Contingency Tables

Overview

1) **Types of Variables**
2) **Comparing (2) Categorical Variables**
   - Contingency (two-way) tables
   - χ^2 Tests
3) **2 x 2 Tables**
   - Sampling designs
   - Testing for association
   - Estimation of effects
   - Paired binary data
4) **Stratified Tables**
   - Confounding
   - Effect Modification

Factors and Contingency Tables

Definition: A **factor** is a categorical (discrete) variable taking a small number of values that represent the levels of the factor.

Examples

Gender with two levels: 1 = Male and 2 = Female

Disease status with three levels: 1 = Progression, 2 = Stable, 3 = Improved

AgeFactor with 4 levels: 1 = 20-29 yrs, 2 = 30-39, 3 = 40-49, 4 = 50-59

Factors and Contingency Tables

Data description: Form one-way, two-way or multi-way tables of frequencies of factor levels and their combinations

- To assess whether two factors are related, we often construct an R x C table that cross-classifies the observations according to the 2 factors.
- Examining two-way tables of Factor A vs Factor B at each level of a third Factor C shows how the A/B association may be explained or modified by C (later).

Data Summary: Categorical data are often summarized by reporting the proportion or percent in each category. Alternatively, one sometimes sees a summary of the relative proportion (odds) in each category (relative to a “baseline” category).

Testing: We can test whether the factors are related using a χ^2 test.

Categorical Data

Example: From Doll and Hill (1952) - retrospective assessment of smoking frequency. The table displays the daily average number of cigarettes for lung cancer patients and control patients. Note there are equal numbers of cancer patients and controls.

	Daily # cigarettes						
	None	< 5	5-14	15-24	25-49	50+	Total
Cancer	7	55	489	475	293	38	1357
	0.5%	4.1%	36.0%	35.0%	21.6%	2.8%	
Control	61	129	570	431	154	12	1357
	4.5%	9.5%	42.0%	31.8%	11.3%	0.9%	
Total	68	184	1059	906	447	50	2714

χ^2 Test

We want to test whether the smoking frequency is the same for each of the populations sampled. We want to test whether the **groups** are **homogeneous** with respect to a characteristic.

H_0: smoking probability same in both groups

H_A: smoking probability not the same

Q: What does H_0 predict we would observe if all we knew were the marginal totals?

	Daily # cigarettes						
	None	< 5	5-14	15-24	25-49	50+	Total
Cancer							1357
Control							1357
Total	68	184	1059	906	447	50	2714

χ^2 Test

A: H_0 predicts the following **expectations**:

	Daily # cigarettes						
	None	< 5	5-14	15-24	25-49	50+	Total
Cancer	34	92	529.5	453	223.5	25	1357
Control	34	92	529.5	453	223.5	25	1357
Total	68	184	1059	906	447	50	2714

Each group has the same proportion in each cell as the overall **marginal proportion.** The “equal” expected number for each group is the result of the equal sample size in each group (what would change if there were half as many cases as controls?)

χ^2 Test

Summing the differences between the observed and expected counts provides an overall assessment of H_0.

$$X^2 = \sum_{i,j} \frac{\left(O_{ij} - E_{ij}\right)^2}{E_{ij}} \sim \chi^2\left((r-1)\times(c-1)\right)$$

X^2 is known as the **Pearson's Chi-square Statistic.**

- Large values of X^2 suggests the data are not consistent with H_0
- Small values of X^2 suggests the data are consistent with H_0

χ^2 Test

In example 3 the contributions to the X^2 statistic are:

	Daily # cigarettes						
	None	< 5	5-14	15-24	25-49	50+	Total
Cancer	$\frac{(7-34)^2}{34}$	$\frac{(55-92)^2}{92}$	etc.				
Control	$\frac{(61-34)^2}{34}$						
Total							

	Daily # cigarettes						
	None	< 5	5-14	15-24	25-49	50+	Total
Cancer	21.44	14.88	3.10	1.07	21.61	6.76	
Control	21.44	14.88	3.10	1.07	21.61	6.76	
Total							

$$X^2 = \sum_{i,j} \frac{\left(O_{ij} - E_{ij}\right)^2}{E_{ij}} = 137.7$$

$p = P(X^2 > \chi^2(5) \mid H_0 \text{ true}) < 0.0001$

Conclusion?

χ^2 Test

	Factor Levels				
	1	2	…	C	Total
1	O_{11}	O_{12}	…	O_{1C}	N_1
Group 2	O_{21}				N_2
3	O_{31}				N_3
⋮	⋮				
R	O_{R1}			O_{RC}	N_R
Total	M_1	M_2		M_C	T

1. Compute the expected cell counts under homogeneity assumption:

$$E_{ij} = N_i M_j / T$$

2. Compute the chi-square statistic:

$$X^2 = \sum_{i,j} \frac{\left(O_{ij} - E_{ij}\right)^2}{E_{ij}}$$

3. Compare X^2 to $\chi^2(df)$ where

$$df = (R-1) \times (C-1)$$

4. Interpret acceptance/rejection or p-value.

2 x 2 Tables

Example 1: Pauling (1971)

Patients are randomized to either receive Vitamin C or placebo. Patients are followed-up to ascertain the development of a cold.

	Cold - Y	Cold - N	Total
Vitamin C	17	122	139
Placebo	31	109	140
Total	48	231	279

Q: Is treatment with Vitamin C associated with a reduced probability of getting a cold?

Q: If Vitamin C is associated with reducing colds, then what is the magnitude of the effect?

2 x 2 Tables

Example 2: Keller (AJPH, 1965)

Patients with (cases) and without (controls) oral cancer were surveyed regarding their smoking frequency (this table collapses over the smoking frequency categories).

	Case	Control	Total
Smoker	484	385	869
Non-Smoker	27	90	117
Total	511	475	986

Q: Is oral cancer associated with smoking?

Q: If smoking is associated with oral cancer, then what is the magnitude of the risk?

2 x 2 Tables

Example 3: Sex-linked traits

Suppose we collect a random sample of Drosophila and cross classify eye color and sex.

	male	female	Total
red	165	300	465
white	176	81	257
Total	341	381	722

Q: Is eye color associated with sex?

Q: If eye color is associated with sex, then what is the magnitude of the effect?

2 x 2 Tables

Example 4: Matched case control study

213 subjects with a history of acute myocardial infarction (AMI) were ***matched*** by age and sex with one of their siblings who did not have a history of AMI. The prevalence of a particular polymorphism was compared between the siblings

	AMI		
	carrier	noncarrier	Total
carrier	73	14	87
No AMI			
noncarrier	23	103	126
Total	96	117	213

Q: Is there an association between the polymorphism and AMI?

Q: If there is an association then what is the magnitude of the effect?

2 x 2 Tables

Each of these tables (except for example 4) can be represented as follows:

Disease Status

Exposure Status

	D	not D	Total
E	a	b	(a + b) = n_1
not E	c	d	(c + d) = n_2
Total	(a + c) = m_1	(b + d) = m_2	N

The question of association can be addressed with **Pearson's** X^2 (except for example 4) We compute the **expected** cell counts as follows:

Expected:

	D	not D	Total
E	n_1m_1/N	n_1m_2/N	(a + b) = n_1
not E	n_2m_1/N	n_2m_2/N	(c + d) = n_2
Total	(a + c) = m_1	(b + d) = m_2	N

2 x 2 Tables

Pearson's chi-square is given by:

$$X^2 = \sum_{i=1}^{4} \left(O_i - E_i\right)^2 / E_i$$

$$= \left(a - \frac{n_1 m_1}{N}\right)^2 / \left(\frac{n_1 m_1}{N}\right) + \left(b - \frac{n_1 m_2}{N}\right)^2 / \left(\frac{n_1 m_2}{N}\right) +$$

$$\left(c - \frac{n_2 m_1}{N}\right)^2 / \left(\frac{n_2 m_1}{N}\right) + \left(d - \frac{n_2 m_2}{N}\right)^2 / \left(\frac{n_2 m_2}{N}\right) +$$

$$= \frac{N\left(ad - bc\right)^2}{n_1 n_2 m_1 m_2}$$

2 x 2 Tables

Example 1: Pauling (1971)

	Cold - Y	Cold - N	Total
Vitamin C	17 (12%)	122 (88%)	139
Placebo	31 (22%)	109 (78%)	140
Total	48	231	279

H_0 : probability of disease does not depend on treatment

H_A : probability of disease does depend on treatment

$$X^2 = \frac{N(ad - bc)^2}{n_1 n_2 m_1 m_2}$$

$$= \frac{279(17 \times 109 - 31 \times 122)^2}{139 \times 140 \times 48 \times 231}$$

$$= 4.81$$

For the p-value we compute P(χ^2(1) > 4.81) = 0.028. Therefore, we reject the homogeneity of disease probability in the two treatment groups.

2 x 2 Tables
Applications In Epidemiology

Example 1 fixed the number of E and not E, then evaluated the disease status after a fixed period of time (same for everyone). This is a **prospective study**. Given this design we can estimate the **relative risk**:

$$RR = \frac{P(D \mid E)}{P(D \mid \overline{E})}$$

The range of RR is [0, ∞). By taking the logarithm, we have (- ∞, +∞) as the range for ln(RR) and a better approximation to normality for the estimated $\ln\left(\hat{R}R\right)$:

$$\ln\left(\hat{R}R\right) = \ln\left(\frac{\hat{P}(D \mid E)}{\hat{P}(D \mid \overline{E})}\right) = \ln\left(\frac{p_1}{p_2}\right)$$

$$= \ln\left(\frac{a / n_1}{c / n_2}\right)$$

$$\ln\left(\hat{R}R\right) \sim approx\ N\left(\ln\left(p_1 / p_2\right), \frac{1 - p_1}{p_1 n_1} + \frac{1 - p_2}{p_2 n_2}\right)$$

Relative Risk

	Cold - Y	Cold - N	Total
Vitamin C	17	122	139
Placebo	31	109	140
Total	48	231	279

The estimated relative risk is:

$$\hat{R}R = \frac{\hat{P}\left(D \mid E\right)}{\hat{P}\left(D \mid \overline{E}\right)}$$

$$= \frac{17/139}{31/140} = 0.55$$

We can obtain a 95% confidence interval for the relative risk by first obtaining a confidence interval for the log-RR:

$$\ln\left(\hat{R}R\right) \pm 1.96 \times \sqrt{\frac{1-p_1}{p_1 n_1} + \frac{1-p_2}{p_2 n_2}}$$

and exponentiating the endpoints of the CI.

Note that disease status and exposure status are transposed here compared to previous tables.

```
. csi 17 31 122 109

                 |   Exposed   Unexposed  |     Total
-----------------+------------------------+----------
           Cases |        17          31  |        48
        Noncases |       122         109  |       231
-----------------+------------------------+----------
           Total |       139         140  |       279
                 |                        |
            Risk |  .1223022    .2214286  |   .172043
                 |                        |
                 |      Point estimate    |  [95% Conf. Interval]
                 |------------------------+----------------------
 Risk difference |        -.0991264       | -.1868592   -.0113937
      Risk ratio |         .5523323       |  .3209178    .9506203
 Prev. frac. ex. |         .4476677       |  .0493797    .6790822
 Prev. frac. pop |         .2230316       |
                 +-----------------------------------------------
                              chi2(1) =     4.81  Pr>chi2 = 0.0283
```

2 x 2 Tables

Example 2: Keller (AJPH, 1965)

Patients with (cases) and without (controls) oral cancer were surveyed regarding their smoking frequency (this table collapses over the smoking frequency categories).

	Case	Control	Total
Smoker	484	385	869
Non-Smoker	27	90	117
Total	511	475	986

Q: Is oral cancer associated with smoking?

Q: If smoking is associated with oral cancer, then what is the magnitude of the risk?

2 x 2 Tables
Applications In Epidemiology

In **Example 2** we fixed the number of **cases** and **controls** then ascertained exposure status. Such a design is known as **case- control study**. Based on this we are able to directly estimate:

$$P(E \mid D) \quad \text{and} \quad P(E \mid \overline{D})$$

However, we generally are interested in the relative risk of disease given exposure, which is not estimable from these data alone - we've fixed the number of diseased and diseased free subjects, and it can be shown that in general:

$$\mathrm{P(D \mid E) \neq P(E \mid D)}$$

$$\frac{\mathrm{P}\left(\mathrm{D|E}\right)}{\mathrm{P}\left(\mathrm{D|\overline{E}}\right)} \neq \frac{\mathrm{P}\left(\mathrm{E|D}\right)}{\mathrm{P}\left(\mathrm{E|\overline{D}}\right)}$$

Odds Ratio

Instead of the relative risk we can estimate the **exposure odds ratio** which (surprisingly) is equivalent to the **disease odds ratio**:

$$\frac{P(E \mid D)/(1-P(E \mid D))}{P(E \mid \overline{D})/(1-P(E \mid \overline{D}))} = \frac{P(D \mid E)/(1-P(D \mid E))}{P(D \mid \overline{E})/(1-P(D \mid \overline{E}))}$$

In other words, **the odds ratio can be estimated regardless of the sampling scheme.**

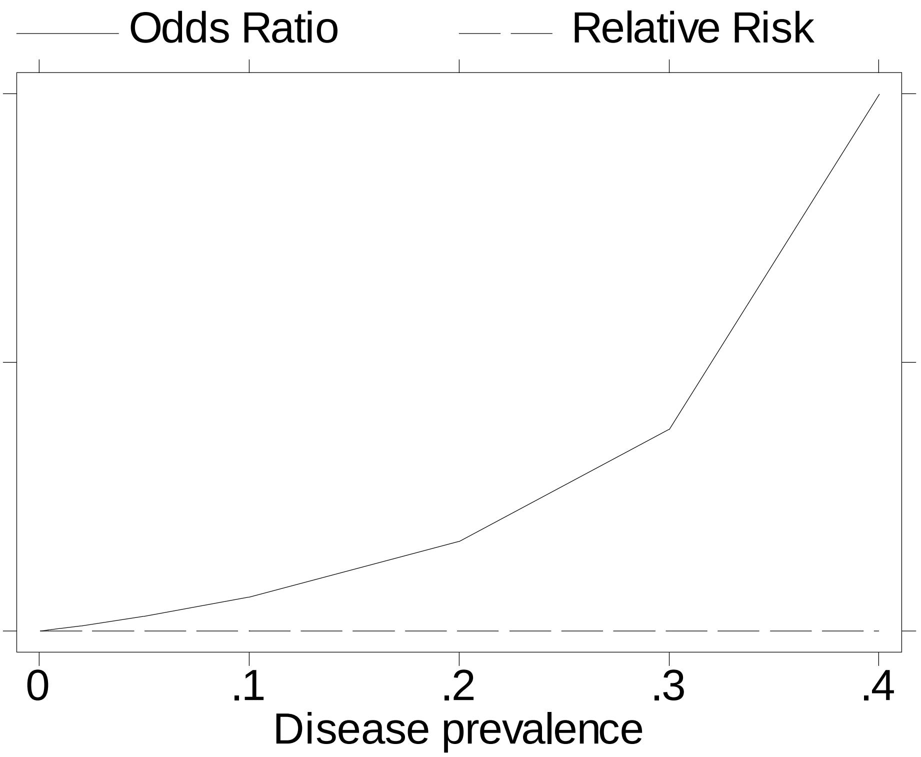
Furthermore, <u>for rare diseases</u>, P(D | E) ≈ 0 so that the disease odds ratio <u>approximates</u> the relative risk:

$$\frac{P(D \mid E)/(1-P(D \mid E))}{P(D \mid \overline{E})/(1-P(D \mid \overline{E}))} \approx \frac{P(D \mid E)}{P(D \mid \overline{E})}$$

Since with case-control data we are able to effectively estimate the exposure odds ratio we are then able to equivalently estimate the disease odds ratio which for rare diseases approximates the relative risk.

For rare diseases (e.g., prevalence <5%), the (sample) odds ratio estimates the (population) relative risk.

Odds Ratio



Odds Ratio

Like the relative risk, the odds ratio has [0, ∞) as its range. The **log odds ratio** has (- ∞, +∞) as its range and the normal approximation is better as an approximation to the dist of the estimated log odds ratio.

$$OR = \frac{p_1 / 1 - p_1}{p_2 / 1 - p_2}$$

$$\hat{O}R = \frac{\hat{p}_1 / 1 - \hat{p}_1}{\hat{p}_2 / 1 - \hat{p}_2}$$

$$\hat{O}R = \frac{ad}{bc}$$

Confidence intervals are based upon:

$$\ln\left(\hat{O}R\right) \sim \mathrm{N}\left(\ln(\mathrm{OR}), \frac{1}{\mathrm{n}_1 p_1} + \frac{1}{\mathrm{n}_1(1 - p_1)} + \frac{1}{\mathrm{n}_2 p_2} + \frac{1}{\mathrm{n}_2(1 - p_2)} \right)$$

Therefore, a 95% confidence interval for the log odds ratio is given by:

$$\ln\left(\frac{ad}{bc}\right) \pm 1.96 \times \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$$

Odds Ratio

```
. cci 484 27 385 90
                                                       Proportion
                 |   Exposed   Unexposed  |     Total    Exposed
-----------------+------------------------+---------------------
           Cases |       484          27  |       511     0.9472
        Controls |       385          90  |       475     0.8105
-----------------+------------------------+---------------------
           Total |       869         117  |       986     0.8813
                 |                        |
                 |      Point estimate    | [95% Conf. Interval]
                 |------------------------+---------------------
      Odds ratio |         4.190476       |  2.633584    6.836229  (exact)
 Attr. frac. ex. |         .7613636       |  .6202893    .8537205  (exact)
 Attr. frac. pop |          .721135       |
                 +----------------------------------------------
                            chi2(1) =    43.95  Pr>chi2 = 0.0000
```

Interpreting Odds ratios

1. What is the outcome of interest? (i.e. disease)
2. What are the two groups being contrasted? (i.e. exposed and unexposed)

$$\text{OR} = \frac{\text{odds of OUTCOME in EXPOSED}}{\text{odds of OUTCOME in UNEXPOSED}}$$

- Similar to RR for rare diseases
- Meaningful for both cohort and case-control studies
- OR > 1 $\Rightarrow$ increased risk of OUTCOME with EXPOSURE
- OR < 1 $\Rightarrow$ decreased risk of OUTCOME with EXPOSURE

2 x 2 Tables

Example 3: Sex-linked traits

Suppose we collect a random sample of Drosophila and cross classify eye color and sex.

	male	female	Total
red	165	300	465
white	176	81	257
Total	341	381	722

Q: Is eye color associated with sex?

Q: If eye color is associated with sex, then what is the magnitude of the effect?

2 x 2 Tables
Applications in Epidemiology

Example 3 is an example of a **cross-sectional** study since only the total for the entire table is fixed in advance. The row totals or column totals are not fixed in advance.

	male	female	Total
red	165 (48%)	300 (79%)	465
white	176	81	257
Total	341	381	722

Cross-sectional studies

- Sample from the entire population, not by disease status or exposure status
- Use chi-square test to test for association
- Use RR or OR to summarize association
- Cases of disease are **prevalent** cases (compared to incident cases in a prospective or cohort study)

2 x 2 Tables
Applications in Epidemiology

Case = red eye color
Noncase = white eye color

```
                        male        female
-----------------+------------------------+------------
           Cases |       165         300  |         465
        Noncases |       176          81  |         257
-----------------+------------------------+------------
           Total |       341         381  |         722
            Risk |   .483871    .7874016  |    .6440443
                 |                        |
                 |      Point estimate    |    [95% Conf. Interval]
                 |------------------------+------------------------
 Risk difference |         -.3035306      |   -.3706217   -.2364395
      Risk ratio |          .6145161      |     .544263    .6938375
 Prev. frac. ex. |          .3854839      |    .3061625     .455737
 Prev. frac. pop |          .1820637      |
      Odds ratio |           .253125      |    .1830613    .3500144
                 +-------------------------------------------------
                               chi2(1) =     72.32  Pr>chi2 = 0.0000
```

2 x 2 Tables

Example 4: Matched case control study

213 subjects with a history of acute myocardial infarction (AMI) were ***matched*** by age and sex with one of their siblings who did not have a history of AMI. The prevalence of a particular polymorphism was compared between the siblings

		AMI		
		carrier	noncarrier	Total
No AMI	carrier	73	14	87
	noncarrier	23	103	126
Total		96	117	213

Q: Is there an association between the polymorphism and AMI?

Q: If there is an association then what is the magnitude of the effect?

Paired Binary Data

Example 4 measures a binary response in sibs. This is an example of **paired binary data**. One way to display these data is the following:

	Carrier	Noncarrier	Total
AMI	96	117	213
No AMI	87	126	213
Total	183	243	426

Q: Can't we simply use X^2 Test of Homogeneity to assess whether this is evidence for an increase in knowledge?

A: NO!!! The X^2 tests assume that the rows are **independent** samples. In this design the 213 with AMI are genetically related to the 213 w/o AMI.

Paired Binary Data

For paired binary data we display the results as follows:

	AMI	
	1	0
No AMI 1	n_{11}	n_{10}
0	n_{01}	n_{00}

This analysis explicitly recognizes the heterogeneity of subjects. Thus, those that score (0,0) and (1,1) provide no information about the association between AMI and the polymorphism. These are known as the **concordant pairs**. The information regarding the association is in the **discordant pairs**, (0,1) and (1,0).

$$p_1 = P(\text{carrier} \mid \text{AMI})$$

$$p_0 = P(\text{carrier} \mid \text{No AMI})$$

$$H_0 : p_1 = p_0$$

$$H_A : p_1 \neq p_0$$

$$\hat{p}_1 - \hat{p}_0 = \frac{n_{11} + n_{01}}{N} - \frac{n_{11} + n_{10}}{N} = \frac{n_{01} - n_{10}}{N}$$

Paired Binary Data
McNemar's Test

Under the null hypothesis, H_0 : $p_1 = p_0$, we expect equal numbers of 01's and 10's. ($E[n_{01}] = E[n_{10}]$). Specifically, under the null:

$$M = n_{01} + n_{10}$$

$$n_{10} \mid M \sim Bin\left(M , \frac{1}{2} \right)$$

$$Z = \frac{n_{10} - M\frac{1}{2}}{\sqrt{M\frac{1}{2}\left(1 - \frac{1}{2}\right)}}$$

Under H_0, $Z^2 \sim \chi^2(1)$, and forms the basis for **McNemar's Test for Paired Binary Responses**.

The odds ratio comparing the odds of carrier in those with AMI to odds of carrier in those w/o AMI is estimated by:

$$\hat{O}R = \frac{n_{01}}{n_{10}}$$

Confidence intervals can be obtained as described in Breslow and Day (1981), section 5.2, or in Armitage and Berry (1987), chapter 16.

Example 4:

		AMI		
		carrier	noncarrier	Total
No AMI	carrier	73	14	87
	noncarrier	23	103	126
	Total	96	117	213

We can test H_0: $p_1 = p_2$ using **McNemar's Test:**

$$Z = \frac{n_{01} - M\frac{1}{2}}{\sqrt{M\,\frac{1}{2}\left(\frac{1}{2}\right)}}$$

$$= \frac{23 - \left(23 + 14\right)/2}{\sqrt{\left(23 + 14\right)/4}}$$

$$= 1.48$$

Comparing 1.48^2 to a χ^2 (1) we find that $p > 0.05$. Therefore, we do not reject the null hypothesis and find little evidence of association between gene and disease.

We estimate the odds ratio as $\hat{OR} = 23/14 = 1.64.$

Matched case-control data

```
. mcci 73 23 14 103

                 | Controls               |
Cases            |   Exposed   Unexposed  |      Total
-----------------+------------------------+------------
         Exposed |        73          23  |         96
       Unexposed |        14         103  |        117
-----------------+------------------------+------------
           Total |        87         126  |        213

McNemar's chi2(1) =      2.19    Prob > chi2 = 0.1390
Exact McNemar significance probability       = 0.1877

Proportion with factor
        Cases       .4507042
        Controls    .4084507     [95% Conf. Interval]
                   ---------     --------------------
        difference  .0422535     -.0181247   .1026318
        ratio       1.103448      .9684942   1.257207
        rel. diff.  .0714286     -.0197486   .1626057

        odds ratio  1.642857      .8101776   3.452833   (exact)
```

Two way tables - Review

- How were data collected?
  - Cohort design
  - Case-control design
  - Cross-sectional design
  - Matched pairs
- Is there an association?
  - R x C Tables
    - Chi-square tests of Homogeneity & Independence
  - 2 x 2 Tables
    - Chi-square test
    - Paired data and McNemar's
- What is the magnitude of the association?
  - Relative risk
  - Odds ratio (≈ relative risk for rare diseases)
  - Risk difference (attributable risk)

SUMMARY
Measures of Association for 2 x 2 Tables

RD = p_1 - p_2 = risk difference (null: RD = 0)

- also known as **attributable risk** or **excess risk**
- measures **absolute effect** – the proportion of cases among the exposed that can be attributed to exposure

RR = p_1/ p_2 = relative risk (null: RR = 1)

- measures **relative effect** of exposure
- bounded above by 1/p_2

OR = [p_1(1-p_2)]/[p_2 (1-p_1)] = odds ratio (null: OR = 1)

- range is 0 to ∞
- approximates RR for rare events
- invariant of switching rows and cols
- good behavior of p-values and CI even for small to moderate sample size

SUMMARY
Models for 2 x 2 Tables

1. **Cohort** ("Prospective", "Followup")
   - Sample n_1 "exposed" and n_2 "unexposed"
   - Follow everyone for equal period of time
   - Observe incident disease – r_1 cases among exposed, r_2 cases among unexposed
   - Model: Two independent binomials

     $r_1 \sim \text{binom}(p_1,n_1)$

     $r_2 \sim \text{binom}(p_2,n_2)$

     $p_1 = P(D|E)$

     $p_2 = P(D|\overline{E})$
   - Useful measures of association – RR,OR,RD
   - Examples:

     r_i = number of cases of HIV during 1 year followup of n_i individuals in arm i of HIV prevention trial

     r_i = number of low birthweight babies among n_i live births

SUMMARY
Models for 2 x 2 Tables

2. Case-Control

- Sample n_1 “cases” and n_2 “controls”
- Observe exposure history – r_1 exposed among cases, r_2 exposed among controls
- Model: Two independent binomials

$$r_1 \sim \text{binom}(q_1,n_1)$$

$$r_2 \sim \text{binom}(q_2,n_2)$$

$$q_1 = P(E|D)$$

$$q_2 = P(E|\overline{D})$$

- Useful measures of association – OR
- Examples:

r_i = consistent condom use (yes/no) among those with/without HPV infection

r_i = number exposed to alcohol during pregnancy among n_i low birthweight/normal birthweight babies

SUMMARY
Models for 2 x 2 Tables

3. Cross-sectional

- Sample n individuals from population
- Observe both "exposure" and (prevalent) "disease" status.
- No longitudinal followup
- Useful measures of association – RR,OR,RD
- Example:

  n_{ij} = number of gay men with gonorrhea in random sample of STD clinic attendees