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Statistics in Evidence Based Medicine

Lecture 7: Research Questions for Two Groups

Rizwana Rehman, PhD

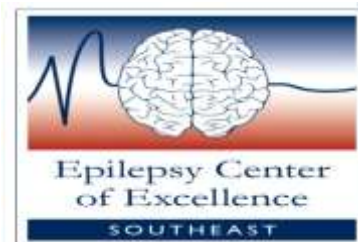
Regional Statistician

Southeast Epilepsy Center of Excellence

Durham VA Medical Center, Durham NC

Rizwana.Rehman@va.gov

(919)286-0411 ext: 5024





Summary of One Group Methods

Nature of problem	Test
Interval & normal	One –sample t test
Ordinal or interval, non normal	Sign test
Dependent groups; interval & normal	Paired t test
Dependent groups; ordinal or interval	Wilcoxon signed rank test, Sign test
Single proportion	z approximation, exact binomial
Dependent groups; proportion	McNemar



Overview

- Difference of means in two normally distributed groups
- Nonparametric test for two independent means
- Statistical difference between computed proportions
- Fisher's Exact test



Normal Data with Same Standard Deviations

- Are two studied groups from the same population?
- t test is used for quantitative data under the following assumptions.
 - Both samples are normally distributed.
 - Both come from distributions with same value of standard deviation.
 - Observations are independent of each other.

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{S_p^2}{n_1} + \frac{S_p^2}{n_2}}} \quad \text{with } n_1 + n_2 - 2 \text{ d.f, } s_p \text{ is pooled SD.}$$



Why Assumptions Matter?

- When assumptions are not met, α increases.
 - If t test is used on highly skewed data with less than 30 observations, then confidence intervals are erroneously narrow and p value is smaller than it should be.
 - Same happens when observations are not independent due to less effective sample size.
 - Similarly pooled SD is not accurate if standard deviations are markedly different increasing type I error rate.



How To Check for Assumptions?

- Normality
 - For large data sets normality does not matter
 - For small data
 - Eyeball data sets
 - A normality test can be run
- Independence
 - One's decision
- Equal standard deviations
 - For equal sample sizes equal SD is not needed.
 - If ratio of larger to smaller SD is less than 2, OK
 - Run a test such as F test for equal variance



What if Standard Deviations are Different?

- If standard deviations are noticeably different, then use another approximate test by Satterthwaite also known as Welch test.
- Openstat gives results for both equal and unequal standard deviations.



Openstat for Two Independent Means

Assume that FEV_1 levels for following data are normally distributed. Are FEV_1 levels different in two groups?

Asthmatics' FEV_1 : $n_1 = 5, \bar{x}_1 = 1.86, s_1 = 0.378$

Controls' FEV_1 : $n_2 = 6, \bar{x}_2 = 2.51, s_2 = 0.210$

Medical Statistics A Common Sense Approach A5

Two Independent Groups t Test in Openstat

$$H_0: \mu_1 = \mu_2$$

$$H_A: \mu_1 \neq \mu_2$$



Entering Data in Openstat

Comparison of Two Sample Means

Data Entry By:

- ☒ Values Entered On This Form
- ☐ Values in the Data Grid

Assume:

- ☒ Independent Scores
- ☐ Correlated Scores

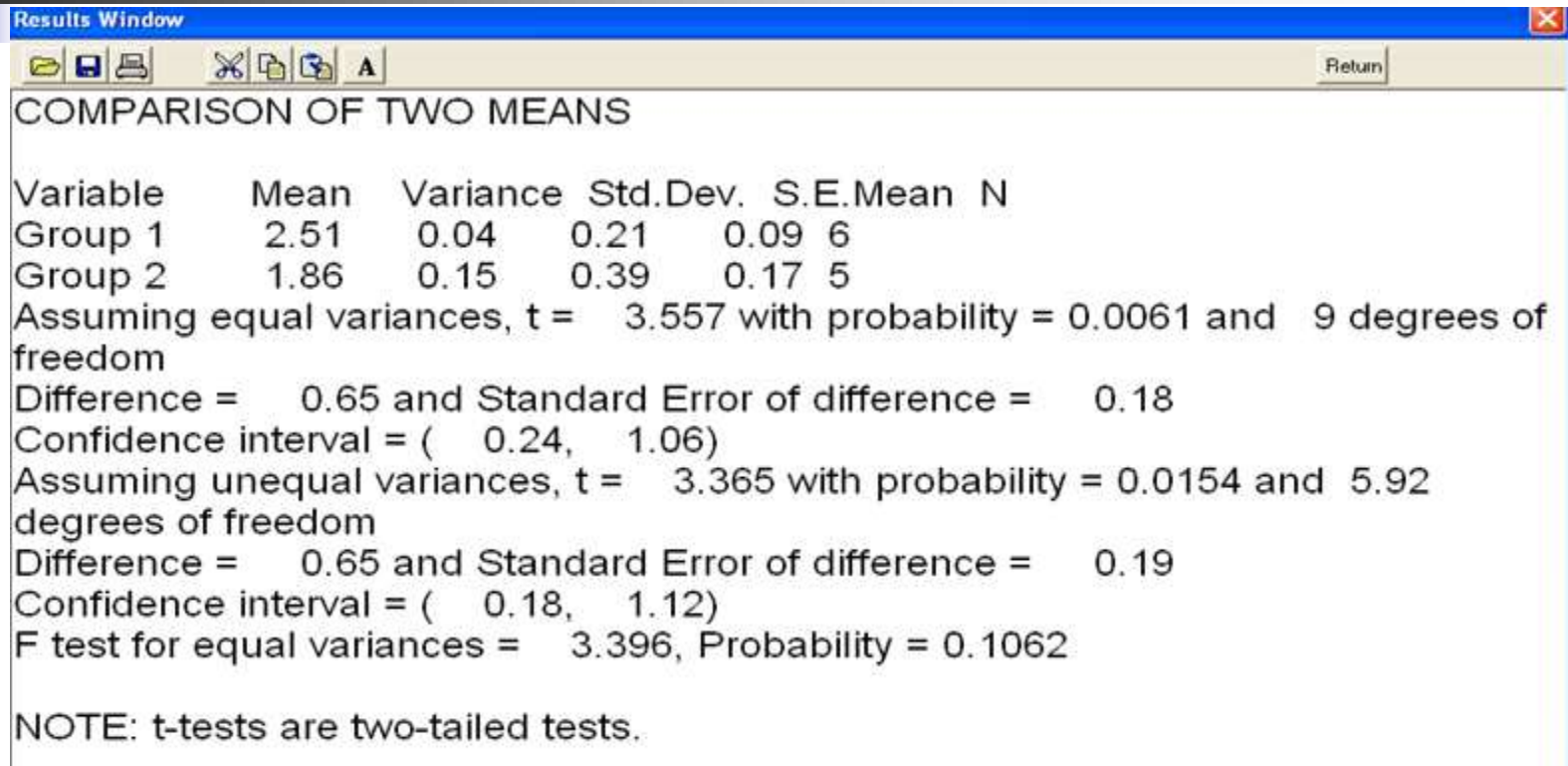
Mean 1: 2.51 Std. Dev. 1: 0.210 Sample Size 1: 6

Mean 2: 1.86 Std. Dev. 2: 0.387 Sample Size 2: 5

Percent Confidence Interval: 95

Reset Cancel Continue

Results from Openstat



The screenshot shows the 'Results Window' of the Openstat software. The window title is 'Results Window' with a standard Windows-style title bar (minimize, maximize, close buttons). Below the title bar is a toolbar with icons for file operations (open, save, print, copy, paste) and a text editor icon. A 'Return' button is located on the right side of the toolbar. The main content area displays the results of a 'COMPARISON OF TWO MEANS' test. The results are presented in a table format with columns for Variable, Mean, Variance, Std.Dev., S.E.Mean, and N. The data shows Group 1 with a mean of 2.51 and Group 2 with a mean of 1.86. Below the table, the results of the t-test are displayed, including the t-value, probability, degrees of freedom, and confidence intervals for both equal and unequal variances. The F-test result is also shown. A note at the bottom states that t-tests are two-tailed tests.

Variable	Mean	Variance	Std.Dev.	S.E.Mean	N
Group 1	2.51	0.04	0.21	0.09	6
Group 2	1.86	0.15	0.39	0.17	5

Assuming equal variances, $t = 3.557$ with probability = 0.0061 and 9 degrees of freedom
Difference = 0.65 and Standard Error of difference = 0.18
Confidence interval = (0.24, 1.06)
Assuming unequal variances, $t = 3.365$ with probability = 0.0154 and 5.92 degrees of freedom
Difference = 0.65 and Standard Error of difference = 0.19
Confidence interval = (0.18, 1.12)
F test for equal variances = 3.396, Probability = 0.1062

NOTE: t-tests are two-tailed tests.

Reject H_0 , means in two groups are statistically significantly different



Mean Difference for Non Normal Data

- Use Mann-Whitney using the following assumptions.
 - Data are ordinal or continuous.
 - Two groups are independent.
 - Two groups are symmetrically distributed.
- Can be used for median or mean.
- As powerful as t test.



Mann-Whitney U Test for $n_1, n_2 \geq 10$

- Combine both data sets and rank them in increasing order. Break for ties.
- Separate the ranks in each group and add ranks for each group.
- Call the smaller rank T and smaller group size n_1
- Use z approximation

$$z = \frac{|T - n_1(n_1 + n_2 + 1)/2|}{\sqrt{n_1 n_2 (n_1 + n_2 + 1)/12}}$$

- For smaller samples use tables



Example of Non Normal data

H_0 : New treatment B does not change the plasma globulin.

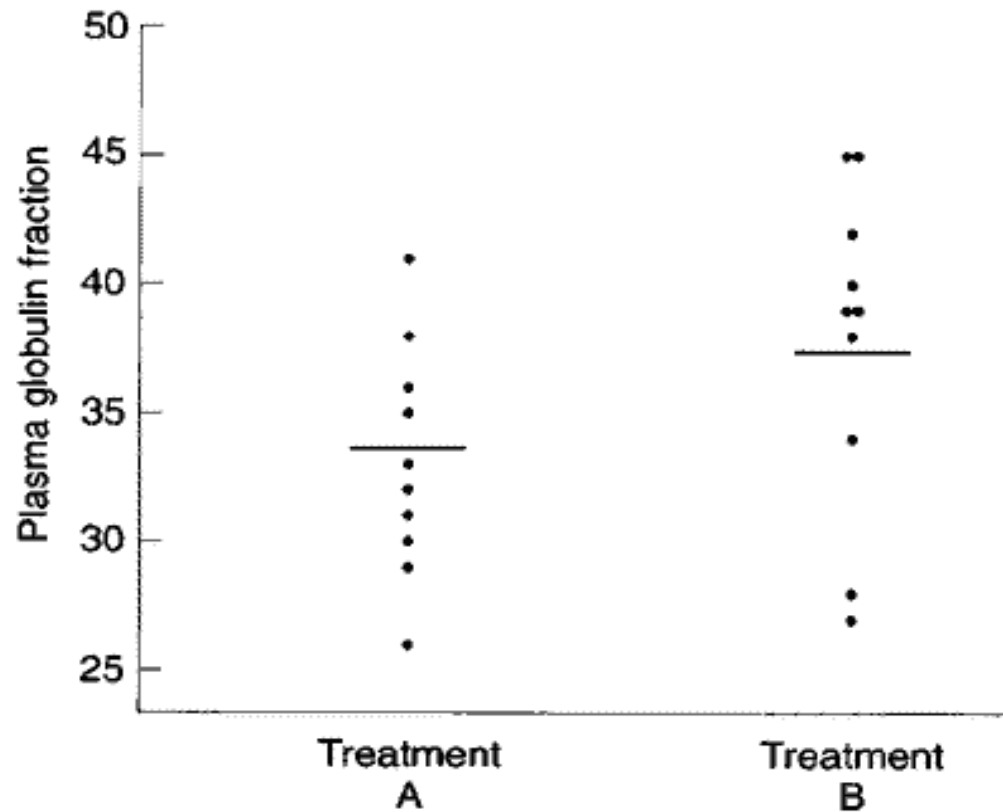
H_A : New treatment B changes the plasma globulin.

Plasma globulin fraction after randomization to treatments A or B

Treatment A	38	26	29	41	36	31	32	30	35	33
Treatment B	45	28	27	38	40	42	39	39	40	45

Statistic at Square One: Chapter 10

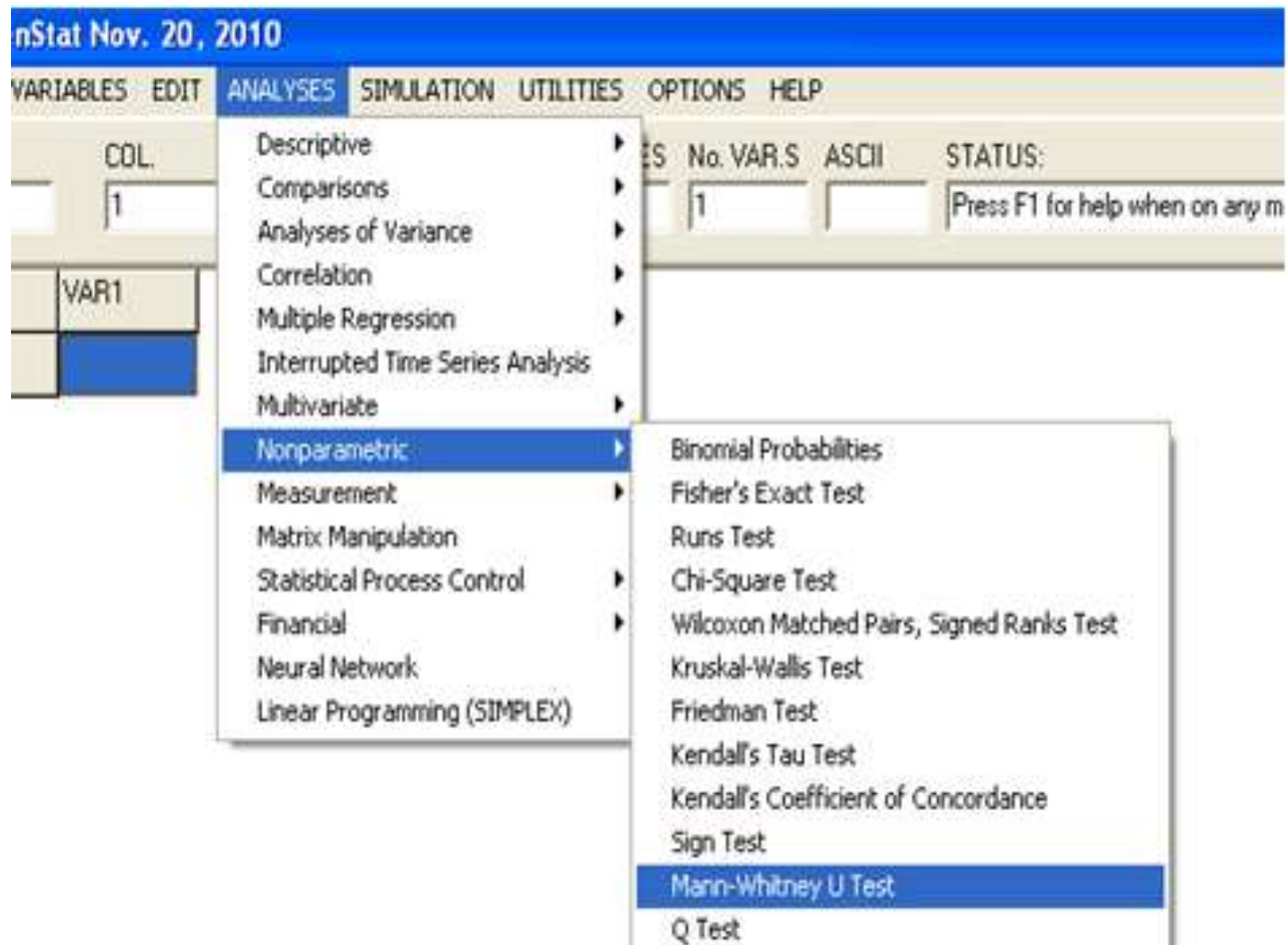
Symmetry



Plasma globulin fraction after treatments A or B with mean values.

Statistic at Square One: Chapter 10

Mann –Whitney in Openstat



Entering Data for Analysis

OpenStat Nov. 20, 2010

FILES VARIABLES EDIT ANALYSES SIMULATION UTILITIES OPTIONS HELP

ROW COL. Cell Edit (Return to finish) N CASES No. VAR.S ASCII S

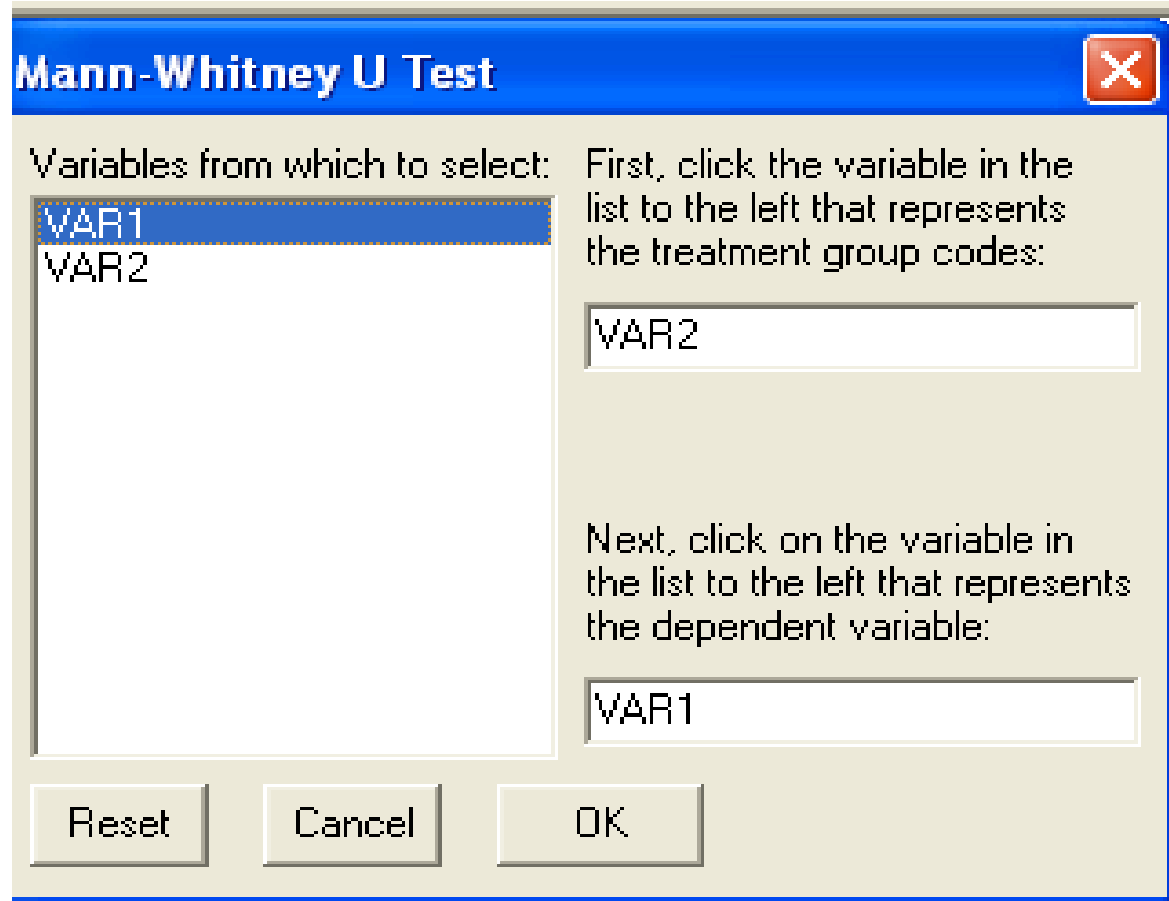
1 1 38.0 20 2 46 F

UNITS	VAR1	VAR2
CASE 1	38.0	1.0
2	26.0	1.0
3	29.0	1.0
4	41.0	1.0
	36.0	1.0
	31.0	1.0
	32.0	1.0
	30.0	1.0
9	35.0	1.0
1	33.0	1.0
11	45.0	2.0
12	28.0	2.0
13	27.0	2.0
14	38.0	2.0
15	40.0	2.0
16	42.0	2.0
17	39.0	2.0
18	39.0	2.0
19	34.0	2.0
20	45.0	2.0

1. Enter observations from both datasets under VAR1

2. Enter "1" for observations from first group and "2" for observations from second group in VAR2.

Getting Results



The image shows a 'Mann-Whitney U Test' dialog box. It has a blue title bar with the text 'Mann-Whitney U Test' and a red close button. The main area is divided into two sections. The left section, titled 'Variables from which to select:', contains a list box with 'VAR1' and 'VAR2'. 'VAR1' is selected. The right section contains two text boxes. The first is labeled 'First, click the variable in the list to the left that represents the treatment group codes:' and contains 'VAR2'. The second is labeled 'Next, click on the variable in the list to the left that represents the dependent variable:' and contains 'VAR1'. At the bottom are three buttons: 'Reset', 'Cancel', and 'OK'.

Mann-Whitney U Test

Variables from which to select:

VAR1
VAR2

First, click the variable in the list to the left that represents the treatment group codes:

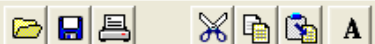
VAR2

Next, click on the variable in the list to the left that represents the dependent variable:

VAR1

Reset Cancel OK

Results

Results Window		
		
Return		
Mann-Whitney U Test		
See pages 116-127 in S. Siegel's Nonparametric Statistics for the Behavioral Sciences		
Score	Rank	Group
26.00	1.00	1
27.00	2.00	2
28.00	3.00	2
29.00	4.00	1
30.00	5.00	1
31.00	6.00	1
32.00	7.00	1
33.00	8.00	1
34.00	9.00	2
35.00	10.00	1
36.00	11.00	1
38.00	12.50	2
38.00	12.50	1
39.00	14.50	2
39.00	14.50	2
40.00	16.00	2
41.00	17.00	1
42.00	18.00	2

Results (cont'd)

Results Window

35.00	10.00	1
36.00	11.00	1
38.00	12.50	2
38.00	12.50	1
39.00	14.50	2
39.00	14.50	2
40.00	16.00	2
41.00	17.00	1
42.00	18.00	2
45.00	19.50	2
45.00	19.50	2

**For two tailed test
 $p \approx 0.076$, can't reject H_0**

Sum of Ranks in each Group

Group	Sum	No. in Group
1	81.50	10
2	128.50	10

No. of tied rank groups = 3

Statistic U = 26.5000

z Statistic (corrected for ties) = 1.7764, Prob. > z = 0.0378

z test is approximate. Use tables of exact probabilities in Siegel.

(Table J or K, pages 271-277)



Questions About Independent Proportions

- Test the hypothesis of equal proportions using the approximate z test.
- Test the hypothesis of expected frequencies using a chi-square test.



z Test for Independent Proportions

- We use the standard normal or **z** distribution as an approximation to binomial distribution for difference of proportions

- $$z = \frac{p_1 - p_2}{\sqrt{p(1-p)(1/n_1 + 1/n_2)}}$$

p is pooled or average proportion.

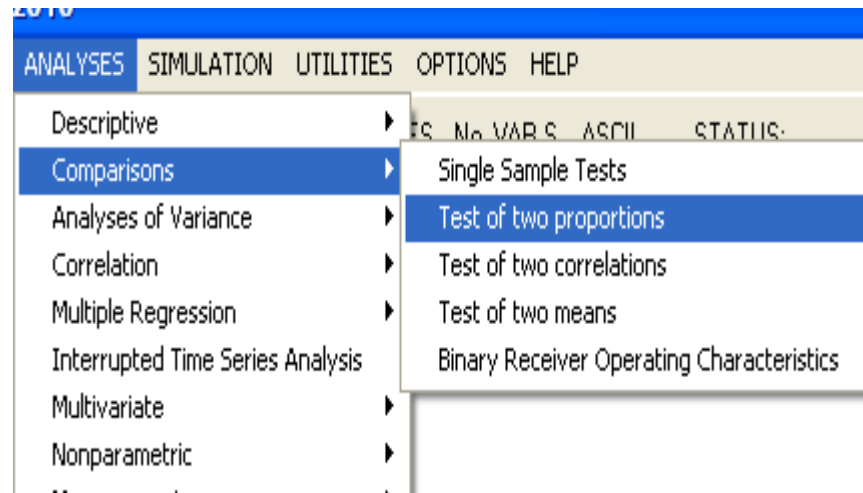


Example of Independent Proportions

		Screen		
		Yes	No	Total
Previous domestic violence (DV) training	Yes	175	27	202
	No	155	111	266

Basic & Clinical Biostatistics: Chapter 3

Openstat for z Approximation



Entering Data

Test of the Equality of Two Proportions

Data Entry By:

- ☒ Values Entered On This Form
- ☐ Values in the Data Grid

Assume:

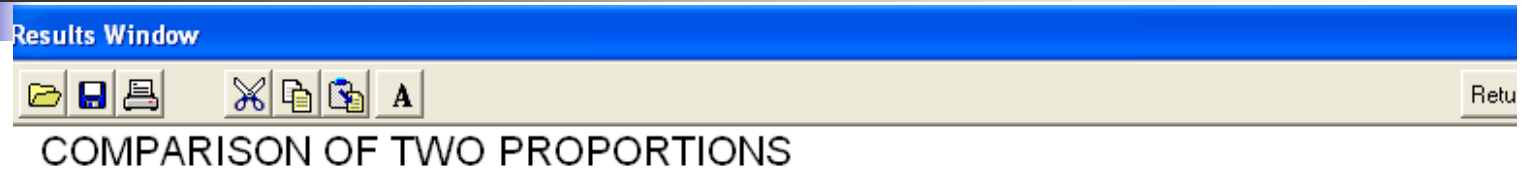
- ☒ Independent Proportions
- ☐ Dependent Proportions

Sample 1 freq.: 175 Sample Size: 202

Sample 2 freq.: 155 Sample Size: 111

Percent Confidence Interval: 95

Getting Results



--> Test for the Difference Between Two Independent Proportions

Sample 1: Frequency = 175 for 202 cases.

Sample 2: Frequency = 155 for 266 cases.

Proportion 1 = 0.8663 Proportion 2 = 0.5827 Difference = 0.2836

Standard Error of Difference = 0.0426

z test statistic = 6.6649 p-value = 0.0000 two-tailed

z value for confidence interval = 1.9600

Confidence Interval 95% = (0.2002, 0.3670)

Reject H_0 , there is a statistically significant difference in proportions of two groups of physicians.



Chi-Square for DV Example

We can answer two questions with one chi-square test using a two by two table.

- 1) Is there a difference in proportions of physicians who screen and who don't screen for DV?
- 2) Is there a relationship (dependency) between a physician's prior DV training & whether the physicians screen for DV?



Logic behind Chi-Square

- The frequencies in two by two table are considered fixed known and marginal frequencies.
- Assuming rows and columns are independent, we calculate the expected frequencies that can occur by chance alone.
- The Chi-Square test compares the observed frequencies with expected frequencies. For no relationship, expected and observed should be close.
- For a two by two table a chi-square statistic has one degree of freedom.



Assumptions of χ^2


- Sample size for two by two table is sufficiently large, total greater than 20.
- Expected value (not the original frequency) in any cell of two by two table is greater than 5.
- The data are independent.



What Happens if Assumptions are Violated?

- The **type II error rate β** increases if chi-square is conducted on a smaller sample size.
- Can use Yates' continuity correction for small samples.
- Can use Fisher's exact test for small samples.

DV Example in Openstat

 OpenStat Nov. 20, 2010

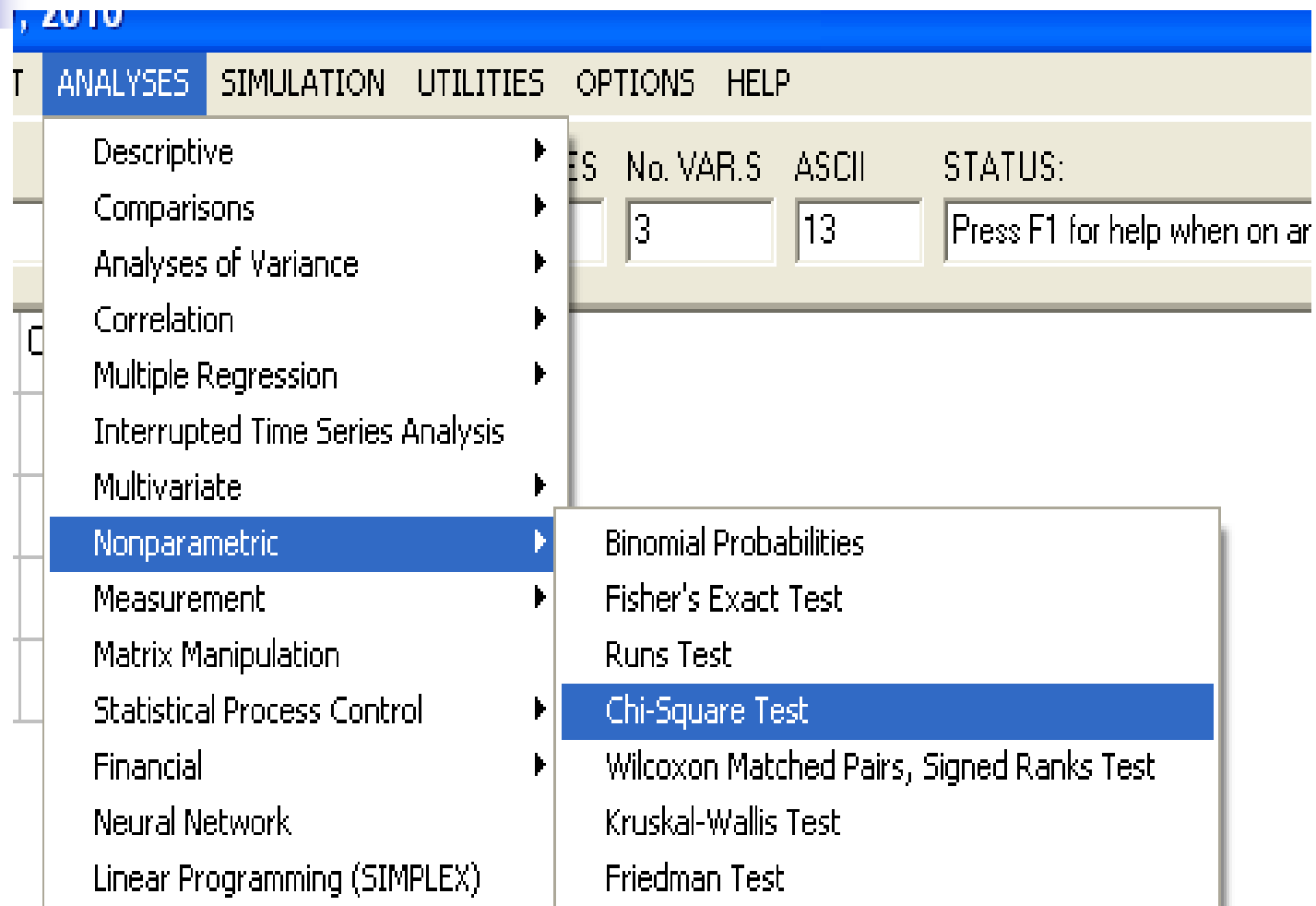
FILES VARIABLES EDIT ANALYSES SIMULATION UTILITIES OPTIONS HELP

ROW COL Cell Edit (Return to finish) N CASES No. VAR.S AS

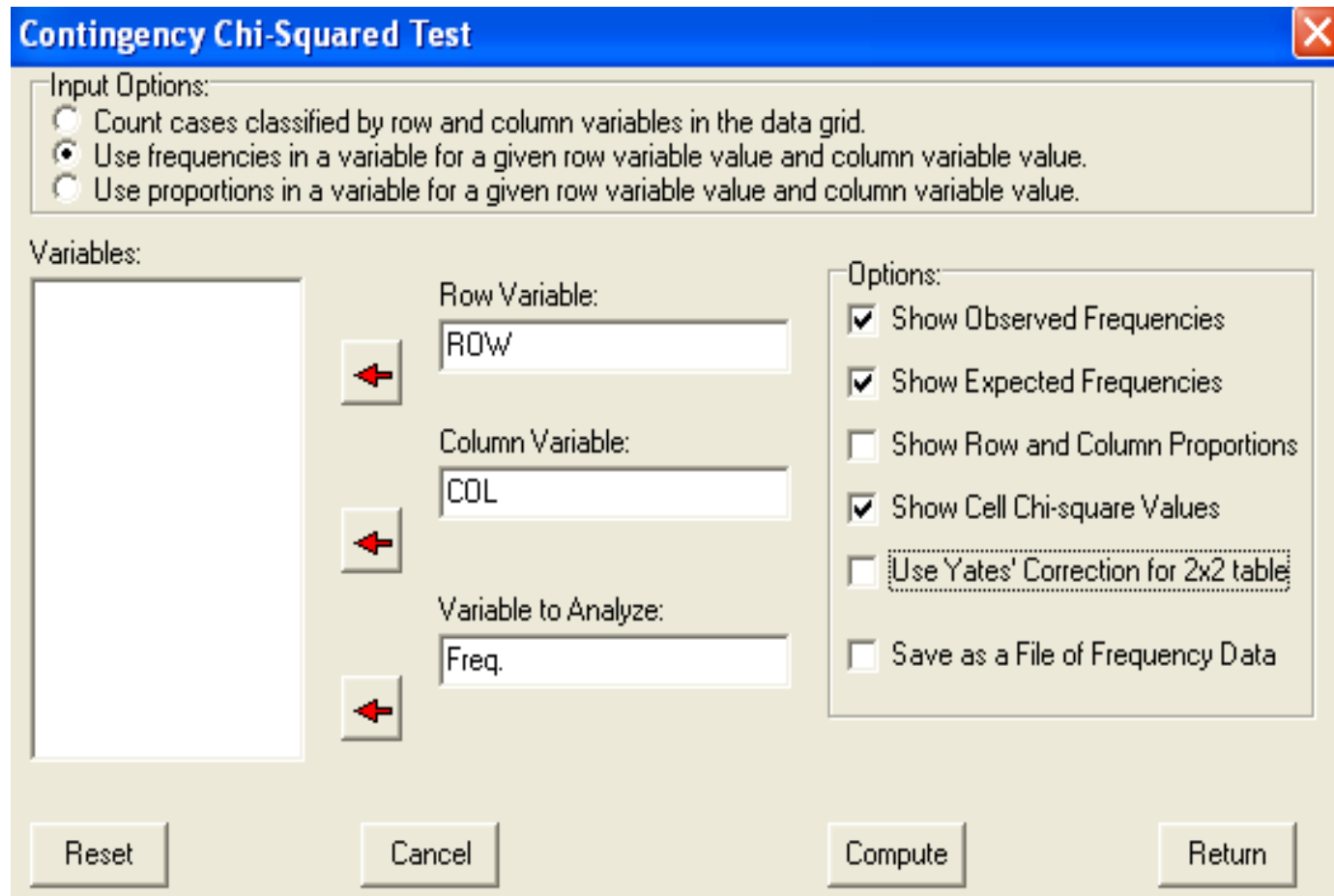
4 3 111.00 4 3 1:

0	ROW	COL	Freq.
1	1.00	1.00	175.00
2	1.00	2.00	27.00
3	2.00	1.00	155.00
4	2.00	2.00	111.00

Chi-Square in Openstat



Getting Results



The image shows a 'Contingency Chi-Squared Test' dialog box. It has a blue title bar with a close button. The main area is divided into three sections: 'Input Options', 'Variables', and 'Options'. The 'Input Options' section has three radio buttons. The 'Variables' section has a list box on the left and three input fields on the right, each with a red arrow button. The 'Options' section has five checkboxes. At the bottom are four buttons: 'Reset', 'Cancel', 'Compute', and 'Return'.

Contingency Chi-Squared Test

Input Options:

- ☐ Count cases classified by row and column variables in the data grid.
- ☒ Use frequencies in a variable for a given row variable value and column variable value.
- ☐ Use proportions in a variable for a given row variable value and column variable value.

Variables:

Row Variable: ROW

Column Variable: COL

Variable to Analyze: Freq.

Options:

- ☒ Show Observed Frequencies
- ☒ Show Expected Frequencies
- ☐ Show Row and Column Proportions
- ☒ Show Cell Chi-square Values
- ☐ Use Yates' Correction for 2x2 table
- ☐ Save as a File of Frequency Data

Reset Cancel Compute Return

Chi-Square Results

Results Window			
	COL. 1	COL. 2	Total
Row 1	175	27	202
Row 2	155	111	266
Total	330	138	468
EXPECTED FREQUENCIES			
	Expected Values		
	COL. 1	COL. 2	
Row 1	142.436	59.564	
Row 2	187.564	78.436	
CHI-SQUARED VALUE FOR CELLS			
	Chi-square Values		
	COL. 1	COL. 2	
Row 1	7.445	17.803	
Row 2	5.654	13.520	
Chi-square = 44.421 with D.F. = 1. Prob. > value = 0.000			

Reject H_0 , there is a difference in proportions of two groups of physicians.



Versatility of Chi-Square

- Distribution of a categorical variable in one sample can be compared with distribution of a categorical variable in another sample.
- Chi-Square can be used to compare an observed data with a theoretical distribution.
- Can be used to test difference between two counts.
- Can be extended to look at the effect of more than one input variable.

Fisher's Exact Test for Small Data Sets

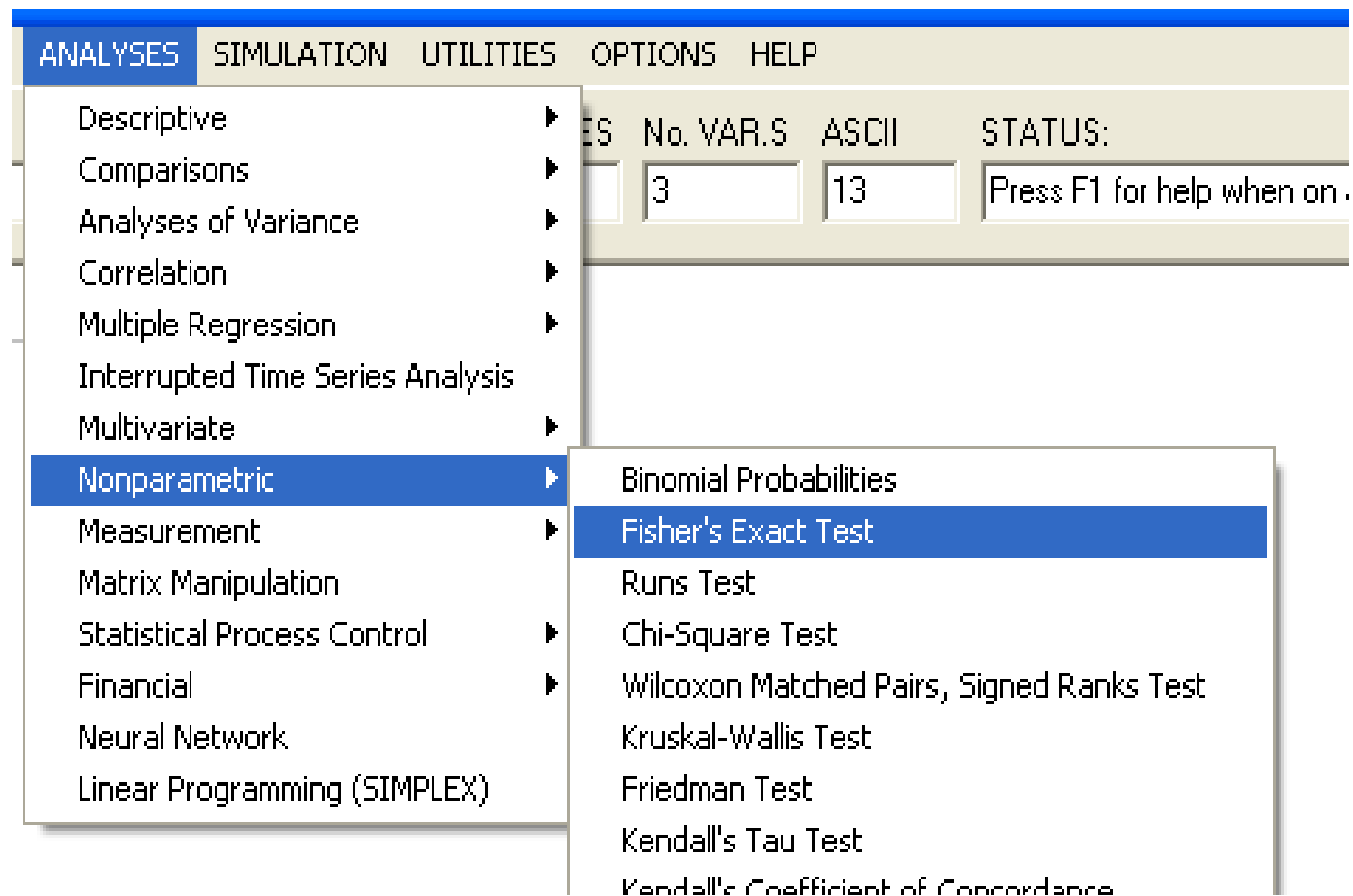
Deaths in six months after fractured neck of femur in a specialised orthopedic ward (A) and a general ward (B)

		Ward			
		A	B	Total	
Deaths	Yes	2	6	8	
	No	18	14	32	
Total		20	20	40	

Medical Statistics A Commonsense Approach A8

H_0 : There is no difference in deaths for two wards.

Fisher's Exact in Openstat



Entering Data

Fisher's Exact Test [X]

Input Options:

- ☐ Count cases classified by row and column variables in the data grid.
- ☐ Use frequencies in a variable for a given row variable value and column variable value.
- ☐ Use proportions in a variable for a given row variable value and column variable value.
- ☒ Enter Frequencies on this form.

	COL. 1	COL. 2
ROW 1	<input type="text" value="2"/>	<input type="text" value="6"/>
Row 2	<input type="text" value="18"/>	<input type="text" value="14"/>

Reset

Cancel

Compute

Return



Results

Fisher Exact Probability Test

Accumulating Values of the Hypergeometric Distribution

Contingency Table for Fisher Exact Test

Row	Column	
	1	2
1	2	6
2	18	14
Probability = 0.0958		

Cumulative Probability = 0.0958

Contingency Table for Fisher Exact Test

Row	Column	
	1	2
1	1	7
2	19	13
Probability = 0.0202		

Results Cont'd

Probability = 0.0202

Cumulative Probability = 0.1159

Contingency Table for Fisher Exact Test

Row	Column	
	1	2
1	0	8
2	20	12

Probability = 0.0016

**Two tailed $p \approx 0.23$
can't reject H_0**

Cumulative Probability = 0.1176

Tocher ratio computed: 0.295

A random value of 0.549 selected was greater than the Tocher value.

Conclusion: Accept the null Hypothesis

Chi-squared = 2.500 with 1 d.f. and prob. > chi-square = 0.1138



Summary of Two Groups Methods

Nature of problem	Test
Interval & normal	Two independent sample t
Ordinal or interval, non normal	Mann-Whitney U
Independent Proportions	Z approximation
Independent proportions large sample size	Chi-Square
Independent Proportions small sample size	Fisher's Exact



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Questions/Comments

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Next lecture's highlights

Study Designs, Odds Ratio, Relative Risk