

BIOS 662 Fall 2016

Categorical Data: Contingency Tables

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Contingency Tables

- Two-way $(r \times c)$ contingency table:

	j			
	1	2	\dots	c
1	n_{11}	n_{12}	\dots	n_{1c}
2	n_{21}	n_{22}	\dots	n_{2c}
i	\vdots	\vdots	\vdots	\vdots
r	n_{r1}	n_{r2}	\dots	n_{rc}

- Notation:

$$n_{i.} = \sum_{j=1}^c n_{ij} \quad n_{.j} = \sum_{i=1}^r n_{ij}$$

Contingency Tables

- Two scenarios where $r \times c$ tables arise
 1. Sample from a population and measure two characteristics, say X and Y

$$\Pr[X = i, Y = j] = \pi_{ij}; \quad \sum_{i=1}^r \sum_{j=1}^c \pi_{ij} = 1$$

2. Each row corresponds to a sample from a different population

$$\sum_{j=1}^c \pi_{ij} = 1$$

Contingency Table: Example I

- A survey of physicians asked about the size of the community in which they were reared and the size of the community in which they practice

Reared	Practice				Total
	<5K	5-49K	50-99K	$\geq 100K$	
<5K	40	38	32	37	147
5-49K	26	42	35	33	136
50-99K	24	26	34	31	115
$\geq 100K$	30	39	53	60	182
	120	145	154	161	580

Contingency Table: Example II

- A case-control study of women was conducted to investigate the relationship between age at which they first gave birth and breast cancer

	Age at first childbirth					Total
	<20	20-24	25-29	30-34	≥ 35	
Case	320	1206	1011	463	220	3220
Control	1422	4432	2893	1092	406	10245
	1742	5638	3904	1555	626	13465

Contingency Tables

- For the physicians example, H_0 : size of community in which practice is independent of size of community in which reared

$$H_0 : \pi_{ij} = \pi_{i.}\pi_{.j}$$

- Test of independence, $X \perp Y$

$$\Pr[X = i, Y = j] = \Pr[X = i] \Pr[Y = j]$$

for $i = 1, \dots, r$; $j = 1, \dots, c$

Contingency Tables

- For the breast cancer example, H_0 : distribution of age at first childbirth is the same for cases and controls

$$H_0 : \pi_{ij} = \pi_{i'j}; \quad j = 1, 2, \dots, c$$

- Test of homogeneity/association

Test of Independence or No Association

- Under either H_0 , the estimated expected frequency in the (i, j) cell is

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

- Consider the breast cancer example

- The overall proportion of women <20 is

$$\frac{n_{11} + n_{21}}{N} = \frac{n_{.1}}{N}$$

- There are $n_{1.}$ cases, so if H_0 is true we would expect

$$E_{11} = n_{1.} \frac{n_{.1}}{N} = \frac{n_{1.}n_{.1}}{N}$$

cases to be <20 years old

Test of Independence or Association

- Under H_0 , the expected frequency in the (i, j) cell is

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

- Let

$$X^2 = \sum_{i=1}^r \sum_{j=1}^c \frac{(O_{ij} - E_{ij})^2}{E_{ij}}$$

that is,

$$X^2 = \sum_{i=1}^r \sum_{j=1}^c \frac{(n_{ij} - n_{i.}n_{.j}/N)^2}{n_{i.}n_{.j}/N}$$

Test of Independence

- Under H_0 ,

$$X^2 \sim \chi^2_{(r-1)(c-1)}$$

- Physicians example:

$$(r - 1)(c - 1) = 3 \times 3 = 9$$

$$C_{0.05} = \{X^2 : X^2 > \chi^2_{9,0.95} = 16.92\}$$

Physicians Example

- Expected values

Reared	Practice				Total
	<5K	5-49K	50-99K	$\geq 100K$	
<5K	30.4	36.8	39.0	40.8	147
5-49K	28.1	34.0	36.1	37.8	136
50-99K	23.8	28.8	30.5	31.9	115
$\geq 100K$	37.7	45.5	48.3	50.5	182
	120	145	154	161	580

Physicians Example cont.

- Calculate the test statistic

$$\begin{aligned} X^2 &= \frac{(40 - 30.4)^2}{30.4} + \frac{(38 - 36.8)^2}{36.8} + \dots + \frac{(60 - 50.5)^2}{50.5} \\ &= 12.81 \end{aligned}$$

- Do not reject H_0 .
- There is insufficient evidence to conclude that the size of the community in which practice and that of the community in which reared are dependent; the data are consistent with the null hypothesis that size of community in which practice and that in which reared are independent

Breast Cancer Example

- Underlying probabilities

	Age at first childbirth					
	<20	20-24	25-29	30-34	≥ 35	Total
Case	π_{11}	π_{12}	π_{13}	π_{14}	π_{15}	1
Control	π_{21}	π_{22}	π_{23}	π_{24}	π_{25}	1

- Null hypothesis

$$H_0 : \pi_{1j} = \pi_{2j} \text{ for } j = 1, 2, 3, 4, 5$$

- We can use the same statistic

$$X^2 = \sum_{i=1}^2 \sum_{j=1}^c \frac{(O_{ij} - E_{ij})^2}{E_{ij}} \sim \chi^2_{(c-1)}$$

Breast Cancer Example cont.

- Expected frequencies

	Age at first childbirth					Total
	<20	20-24	25-29	30-34	≥ 35	
Case	416.6	1348.3	933.6	371.9	149.7	3220
Control	1325.4	4289.7	2970.4	1183.1	476.3	10245
	1742	5638	3904	1555	626	13465

Breast Cancer Example cont.

- Test statistic

$$X^2 = \frac{(320 - 416.6)^2}{416.6} + \dots + \frac{(406 - 476.3)^2}{476.3} = 130.3$$

- Rejection region

$$C_{0.05} = \{X^2 : X^2 > \chi_{4,0.95}^2 = 9.49\}$$

- Reject H_0
- Conclude that the age distributions are not the same

Asymptotic Approximation

- Note that the χ^2 distribution for X^2 is an approximation
- The approximation works well if $E_{ij} \geq 5$ for all i, j
- If $E_{ij} < 5$, a generalization of Fisher's exact test can be employed or categories combined

Test of Independence

- For $r = c = 2$, one can show that

$$\begin{aligned} X^2 &= \sum_{i=1}^2 \sum_{j=1}^2 \frac{(n_{ij} - n_{i.}n_{.j}/N)^2}{n_{i.}n_{.j}/N} \\ &= \frac{N(n_{11}n_{22} - n_{12}n_{21})^2}{n_{1.}n_{.1}n_{2.}n_{.2}} \end{aligned}$$

- This is the *Pearson chi-square statistic* we saw for comparing two proportions

Test for Trend

- Consider a $2 \times c$ table
- The χ^2 test for homogeneity does not tell us how the probabilities differ
- Rather, it tests just whether they differ
- If the categories of the column variable are ordered, a more powerful test is possible

Test for Trend

- Suppose the columns correspond to ordered levels of an exposure
- Suppose the rows correspond to disease (yes/no)
- We are interested in detecting alternatives where the probability of disease increases (or decreases) with exposure level
- That is, we are looking for a monotonic dose-response type of relationship

Test for Trend: Example

- Example 7.3 in the text: Risk of catheter-related infection and the duration of catheterization

	Duration (days)			
Culture	1	2	3	4+
Positive	1	5	5	14
Negative	46	64	39	76
Total	47	69	44	90

- Let ρ_j denote the conditional probability of being in row 1 given in column j
- For this catheter example, ρ_j is the probability of a positive culture given in the j^{th} duration category

Test for Trend

- Test

$$H_0 : \rho_1 = \rho_2 = \cdots = \rho_c$$

versus

$$H_A : \rho_1 \leq \rho_2 \leq \cdots \leq \rho_c$$

with at least one strict inequality, or

$$H_A : \rho_1 \geq \rho_2 \geq \cdots \geq \rho_c$$

with at least one strict inequality

Test for Trend

- Numerical scores must be assigned to the categories:

$$x_j : j = 1, 2, \dots, c$$

- Example: $x_j = j$
- In the breast cancer example, use the mid-range of age categories

Test for Trend

- Let

$$[n_1x] \equiv \sum_{j=1}^c n_{1j}x_j - \frac{n_{1\cdot} \sum_{j=1}^c n_{\cdot j}x_j}{N}$$

$$[x^2] \equiv \sum_{j=1}^c n_{\cdot j}x_j^2 - \frac{(\sum_{j=1}^c n_{\cdot j}x_j)^2}{N}$$

and

$$p \equiv \frac{n_{1\cdot}}{N}$$

- Then the chi-square test for trend (text, p 215) is

$$X_{\text{trend}}^2 \equiv \frac{[n_1x]^2}{[x^2]p(1-p)}$$

Test for Trend

- Huh?
- Compute the average score in row 1:

$$\bar{x} \equiv \sum_{j=1}^c \frac{n_{1j}x_j}{n_{1.}}$$

- Compute the finite-sample expected value under the null:

$$E(\bar{x}) \equiv E(x) \equiv \sum_{j=1}^c \frac{n_{.j}x_j}{N}$$

Test for Trend

- Compute the finite-sample variance:

$$\text{Var}(\bar{x}) \equiv \left(\frac{1-f}{n_{1.}} \right) \left[E(x^2) - E(x)^2 \right]$$

where $f = n_{1.}/N$ is the sampling fraction and

$$E(x^2) \equiv \sum_{j=1}^c \frac{n_{.j} x_j^2}{N}$$

- Then the chi-square test for trend can equivalently be written as

$$X_{\text{trend}}^2 = \frac{(\bar{x} - E(\bar{x}))^2}{\text{Var}(\bar{x})}$$

Test for Trend

- Under H_0 ,

$$X_{\text{trend}}^2 \sim \chi_1^2$$

$$C_\alpha = \{X^2 : X^2 > \chi_{1,1-\alpha}^2\}$$

$$p = \Pr[\chi_1^2 > x^2]$$

- Note that here χ^2 has 1 degree of freedom regardless of c

Test for Trend: Example

- Catheter example

Culture	Duration			
	1	2	3	4+
Positive	1	5	5	14
Negative	46	64	39	76
Total	47	69	44	90

- $X^2_{\text{trend}} = 6.98$; $p = 0.008$; reject H_0 and conclude that the probability of a positive culture increases with duration of catheterization

Test for Trend: R

```
# Also if prop.trend.test(c(1,5,5,14),c(47,69,44,90),c(1,2,3,4))  
# or      prop.trend.test(c(1,5,5,14),c(47,69,44,90),c(4,3,2,1))  
> prop.trend.test(c(1,5,5,14),c(47,69,44,90))
```

Chi-squared Test for Trend in Proportions

```
data:  c(1, 5, 5, 14) out of c(47, 69, 44, 90) ,  
      using scores: 1 2 3 4  
X-squared = 6.9764, df = 1, p-value = 0.008259
```

```
> prop.trend.test(c(1,5,5,14),c(47,69,44,90),c(1,2,3,6))
```

Chi-squared Test for Trend in Proportions

```
data:  c(1, 5, 5, 14) out of c(47, 69, 44, 90) ,  
      using scores: 1 2 3 6  
X-squared = 6.4248, df = 1, p-value = 0.01125
```

Test for Trend: SAS

```
data trend; input culture $1-8 duration count;
cards;
positive 1 1
positive 2 5
positive 3 5
positive 4 14
negative 1 46
negative 2 64
negative 3 39
negative 4 76
;

proc freq data=trend order=data;
  tables culture*duration / chisq nopct norow trend;
  weight count;
```

culture		duration				
Frequency						
Col	Pct	1	2	3	4	Total
-----+-----+-----+-----+-----+						
positive		1	5	5	14	25
		2.13	7.25	11.36	15.56	
-----+-----+-----+-----+-----+						
negative		46	64	39	76	225
		97.87	92.75	88.64	84.44	
-----+-----+-----+-----+-----+						
Total		47	69	44	90	250

Test for Trend: SAS, cont.

Statistics for Table of culture by duration

Statistic	DF	Value	Prob

Chi-Square	3	6.9951	0.0721
Mantel-Haenszel Chi-Square	1	6.9485	0.0084

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

Cochran-Armitage Trend Test

Statistic (Z)	2.6413
One-sided Pr > Z	0.0041
Two-sided Pr > Z	0.0083

χ^2 Test of Goodness of Fit

- Goal: Assess how well a particular model fits the data
- General form

$$\chi^2 = \sum_i \frac{(O_i - E_i)^2}{E_i} \sim \chi_{\text{df}}^2$$

- E_i computed under H_0
- Rejecting the null implies the model does not provide an adequate fit to the data

χ^2 Test of Goodness of Fit

- Multinomial: Generalization of binomial from 2 to K categories
- Suppose there are n independent trials, each with K possible outcomes having probabilities π_1, \dots, π_K
- Let n_i be the number of trials having outcome i , $i = 1, \dots, K$, such that

$$n = \sum_{i=1}^K n_i$$

- Then

$$E(n_i) = n\pi_i \quad \text{and} \quad \text{Var}(n_i) = n\pi_i(1 - \pi_i)$$

χ^2 GOF: Genetics Example

- Example: Mendelian genetics hypothesizes a particular genotype should occur in the proportions

1 : 2 : 1 (dominant, heterozygous, recessive)

- $H_0 : \pi_1 = 0.25, \pi_2 = 0.5, \pi_3 = 0.25$
- H_A : at least one of the equalities is false (in which case at least two must be false)
- Suppose in a study the genotypes have frequencies
 $n_1 = 21, n_2 = 62, n_3 = 17$

χ^2 GOF: Genetics Example cont.

- When the expected values are known, in general

$$X^2 = \sum_{i=1}^K \frac{(O_i - E_i)^2}{E_i} \sim \chi_{K-1}^2$$

$K = 3$ for the genetics example

- Under H_0 ,

$$E_1 = 0.25 \times 100 = 25$$

$$E_2 = 50$$

$$E_3 = 25$$

χ^2 GOF: Genetics Example cont.

- Thus

$$X^2 = \frac{(21 - 25)^2}{25} + \frac{(62 - 50)^2}{50} + \frac{(17 - 25)^2}{25} = 6.08$$

- Because $K = 3$, $\text{df} = 2$, so

$$C_{0.05} = \{X^2 : X^2 \geq \chi_{2,0.95}^2 = 5.99\}$$

- Also,

$$\Pr[\chi_2^2 \geq 6.08] = 1 - 0.952 = 0.048$$

- Reject H_0

χ^2 GOF: Genetics Example Using SAS

```
proc freq order=data;
  tables genotype / testp=(25 50 25);
  weight count;
```

The FREQ Procedure

genotype	Frequency	Percent	Test Percent	Cumulative Frequency	Cumulative Percent
dominant	21	21.00	25.00	21	21.00
heterozygous	62	62.00	50.00	83	83.00
recessive	17	17.00	25.00	100	100.00

Chi-Square Test
for Specified Proportions

```
-----
Chi-Square      6.0800
DF              2
Pr > ChiSq      0.0478
```

χ^2 GOF: DBP Example

- Diastolic blood pressure (DBP) was measured on a random sample from a population of interest
- It is hypothesized that DBP is normally distributed

DBP	Frequency
<50	57
[50, 60)	330
[60, 70)	2132
[70, 80)	4584
[80, 90)	4604
[90, 100)	2119
[100, 110)	659
≥ 110	251
Total	14736

χ^2 GOF: DBP Example cont.

- From the sample (before classifying into intervals)

$$\bar{y} = 80.7 \text{ and } s = 12.00$$

- If DBP is normally distributed with $\mu = 80.7$ and $\sigma = 12$, the expected frequency in an interval between a and b is

$$14736 \times [\Phi((b - 80.7)/12) - \Phi((a - 80.7)/12)]$$

- The expected frequency in the <50 group is

$$14736 \Phi((50 - 80.7)/12) = 14736 \Phi[-2.56] = 77.5$$

χ^2 GOF: DBP Example cont.

DBP	Freq	z	$\Phi(z)$	Prob	E
< 50	57	-2.56	0.0053	0.0053	77.5
$[50, 60)$	330	-1.73	0.0423	0.0370	545.3
$[60, 70)$	2,132	-0.89	0.1863	0.1440	2,122.3
$[70, 80)$	4,584	-0.06	0.4767	0.2905	4,280.2
$[80, 90)$	4,604	0.77	0.7808	0.3041	4,481.0
$[90, 100)$	2,119	1.61	0.9461	0.1653	2,435.7
$[100, 110)$	659	2.44	0.9927	0.0466	686.3
≥ 110	251	∞	1	0.0073	107.7
Total	14,736				14,736.0

χ^2 GOF: DBP Example cont.

- H_0 : data are from a normal distribution
- H_A : data are not from a normal distribution
- Rejection region

$$C_\alpha = \{X^2 : X^2 \geq \chi_{K-S-1, 1-\alpha}^2\}$$

where S = number of parameters estimated

- For the DBP example, $K = 8$ and $S = 2$, so that

$$C_{0.05} = \{X^2 : X^2 \geq \chi_{5, 0.95}^2 = 11.07\}$$

χ^2 GOF: DBP Example cont.

- GOF test statistic

$$X^2 = \sum_{i=1}^K \frac{(O_i - E_i)^2}{E_i} = \frac{(57 - 77.5)^2}{77.5} + \dots = 348.3$$

- Reject H_0
- Read Section 6.6.4 of the text about the distribution of X^2 when parameter estimation is necessary

χ^2 GOF: Mendel Example

- Fisher examined Mendel's experiments (text, Table 6.9)

Experiment	X^2	DF	p
3:1 Ratios	2.14	7	0.95
2:1 Ratios	5.17	8	0.74
Bifactorial	2.81	8	0.95
Gametic ratios	3.67	15	0.999
Trifactorial	15.32	26	0.95
Total	29.11	64	

- If X_1^2, \dots, X_n^2 are independent χ^2 with m_1, \dots, m_n degrees of freedom, then

$$\sum_i X_i^2 \sim \chi_m^2 \quad \text{where} \quad m = \sum_i m_i$$

$$p = \Pr[\chi_{64}^2 > 29.11] = 0.9999474$$

Measurement of Agreement

- Example: Adults were asked to rate their weight as underweight, normal, overweight, or obese; their weight was then measured

Self-report	Measured				Total
	Under	Normal	Over	Obese	
Under	462	178	0	0	640
Normal	72	2868	505	2	3447
Over	0	134	2086	280	2500
Obese	0	0	59	809	868
Total	534	3180	2650	1091	7455

Measure of Agreement: Kappa

- The χ^2 test for independence will reject H_0
- If we want to measure agreement, we might take the proportion on the diagonal:

$$p_a = \frac{462 + 2868 + 2086 + 809}{7455} = 0.835$$

- However, there would be some agreement by chance even if the two classifications were independent

Measure of Agreement: Kappa

- Under independence,

$$E_{11} = (640)(534)/7455 = 45.84$$

$$E_{22} = 1470.35, \quad E_{33} = 888.67, \quad E_{44} = 127.03$$

- Therefore we expect 2531.89 agreements just by chance

$$p_c = \frac{2531.89}{7455} = 0.340$$

Measure of Agreement: Kappa

- Let

p_a = observed proportion of agreement

p_c = expected proportion of agreement

- Kappa statistic

$$\kappa = \frac{p_a - p_c}{1 - p_c}$$

- κ is a chance-adjusted measure of agreement

Measure of Agreement: Kappa

- Note

$$\frac{-p_c}{1 - p_c} \leq \kappa \leq 1$$

$\kappa = 0$ if agreement is totally by chance

$\kappa = 1$ if and only if there is perfect agreement

- There are various categorizations (or guidelines) of values of κ ; the best known is by Landis & Koch (1977). For instance, 0.41-0.60 is classified as “moderate agreement” and 0.61-0.80 as “substantial agreement”.
- My opinion is that the interpretation of κ needs to be context-dependent.

Measure of Agreement: Kappa

- Under $H_0 : \kappa = 0$,

$$\text{Var}(\kappa) = \frac{p_c + p_c^2 - N^{-3} \sum_{i=1}^r (n_{i.}^2 n_{.i} + n_{i.} n_{.i}^2)}{N(1 - p_c)^2}$$

- For moderate sample sizes,

$$z = \frac{\kappa}{\sqrt{\text{Var}(\kappa)}} \sim N(0, 1)$$

under H_0

Measure of Agreement: Kappa

- Weight example revisited:

$$\kappa = \frac{0.835 - 0.34}{1 - 0.34} = 0.75$$

which Landis & Koch would classify as indicating substantial agreement

- Compute variance of κ

$$\text{Var}(\kappa) = \frac{0.34 + 0.34^2 - 0.2631}{7455(0.66)^2} = 5.901 \times 10^{-5}$$

- Therefore

$$z = \frac{0.75}{0.0077} = 97.654$$

Kappa: SAS

```
proc freq order=data;  
  tables self*measured/agree nopct norow nocol;  
  test kappa;  
  weight wt;
```

Simple Kappa Coefficient

Kappa	0.7502
ASE	0.0065
95% Lower Conf Limit	0.7374
95% Upper Conf Limit	0.7629

Test of H0: Kappa = 0

ASE under H0	0.0077
Z	97.6540
One-sided Pr > Z	<.0001
Two-sided Pr > Z	<.0001

Kappa: R

- R has kappa statistics in various libraries. The one below is in the vcd library. Note the uppercase K in Kappa()

```
> table<-matrix(c(462,178,0,0,72,2868,505,2,0,134,2086,280,  
+ 0,0,59,809),nrow=4,byrow=T)
```

```
> Kappa(table)
```

	value	ASE
Unweighted	0.7501581	0.006509663
Weighted	0.8109287	0.013309715

```
> confint(Kappa(table))
```

Kappa	lwr	upr
Unweighted	0.7373994	0.7629169
Weighted	0.7848422	0.8370153

Kappa: R cont.

- R also has a function `kappa2()` in the library `irr`; but it requires the data in a different format – an $n \times 2$ matrix with each row corresponding to an observation (a pair)

```
> col1<-c(rep('under',640),rep('normal',3447),rep('over',2500),  
+   rep('obese',868))
```

```
> col2<-c(rep('under',462),rep('normal',178),rep('under',72),  
+   rep('normal',2868),rep('over',505),rep('obese',2),  
+   rep('normal',134),rep('over',2086),rep('obese',280),  
+   rep('over',59),rep('obese',809))
```

```
> tab2<-cbind(col1,col2)
```

Kappa: R cont.

```
> rbind(tab2[1:5,],tab2[4081:4090,])
```

	col1	col2
[1,]	"under"	"under"
[2,]	"under"	"under"
[3,]	"under"	"under"
[4,]	"under"	"under"
[5,]	"under"	"under"
[6,]	"normal"	"over"
[7,]	"normal"	"over"
[8,]	"normal"	"over"
[9,]	"normal"	"over"
[10,]	"normal"	"over"
[11,]	"normal"	"obese"
[12,]	"normal"	"obese"
[13,]	"over"	"normal"
[14,]	"over"	"normal"
[15,]	"over"	"normal"

Kappa: R cont.

```
> kappa2(tab2)  
Cohen's Kappa for 2 Raters (Weights: unweighted)
```

```
Subjects = 7455
```

```
Raters = 2
```

```
Kappa = 0.75
```

```
z = 97.7
```

```
p-value = 0
```

```
> agree(tab2)  
Percentage agreement (Tolerance=0)
```

```
Subjects = 7455
```

```
Raters = 2
```

```
%-agree = 83.5
```