denoted by E_i).

3. The test procedure is the same regardless of the order of the rows and columns, that is, which row (or column) is designated as first row (or column) is arbitrary.

Mantel-Haenszel Test

The expected value of O_i and variance of O_i is

$$E_i = \mathcal{E}(O_i) = \frac{(a_i + b_i)(a_i + c_i)}{n_i} \tag{122}$$

$$V_i = \mathbf{Var}(O_i) = \frac{(a_i + b_i)(c_i + d_i)(a_i + c_i)(b_i + d_i)}{n_i^2 \, (n_i - 1)} \tag{123}$$

Mantel-Haenszel Test for Association over Different Strata

Mantel-Haenszel Test is used to assess the association between a dichotomous disease and a dichotomous exposure variable after controlling for one or more confounding variables.

Mantel-Haenszel Test for Association over Different Strata

Under H_0, there is no association between disease and exposure, then let

$$O = \sum_{i=1}^{k} O_i = \sum_{i=1}^{k} a_i \tag{124}$$

$$E = \sum_{i=1}^{k} E_i = \sum_{i=1}^{k} \frac{(a_i + b_i)(a_i + c_i)}{n_i} \tag{125}$$

$$V = \sum_{i=1}^{k} V_i = \sum_{i=1}^{k} \frac{(a_i + b_i)(c_i + d_i)(a_i + c_i)(b_i + d_i)}{n_i^2 (n_i - 1)} \tag{126}$$

$$X^2_{MH} = \frac{(\mid O - E \mid -0.5)^2}{V} \overset{\text{asym}}{\sim} \boldsymbol{\chi}^2_1 \tag{127}$$

Mantel-Haenszel Test for Association over Different Strata

1. Under H_0 X^2_{MH} asymptotically follows chi-squared distribution with 1 degree of freedom.

2. For two-sided test with significance level α, we reject H_0 if $X^2_{MH} > \boldsymbol{\chi}^2_{1,1-\alpha}$.

3. p-value $= Pr(\boldsymbol{\chi}^2_1 \geq X^2_{MH})$

Interaction Effect: Confounder and Effect Modifier

1. We stratify the study population into k strata according to the confounding variable, confounder C.

2. If the underling (true) odds ratio is different across the k strata, then there is said to be **interaction** or **effect modification** between risk factor and confounder.

3. Then the confounder C is referred to as an **effect modifier**.

Mantel-Haenszel Test: Chi-square Test for Homogeneity of Odds Ratios over Different Strata (Woolf's Method)

1. The Mantel-Haenszel test provides a test of significance of the relationship between disease and exposure.

2. If we reject the null hypothesis in Mantel-Haenszel test, there exist association of disease and risk factor.

Mantel-Haenszel Test: Chi-square Test for Homogeneity of Odds Ratios over Different Strata (Woolf's Method)

1. Let OR_i is underling odds ratio in the i^{th} stratum.

2. To test the hypothesis

$$H_0 \ : \ OR_1 = OR_2 = \cdots = OR_k; \tag{128}$$

$$\text{vs.} \quad H_A \ : \ \text{at least two of the } OR_i \text{ are significant different} \tag{129}$$

3. This is to test whether **a common odds ratio (homogeneity)** exist when there is association of disease and risk factor given controlling the confounding factor with stratification.

Mantel-Haenszel Test: Chi-square Test for Homogeneity of Odds Ratios over Different Strata (Woolf's Method)

The chi-square test for homogeneity is calculated as following:

Chi-square Test for Homogeneity of Odds Ratios over Different Strata (Woolf's Method)

$$\log(\widehat{OR}_i) = \log\left(\frac{a_i d_i}{b_i c_i}\right) \tag{130}$$

$$\left[\mathbf{Var}\big(\log(\widehat{OR}_i)\big)\right]^{-1} = w_i = \left(\frac{1}{a_i}+\frac{1}{b_i}+\frac{1}{c_i}+\frac{1}{d_i}\right)^{-1} \tag{131}$$

$$\overline{\log OR} = \frac{\sum_{i=1}^{k} w_i \ \log(\widehat{OR}_i)}{\sum_{i=1}^{k} w_i} \tag{132}$$

$$X^2_{HOM} = \sum_{i=1}^{k} w_i \ (\log \widehat{OR}_i - \overline{\log OR})^2 \tag{133}$$

$$X^2_{HOM} \overset{\text{asym}}{\sim} \boldsymbol{\chi}^2_{k-1} \tag{134}$$

Chi-square Test for Homogeneity of Odds Ratios over Different Strata (Breslow-Day Method in SAS)

Similar to Woolf's method

Mantel-Haenszel Test: Chi-square Test for Homogeneity of Odds Ratios over Different Strata (Woolf's Method)

That is, X^2_{MOH} asymptotically follows chi-squared distribution with $(k-1)$ degree of freedom under H_0. For two-sided test with significance level α, we reject H_0 : homogeneity of common odds ratio, if $X^2_{MH} > \boldsymbol{\chi}^2_{k-1,1-\alpha}$.

Mantel-Haenszel Estimator of the Common Odds Ratio for Stratified Data

1. The Mantel-Haenszel test provides a test of significance of the relationship between disease and exposure. If we reject the null hypothesis in Mantel-Haenszel test, there exist association of disease and risk factor.

2. Then we use chi-square test for homogeneity of odds ratios. If we do not reject the null hypothesis of common odds ratio across stratum, we would like to know the common odds ratio.

3. However, chi-square test for homogeneity of odds ratios does not given a measure of the strength of the association.

Mantel-Haenszel Estimator of the Common Odds Ratio for Stratified Data

In general, it is important to test for homogeneity of the stratum-specific odds ratio. If the true odds ratios are different, then it makes no sense to obtain a pooled-odds ratio estimate.

Mantel-Haenszel Estimator of the Common Odds Ratio for Stratified Data

In a collection of $k \times 2 \times 2$ contingency tables, where the i^{th} table, Table 37, corresponding to the ith stratum.

Table 37: Mantel-Haenszel Test: The i^{th} Observed 2×2 Table

i^{th} Stratum	Variable Y		
Variable X	level 1	level 2	Total
level 1	a_i	b_i	$a_i + b_i = n_{1.i}$
level 2	c_i	d_i	$c_i + d_i = n_{2.i}$
Total	$a + c = n_{.1i}$	$b + d = n_{.2i}$	$a + b + c + d = n_{..i} = n_i$

Common Odds Ratio for Stratified Data

$$\widehat{OR}_{MH} = \frac{\sum_i (a_i d_i)/n_i}{\sum_i (b_i c_i)/n_i} \tag{135}$$

$$\mathbf{Var}(\log \widehat{OR}_{MH}) = \frac{\sum \pi_i R_i}{2(\sum_i R_i)^2} + \frac{\sum(\pi_i S_i + Q_i R_i)}{2(\sum R_i)(\sum S_i)} + \frac{\sum Q_i S_i}{2(\sum S_i)^2} \tag{136}$$

$$\text{where } \pi_i = \frac{a_i + d_i}{n_i},\ Q_i = \frac{b_i + c_i}{n_i}, \tag{137}$$

$$R_i = \frac{a_i\, d_i}{n_i},\ S_i = \frac{b_i\, c_i}{n_i} \tag{138}$$

$(1-\alpha) \times 100\%$C.I. :

$$\exp\left[\ \log \widehat{OR}_{MH} \pm Z_{1-\alpha/2}\sqrt{\mathbf{Var}(\log \widehat{OR}_{MH})}\ \right] \tag{139}$$

Mantel-Haenszel Estimator of the Common Odds Ratio for Stratified Data

Alternatively, we can use the equation (132) as the common odds ratio estimator.

$$\log(\widehat{OR}_i) = \log\left(\frac{a_i d_i}{b_i c_i}\right) \tag{140}$$

$$\left[\mathbf{Var}\big(\log(\widehat{OR}_i)\big)\right]^{-1} = w_i = \left(\frac{1}{a_i} + \frac{1}{b_i} + \frac{1}{c_i} + \frac{1}{d_i}\right)^{-1} \tag{141}$$

$$\overline{\log OR} = \frac{\sum_{i=1}^{k} w_i \ \log(\widehat{OR}_i)}{\sum_{i=1}^{k} w_i} \tag{142}$$

Example: Coronary Artery Disease

1. For the Table of "Gender and Disease", Pearson's Chi-Square Test X^2 is 7.035, p-value is 0.008.

2. For female, ECG > 0.1 ST depression and Disease, X^2 is 1.117, p-value is 0.290. OR is 2.2.

3. For male: ECG > 0.1 ST depression and Disease, X^2 is 3.750, p-value is 0.053. OR is 3.5.

Example: Coronary Artery Disease

4. X^2_{MH} is 4.503 (1 df) and p-value is 0.034.

5. There is association between ECG and disease after controlling gender.

6. X^2_{HOM} is 0.215 (1 df) and p-value is 0.643.

7. A common odds ratio exists between ECG and disease.

8. The common odds ration, $\widehat{OR}_{MH}$, is 2.847, and 95% C.I. is (1.083, 7.482).

Notes: Stratification

1. The fact that a marginal table (i.e. pool over gender) may exhibit an association completed different from a partial tables (individual tables for male and female) is known as **Simpson's Paradox** (Simpson 1951).

2. We should analyze the data following the design of original study.

Example: Coronary Artery Disease

```
> CAD <-array(c(8, 4, 10, 11,
                21, 6, 9, 9,),
              dim = c(2, 2, 2),
              dimnames = list(
                  EKG = c(">=0.1 ST Dep", "< 0.1 ST Dep"),
                  Response = c("Case", "Control"),
                  Penicillin.Level = c("Female", "Male")))
```

Example: Coronary Artery Disease

```
> CAD
, , Penicillin.Level = Female
                Response
EKG              Case Control
  >=0.1 ST Dep    8      10
  < 0.1 ST Dep    4      11

, , Penicillin.Level = Male
                Response
EKG              Case Control
  >=0.1 ST Dep   21       9
  < 0.1 ST Dep    6       9
```

Example: Coronary Artery Disease

```
> mantelhaen.test(CAD,correct=FALSE)

Mantel-Haenszel chi-squared test without continuity correction
data:  CAD
Mantel-Haenszel X-squared = 4.5026, df = 1, p-value = 0.03384
alternative hypothesis: true common odds ratio is not equal to 1

95 percent confidence interval:
 1.076514 7.527901
sample estimates:
common odds ratio
         2.846734
```

Example: Coronary Artery Disease

```
> mantelhaen.test(CAD)

Mantel-Haenszel chi-squared test with continuity correction
data:  CAD
Mantel-Haenszel X-squared = 3.5485, df = 1, p-value = 0.0596
alternative hypothesis: true common odds ratio is not equal to 1

95 percent confidence interval:
 1.076514 7.527901
sample estimates:
common odds ratio
         2.846734
```

Example: Coronary Artery Disease

```
> mantelhaen.test(CAD, exact=TRUE)

Exact conditional test of independence in 2 x 2 x k tables
data:  CAD
S = 29, p-value = 0.05418
alternative hypothesis: true common odds ratio is not equal to 1

95 percent confidence interval:
 0.9711574 8.4256184
sample estimates:
common odds ratio
         2.790832
```

Example: Coronary Artery Disease

```
> woolf <- function(x) {
        x <- x + 1 / 2
        k <- dim(x)[3]
        or <- apply(x, 3,
            function(x)(x[1,1]*x[2,2])/(x[1,2]*x[2,1]))
        w <-  apply(x, 3,
            function(x) 1 / sum(1 / x))
        1 - pchisq(sum(w * (log(or)
            - weighted.mean(log(or), w)) ^ 2), k - 1)
      }
```

Example: Coronary Artery Disease

```
> woolf(CAD)
[1] 0.6270651 # p-value
```

Example: Coronary Artery Disease

```
title "Stratified Retrospective Study: kx2x2 Table";
data ca;
   input gender $ ECG $ disease $ count ;
   cards;
   female <0.1  yes   4
   female <0.1  no   11
   female >=0.1 yes   8
   female >=0.1 no   10
   male   <0.1  yes   9
   male   <0.1  no    9
   male   >=0.1 yes  21
   male   >=0.1 no    6;
```

Example: Coronary Artery Disease

```
proc freq;
  weight count;
  tables gender*disease / nocol nopct chisq relrisk ;
  tables gender*ECG*disease / nocol nopct cmh chisq relrisk;
  tables ecg*disease / exact relrisk ;
run;
```

Example: Coronary Artery Disease

Table of gender by disease

gender Frequency Row Pct	disease no	 yes	Total
female	21 63.64	12 36.36	33
male	15 33.33	30 66.67	45
Total	36	42	78

Example: Coronary Artery Disease

Statistics for Table of gender by disease

Statistic	DF	Value	Prob
Chi-Square	1	7.0346	0.0080
Likelihood Ratio Chi-Square	1	7.1209	0.0076
Continuity Adj. Chi-Square	1	5.8681	0.0154

Fisher's Exact Test

Two-sided Pr <= P	0.0114

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	3.5000	1.3646	8.9771

Example: Coronary Artery Disease

Controlling for gender=female

ECG Frequency Row Pct	disease no	 yes	Total
<0.1	11 73.33	4 26.67	15
>=0.1	10 55.56	8 44.44	18
Total	21	12	33

Example: Coronary Artery Disease

Controlling for gender=female

Statistic	DF	Value	Prob
Chi-Square	1	1.1175	0.2905

Fisher's Exact Test

Two-sided Pr <= P	0.4688

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	2.2000	0.5036	9.6107

Example: Coronary Artery Disease

Controlling for gender=male

ECG fREQUENCY | disease Row Pct	no	yes	Total
<0.1	9 50.00	9 50.00	18
>=0.1	6 22.22	21 77.78	27
Total	15	30	45

Example: Coronary Artery Disease

Controlling for gender=male

Statistic	DF	Value	Prob
Chi-Square	1	3.7500	0.0528

Fisher's Exact Test

Two-sided Pr <= P	0.1049

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	3.5000	0.9587	12.7775

Example: Coronary Artery Disease

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
3	General Association	1	4.5026	0.0338

Example: Coronary Artery Disease

Type of Study	Method	Value	95% Confidence Limits	
Case-Control	Mantel-Haenszel	2.8467	1.0765	7.5279

Example: Coronary Artery Disease

```
     Breslow-Day Test for
Homogeneity of the Odds Ratios
------------------------------
Chi-Square                0.2155
DF                             1
Pr > ChiSq                0.6425
Total Sample Size = 78
```