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Statistics in Evidence Based Medicine

Lecture 6: Research Questions for One Group

Rizwana Rehman, PhD

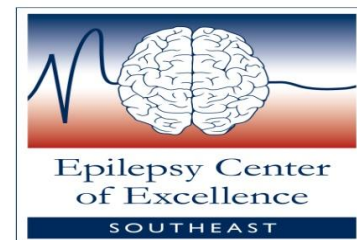
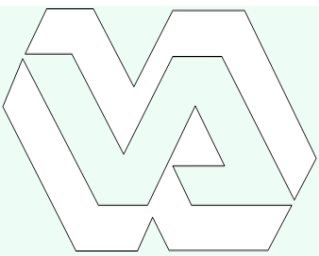
Regional Statistician

Southeast Epilepsy Center of Excellence

Durham VA Medical Center, Durham NC

Rizwana.Rehman@va.gov

(919)286-0411 ext: 5024





Review

- C.I provides information about statistical significance as well as the direction and strength of the effect.
- Hypothesis testing using p value allows for a rapid decision for statistical significance, however this is an overly simplistic approach.
- The two statistical concepts are complimentary.



Overview

- Does our computed mean differ from the typical?
- Is mean difference in variable of interest for before/after study statistically significant?
- How can we test for normality in Openstat?
- Does our computed proportion differ from the typical?
- Is difference in proportions for our before and after study statistically significant?



One Mean with Normal Data

- Is our computed mean statistically different from the typical?
- We use t test for quantitative data under the following assumptions.
 - Our data are normally distributed.
 - Observations are independent of each other.
- $t = \frac{\bar{X} - \mu}{sd / \sqrt{n}}$ with $n - 1$ d.f.



Why Assumptions Matter?

- When assumptions are not met, type I error rate α increases.
 - If we use t test on highly skewed data with less than 30 observations, then CI 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.



How to Check for Assumptions?

- Normality

- For large data sets normality does not matter
- For small data
 - Prior knowledge of variable
 - Eyeball your data
 - Can run a normality test

- Independence

- Decide yourself



One Mean Problem

Estimation of plasma calcium concentration in 18 patients (ages 20-44) with Everley's syndrome gave a mean of 3.02mmol/l, with standard deviation 1.1mmol/l.

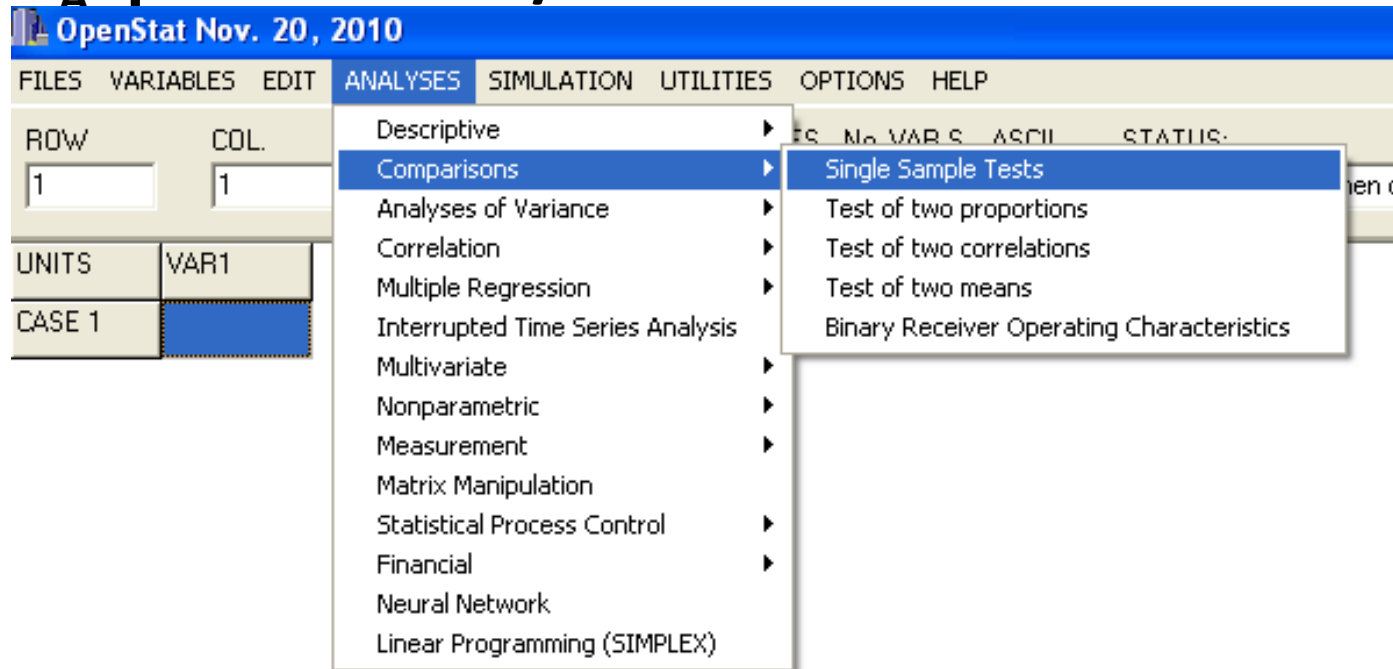
previous studies showed that the mean was commonly close to 2.5 mmol/l in healthy people aged 20-44. Assume that the data are plausibly normally distributed. Is the mean in these patients abnormally high?

Openstat for Everley's Syndrome Example

<http://www.statprograms4u.com/>

$H_0: \mu = 2.5 \text{ mmol/l}$

$H_A: \mu \neq 2.5 \text{ mmol/l}$



Entering Data 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	ASCII	STATUS:
1	1		0	1		Press F1 for help when on any menu item

UNITS	VAR1
CASE 1	

One Sample Tests

Enter Values From:

☒ This Form. ☐ The Data Grid.

Single Sample Test Of:

☒ Sample Mean

☐ Sample Proportion

☐ Sample Correlation

☐ Sample Variance

Sample Statistic: 3.2

Population Parameter: 2.5

Sample Size: 18

Sample Std. Deviation: 1.1

Confidence Level (%): 95

Reset Cancel Continue

Results from OpenStat

Results Window



ANALYSIS OF A SAMPLE MEAN

Sample Mean = 3.200

Population Mean = 2.500

Sample Size = 18

Standard error of Mean = 0.259

t test statistic = 2.700 with probability 0.015

t value required for rejection = 2.110

Confidence Interval = (2.653, 3.747)

Reject H_0 , mean in this sample is unusually statistically high



Mean difference for Before and After Study for Normal Data

- The test is derived from the single sample t test, using the following assumptions.
 - The data are quantitative.
 - The distribution of the differences (not the original data) is plausibly normal.
 - The differences are independent of each other.

$$t = \frac{\bar{d} - \delta}{\frac{sd_d}{\sqrt{n}}} \text{ with } n - 1 \text{ d.f.}$$



Example of Normal Paired Data

FEV₁ from five asthmatics, before and after use of a bronchodilator (liters/sec) with normally distributed data

Before	After
1.5	1.7
1.7	1.9
2.1	2.2
1.6	1.9
2.4	2.4

Medical Statistics A Commonsense Approach: Appendix I

$$H_0: \mu_1 - \mu_2 = 0$$

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

Paired t Test in OpenStat

The screenshot shows the OpenStat software interface. The title bar reads "OpenStat Nov. 20, 2010". The menu bar includes "FILES", "VARIABLES", "EDIT", "ANALYSES", "SIMULATION", "UTILITIES", "OPTIONS", and "HELP". The "ANALYSES" menu is open, displaying a list of statistical tests. The "Comparisons" option is highlighted, which has opened a sub-menu. In this sub-menu, "Test of two means" is highlighted. The background shows a data table with columns "ROW", "COL.", "UNITS", and "VAR1".

ROW	COL.	UNITS	VAR1
5	2	CASE 1	1.5
2			1.7
3			2.1
4			1.6
5			2.4

ANALYSES Menu:

- Descriptive
- Comparisons**
 - Single Sample Tests
 - Test of two proportions
 - Test of two correlations
 - Test of two means**
 - Binary Receiver Operating Characteristics
- Analyses of Variance
- Correlation
- Multiple Regression
- Interrupted Time Series Analysis
- Multivariate
- Nonparametric
- Measurement
- Matrix Manipulation
- Statistical Process Control
- Financial
- Neural Network
- Linear Programming (SIMPLEX)

Entering Data for Analysis

OpenStat Nov. 20, 2010

FILES VARIABLES EDIT ANALYSES SIMULATION UTILITIES OPTIONS HELP

ROW COL Cell Edit (Return)

ROWS	VAR1	VAR2
BASE 1	1.5	1.7
	1.7	1.9
	2.1	2.2
	1.6	1.9
	2.4	2.4

Comparison of Two Sample Means

Data Entry By:

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

Assume:

- ☐ Independent Scores
☒ Correlated Scores

Available Variables:

VAR1
VAR2

First Variable:

VAR1

Second Variable:

VAR2

Directions: For independent group data, first click the variable to be analyzed and then click the variable that contains the group coding. Enter the code value used for group one and for group two.

For dependent groups, it is assumed the data for each pair of scores are entered in two variables for each row of data in a data file. Click on the names of the two variables in the data grid.

Of course, if you are not

Add Variable

FILE: Temporary.TEX

Percent Confidence Interval:

95

Reset

Cancel

Continue

Analysis from OpenStat

Results Window



Return

COMPARISON OF TWO MEANS

Variable	Mean	Variance	Std.Dev.	S.E.Mean	N
VAR1	1.86	0.14	0.38	0.17	5
VAR2	2.02	0.08	0.28	0.12	5

Assuming dependent samples, $t = -3.138$ with probability = 0.0349 and 4 degrees of freedom

Correlation between VAR1 and VAR2 = 0.986

Difference = -0.16 and Standard Error of difference = 0.05

Confidence interval = (-0.30, -0.02)

t for test of equal variances = 3.307 with probability = 0.0455

NOTE: t -tests are two-tailed tests.

The difference in means is statistically significant



Dependent Non-Normal Data

- Use Wilcoxon test under the following assumptions.
 - The paired differences are independent.
 - The differences come from a symmetrical distribution.
- Wilcoxon test can be used for mean & median.
- As powerful as t test.
- For $n \geq 10$, we have a formula, for $n < 10$, use tables.



Wilcoxon Test for $n \geq 10$

- Find the absolute differences between paired observations X_a and X_b . Omit zeros if any.
- Rank the absolute differences breaking for ties.
- Attach positive sign if $X_b > X_a$ and negative sign if $X_b < X_a$.
- Sum positive and negative values; there will be two ranks, positive rank and negative rank.
- The smaller of two is denoted by T .

$$z = \frac{|T - n(n+1)/4|}{\sqrt{n(n+1)(2n+1)/24}}$$



Fetal Movements Before and After Chorionic Villus Sampling

Statistics at Square One: Chapter 10

Patient no (1)	Before (2)	After (3)	Difference (4)
1	25	18	7
2	24	27	-3
3	28	25	3
4	15	20	-5
5	20	17	3
6	23	24	-1
7	21	24	-3
8	20	22	-2
9	20	19	1
10	27	19	8

**H_0 : Chorionic villus sampling does not alter the
percentage of time a fetus spends in moving**

Dot Plot of Difference

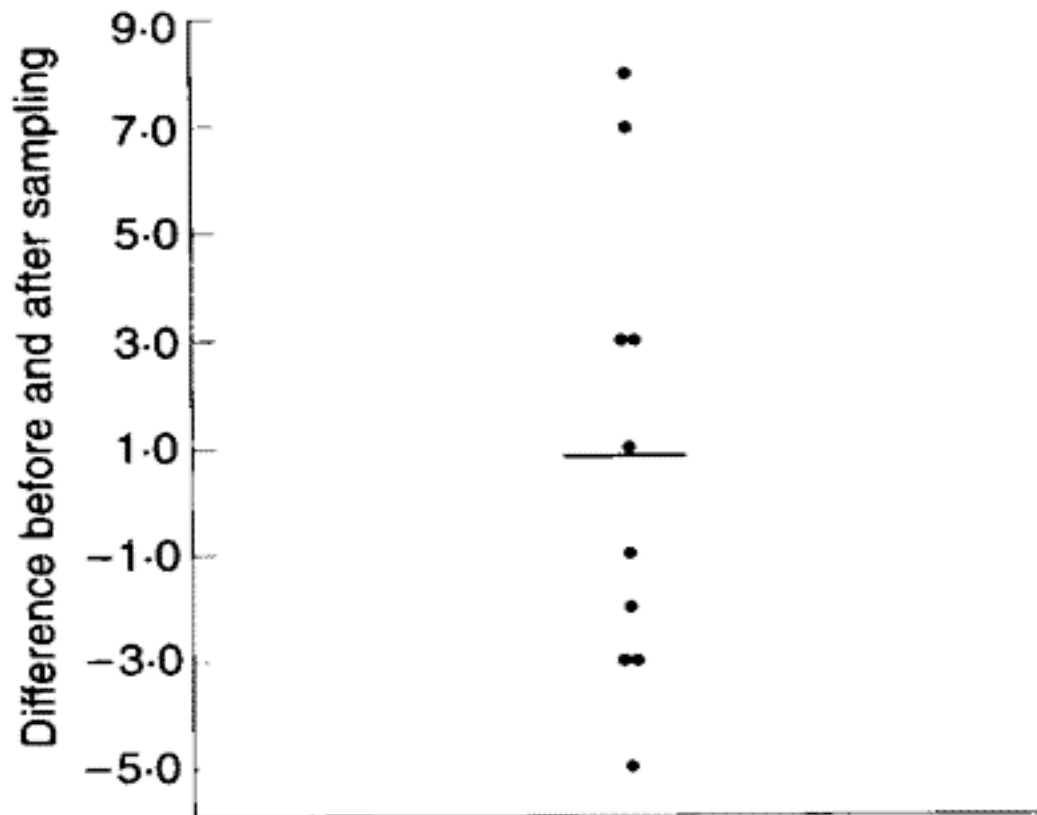
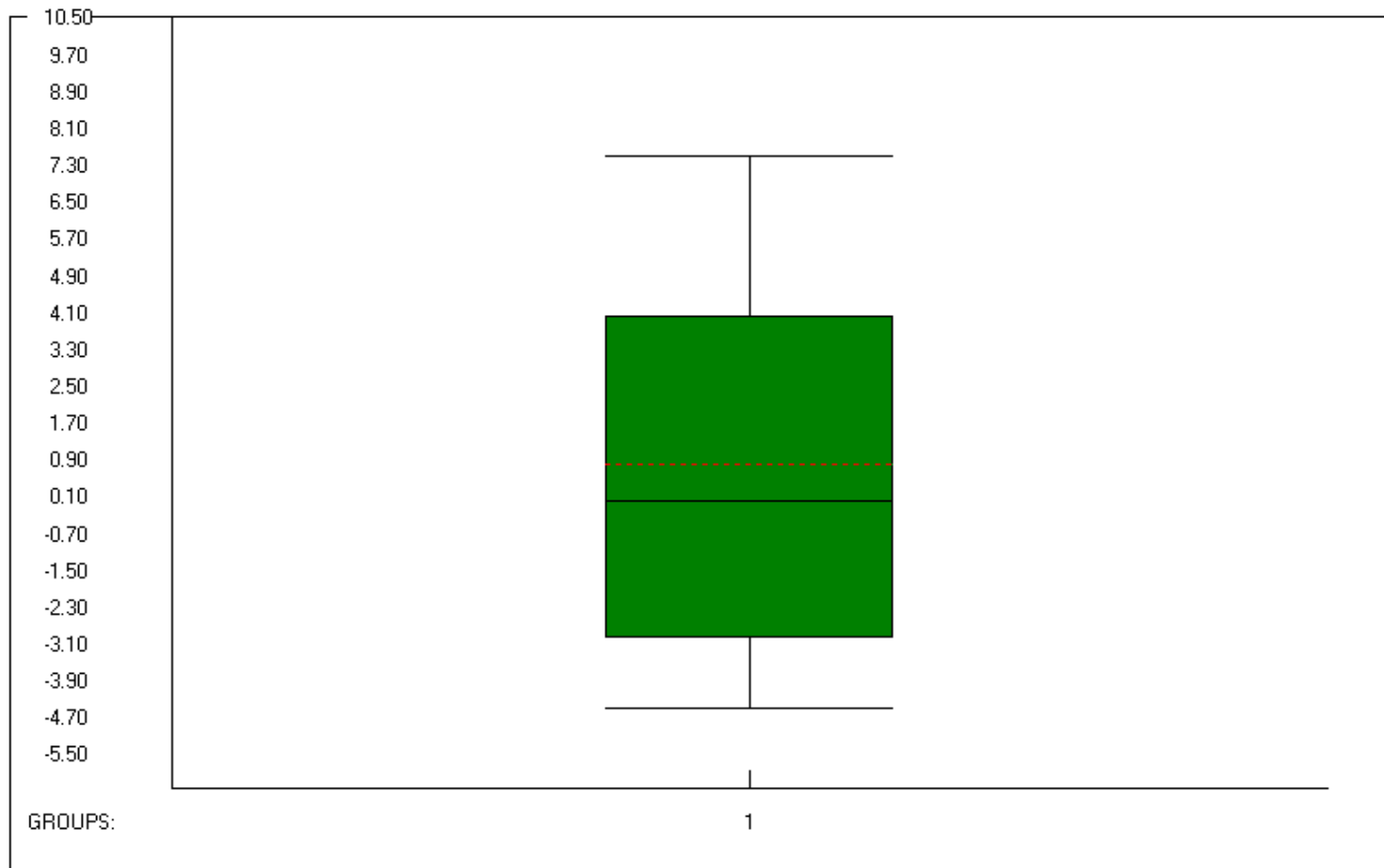


Figure 10.1 Plot of differences in fetal movement with mean value

Box Plot of Difference in OpenStat

BOXPLOT FOR : Temporary.TEX

RED: mean, BLACK: median, BOX: 25th to 75th percentile, WISKERS: 10th and 90th percentile



Comparison to Normal Distribution

nStat Nov. 20, 2010

/VARIABLES		EDIT	ANALYSES	SIMULATION	UTILITIES	OPTIONS	HELP
COL.			Descriptive				Central Tendency, Variability
	1		Comparisons				Frequencies
			Analyses of Variance				Cross Tabulation
			Correlation				Breakdown
			Multiple Regression				Normality Tests
			Interrupted Time Series Analysis				X Versus Y Plot
			Multivariate				Group (integer) Frequency Charts
			Nonparametric				Repeated Measures Bubble Plot
			Measurement				QQ or PP Plot
			Matrix Manipulation				Smooth Data by Averaging
			Statistical Process Control				Compare Two Distributions
			Financial				Compare Observed to Theoretical Distribution
			Neural Network				Three Dimension Rotation
			Linear Programming (SIMPLEX)				Box Plots
							X versus Multiple Y Plot
							Stem and Leaf Plot
							Multiple Group X versus Y Plot

COL.	Difference
	7.0
	-3.0
	3.0
	-5.0
	3.0
	-1.0
	-3.0
	-2.0
	1.0
	8.0

Comparison to Normal Distribution

1

DIRECTIONS:

1. Select the type of theoretical distribution desired.
2. Click the checkbox for printer output if desired.

Cumulative Distributions:

- ☐ Binomial
- ☒ Normal
- ☐ Chi-square
- ☐ Student t
- ☐ F
- ☐ Poisson
- ☐ Beta

Parameters:

X value:

Mean:

Std. Dev.:

Prob.:

1-Prob.:

Status:

Plot Type:

- ☒ 1. Separate observed and theoretic cumulative distributions.
- ☐ 2. Combined observed and theoretic cumulative distributions.
- ☐ 3. Combined observed and theoretic distributions.

☐ Show printer output

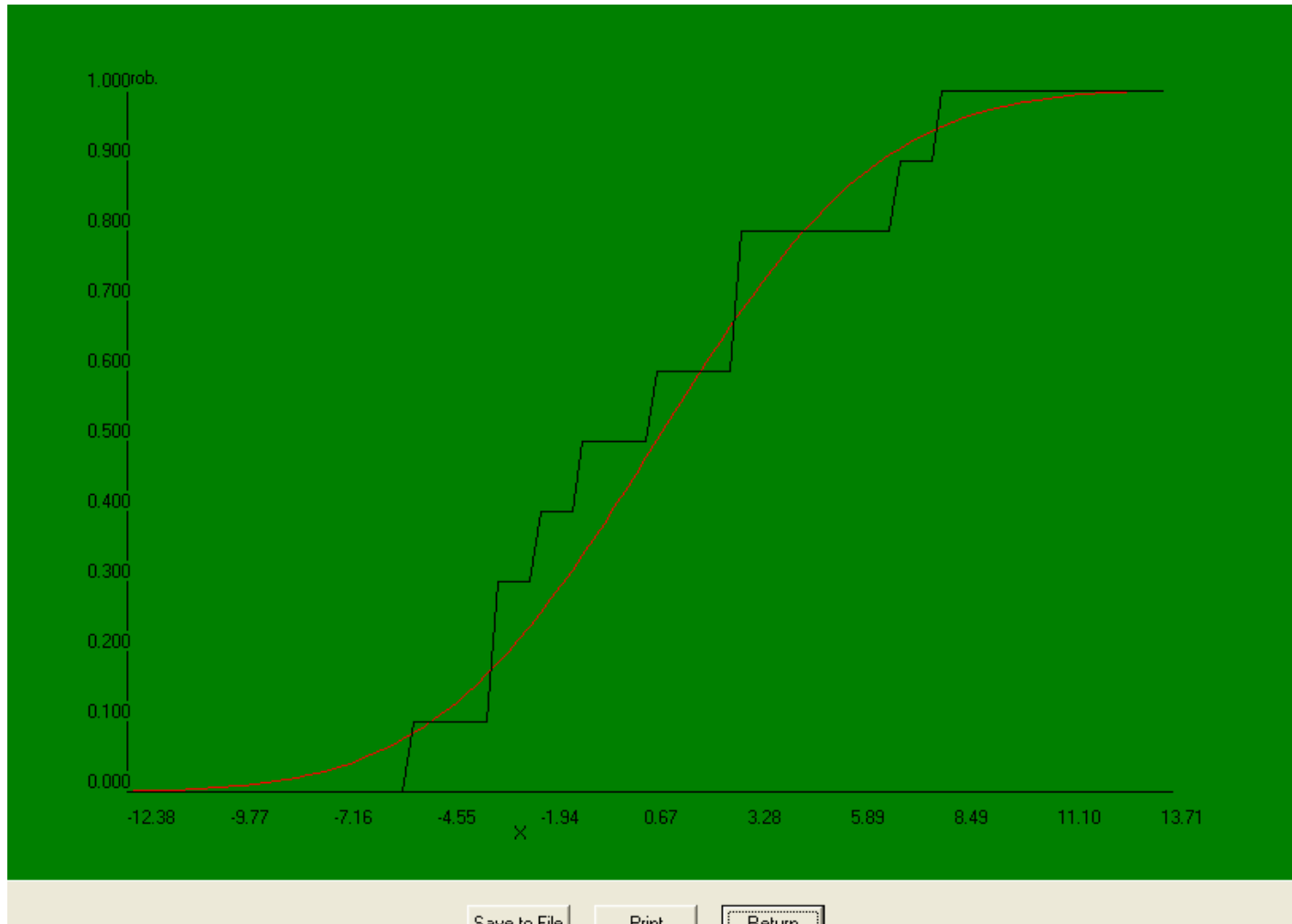
Click the name of your variable:

Difference

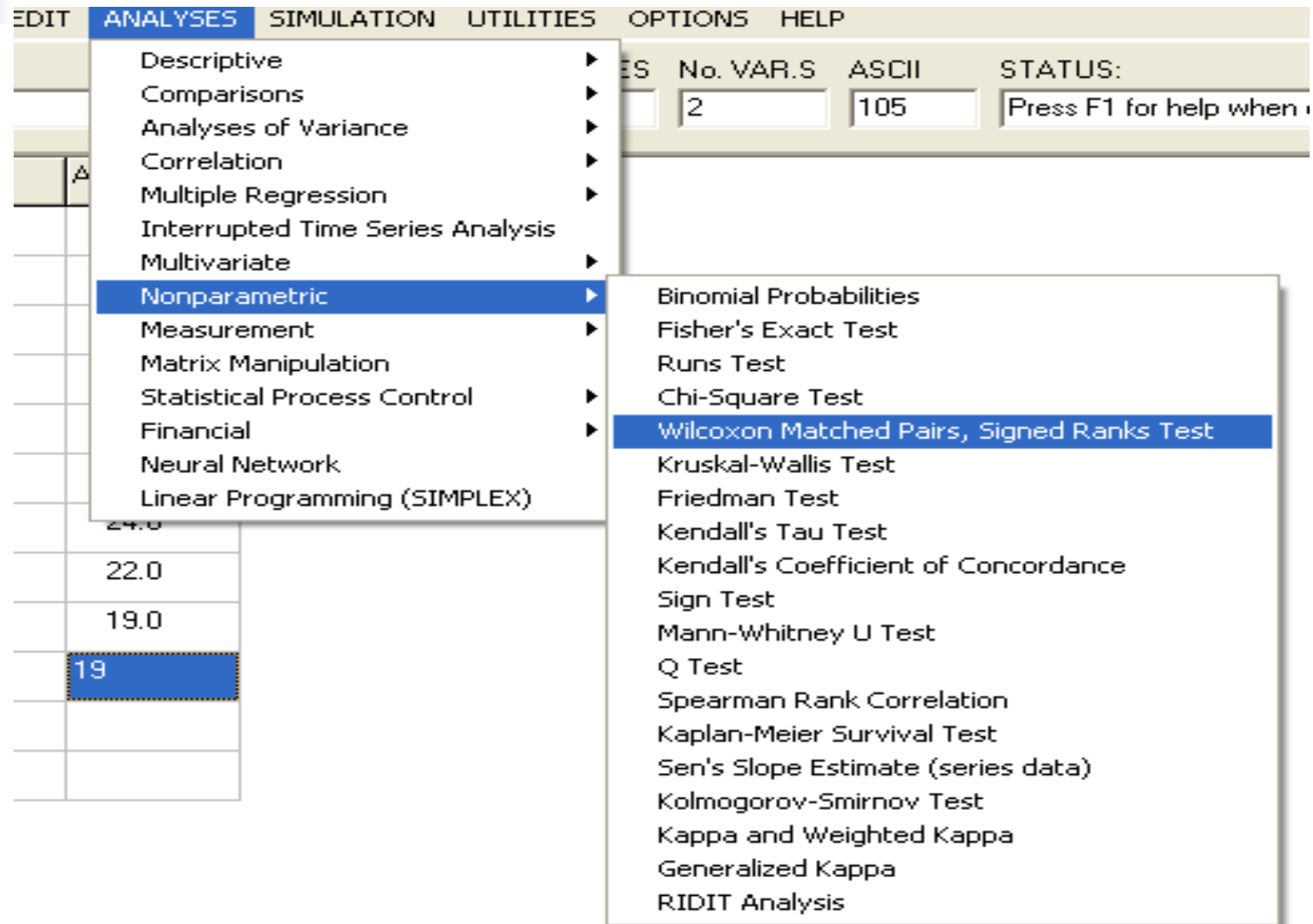
Compute **Exit**

Variable =

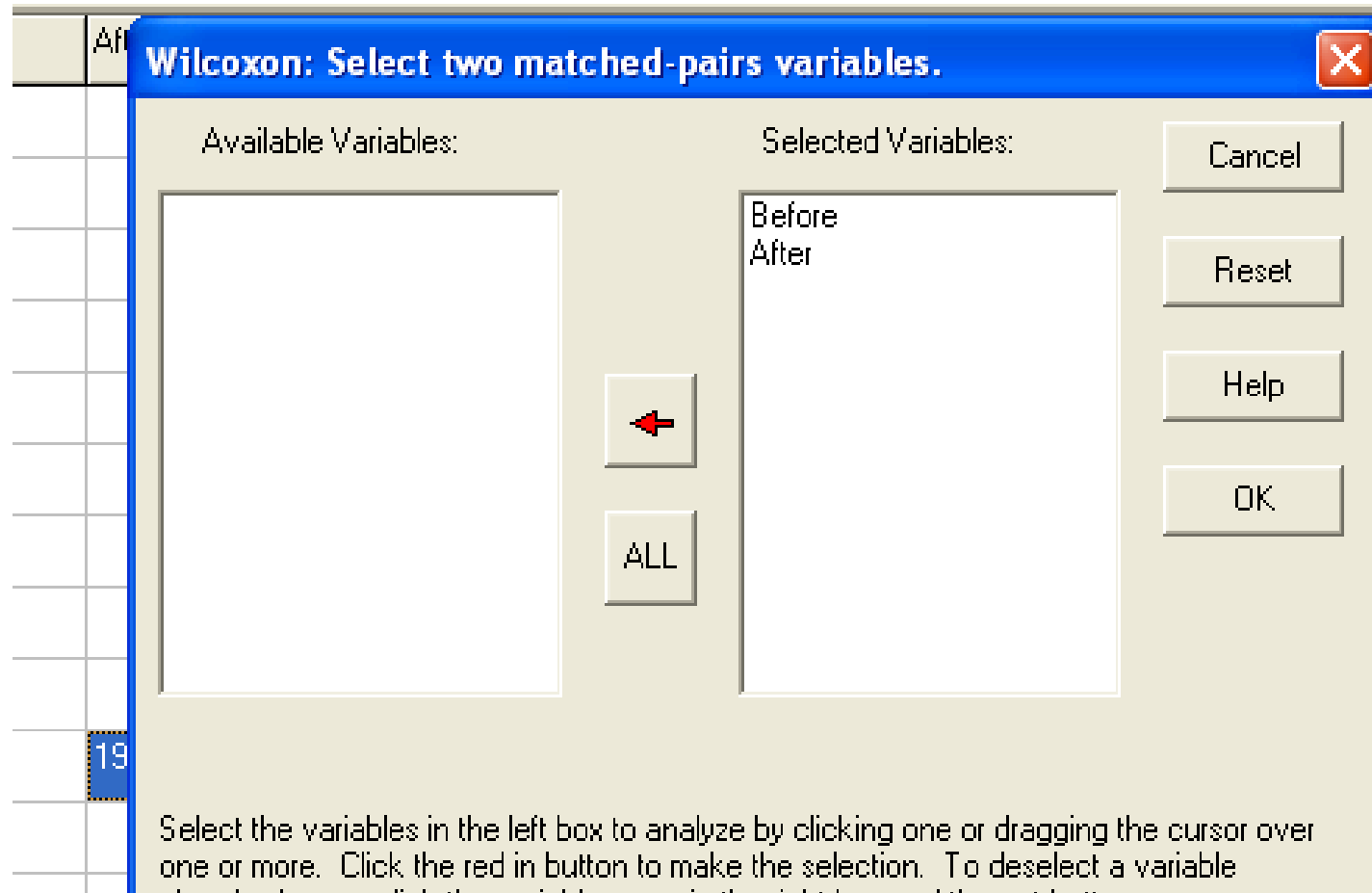
Comparison



Wilcoxon's Test in OpenStat

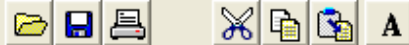


Selecting Variables for Analysis



Results of Wilcoxon's test

Results Window



The Wilcoxon Matched-Pairs Signed-Ranks Test

See pages 75-83 in S. Siegel's Nonparametric Statistics for the Social Sciences

Ordered Cases with cases having 0 differences eliminated:

Number of cases with absolute differences greater than 0 = 10

CASE	Before	After	Difference	Signed Rank
------	--------	-------	------------	-------------

6	23.00	24.00	-1.00	-1.50
9	20.00	19.00	1.00	1.50
8	20.00	22.00	-2.00	-3.00
2	24.00	27.00	-3.00	-5.50
7	21.00	24.00	-3.00	-5.50
3	28.00	25.00	3.00	5.50
5	20.00	17.00	3.00	5.50
4	15.00	20.00	-5.00	-8.00
1	25.00	18.00	7.00	9.00
10	27.00	19.00	8.00	10.00

We conclude that villus sampling doesn't alter the fetal movement.

Smaller sum of ranks (T) = 23.50

Approximately normal z for test statistic T = 0.408

Probability (1-tailed) of greater z = 0.3417

NOTE: For N < 25 use table values for Wilcoxon Test



Sign Test for Asymmetrical Data

- Can be used for matched pairs of sample data.
- Can be used for a claim about population median against a hypothesized value m .
- Less powerful than Wilcoxon test.
- OpenStat provides Sign test for paired data.



Pronethalol for the Prevention of Angina Pectoris

an introduction to medical statistics by Martin Bland

# of Attacks on Placebo	# of Attacks on Pronethalol	Difference	Sign of Difference
71	29	42	+
323	348	-25	-
8	1	7	+
14	7	7	+
23	16	7	+
34	25	9	+
79	65	14	+
60	41	19	+
2	0	2	+
3	0	3	+
17	15	2	+
7	2	5	+

H_0 : Placebo and Pronethalol have the same effect on angina

Selecting Sign Test in Openstat

The screenshot shows the OpenStat software interface. The 'ANALYSES' menu is open, and the 'Sign Test' option is highlighted. The data table on the left contains the following values:

ROW	COL	VAR1	VAR2
1	2	71.0	
2		323.0	
3		8.0	
4		14.0	
5		23.0	
6		34.0	
7		79.0	
8		60.0	41.0
9		2.0	0.0
10		3.0	0.0
11		17.0	15.0
12		7.0	2.0

The 'Sign Test' option is selected in the 'ANALYSES' menu. The status bar at the bottom shows 'Add Variable' and 'FILE: Temporary.TEX'.

Selecting Variables for Analysis

The screenshot shows the OpenStat software interface. The main window displays a data table with columns UNITS, VAR1, and VAR2. The data is as follows:

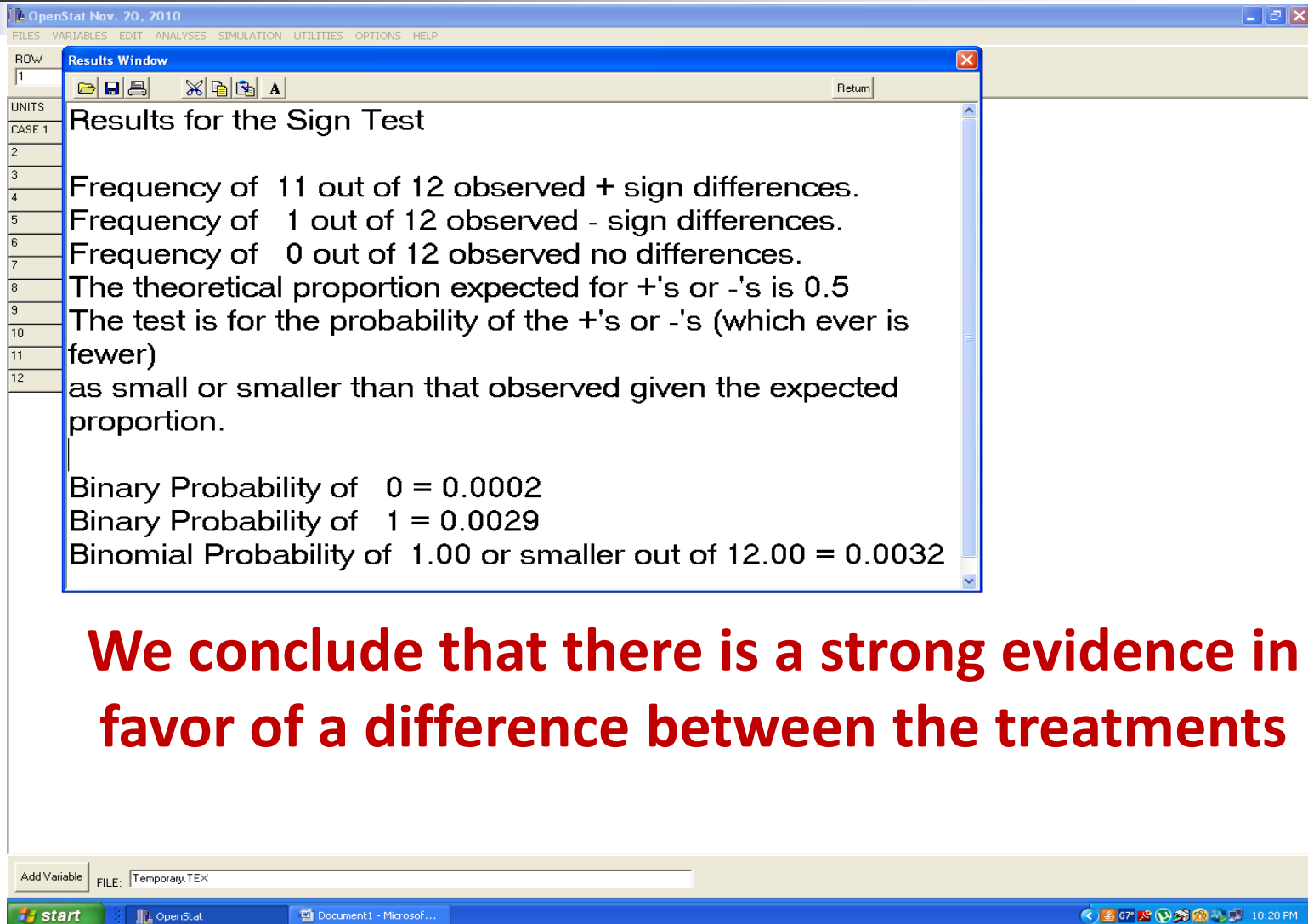
UNITS	VAR1	VAR2
CASE 1	71.0	
2	323.0	
3	8.0	
4	14.0	
5	23.0	
6	34.0	
7	79.0	
8	60.0	
9	2.0	
10	3.0	
11	17.0	
12	7.0	

A dialog box titled "Sign Test: Select Two Matched Pair Variables" is open. It contains two lists: "Available Variables" and "Selected Variables". The "Selected Variables" list contains VAR1 and VAR2. The dialog box also includes buttons for Cancel, Reset, Help, and OK. A red arrow button is visible between the two lists. Below the lists, there is a text box with the following instructions:

Select the variables in the left box to analyze by clicking one or dragging the cursor over one or more. Click the red in button to make the selection. To deselect a variable already chosen, click the variable name in the right box and the out button.

The OpenStat window title bar shows "OpenStat Nov. 20, 2010". The menu bar includes FILES, VARIABLES, EDIT, ANALYSES, SIMULATION, UTILITIES, OPTIONS, and HELP. The status bar at the bottom shows the Windows taskbar with the start button, OpenStat, and Document1 - Microsoft... The system clock shows 10:27 PM.

Results



The screenshot shows the OpenStat software interface. The main window is titled "Results Window" and displays the results for a Sign Test. The results are as follows:

Results for the Sign Test

- Frequency of 11 out of 12 observed + sign differences.
- Frequency of 1 out of 12 observed - sign differences.
- Frequency of 0 out of 12 observed no differences.
- The theoretical proportion expected for +'s or -'s is 0.5
- The test is for the probability of the +'s or -'s (which ever is fewer)
as small or smaller than that observed given the expected proportion.

Binary Probability of 0 = 0.0002
Binary Probability of 1 = 0.0029
Binomial Probability of 1.00 or smaller out of 12.00 = 0.0032

We conclude that there is a strong evidence in favor of a difference between the treatments

The bottom of the screenshot shows the Windows taskbar with the Start button, OpenStat icon, and a Microsoft Word document titled "Document1 - Microsof...". The system clock shows 10:28 PM.

Tests of Normality in OpenStat

OpenStat Nov. 20, 2010

FILES VARIABLES EDIT ANALYSES SIMULATION UTILITIES OPTIONS HELP

ROW COL.

25 1

UNITS	VAR1
CASE 1	1.0
2	1.0
3	2.0
4	2.0
5	3.0
6	3.0
7	4.0
8	5.0
9	5.0
10	6.0
11	7.0
12	7.0
13	8.0
14	10.0
15	20.0
16	22.0
17	25.0
18	27.0
19	33.0
20	40.0

Descriptive

- Central Tendency, Variability
- Frequencies
- Cross Tabulation
- Breakdown
- Normality Tests
- X Versus Y Plot
- Group (integer) Frequency Charts
- Repeated Measures Bubble Plot
- QQ or PP Plot
- Smooth Data by Averaging
- Compare Two Distributions
- Compare Observed to Theoretical Distribution
- Three Dimension Rotation
- Box Plots
- X versus Multiple Y Plot
- Stem and Leaf Plot
- Multiple Group X versus Y Plot

Comparisons

Analyses of Variance

Correlation

Multiple Regression

Interrupted Time Series Analysis

Multivariate

Nonparametric

Measurement

Matrix Manipulation

Statistical Process Control

Financial

Neural Network

Linear Programming (SIMPLEX)

H_0 : Data are normally distributed.

Lilliefors and Shapiro-Wilk W tests

NITS	VAR1
ASE 1	1.0
	1.0
	2.0
	2.0
	3.0
	3.0
	4.0
	5.0
	5.0
0	6.0
1	7.0
2	7.0
3	8.0
4	10.0
5	20.0
6	22.0
7	25.0

Tests of Normality

Variables

Test Normality of:
VAR1

Shapiro-Wilks Results:

W = 0.8117
Probability = 0.0004

Lilliefors Test Results:

Skewness = 1.272
Kurtosis = 0.737
Test Statistic = 0.245
Conclude: Strong evidence against normalit

Cancel Reset Print **Compute** Return



Problems with Normality Tests

- Small samples almost always pass a normality test.
- With large samples, the test may be significant but results of t test are still valid.
- Decisions about using parametric vs. nonparametric tests should be made to cover an entire series of analyses.



Questions about One Proportion

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

- $$Z = \frac{p - \pi}{\sqrt{\frac{\pi(1 - \pi)}{n}}}$$



Example of a Proportion

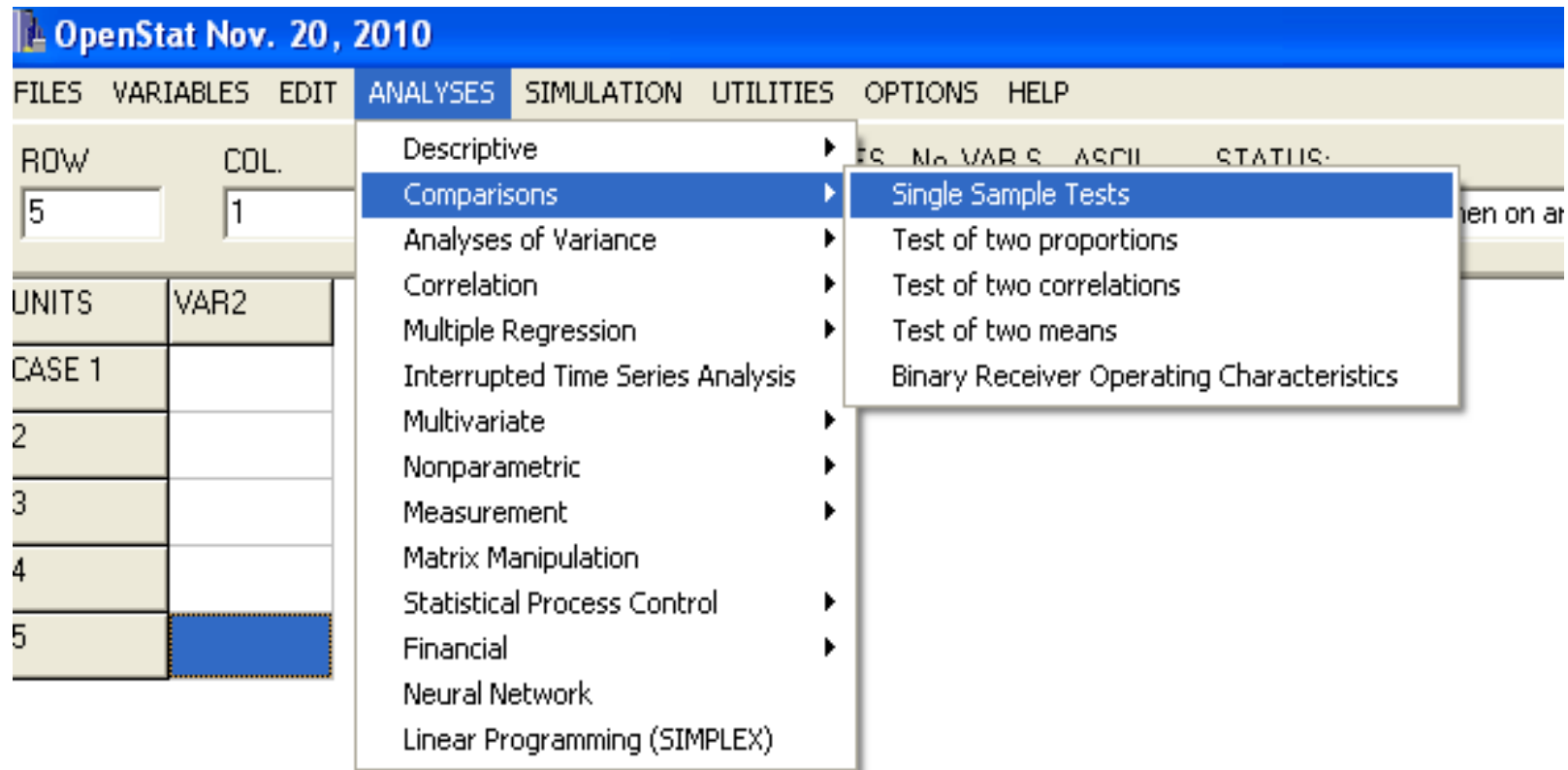
Frey and colleagues wanted to examine the efficacy of different dilutions of smallpox vaccine. The group that received the 1:10 dilution ($n=340$) had a success rate of 97.1%. Investigators wanted to know if this success rate was greater than 95%.

Basic & Clinical Biostatistics: Chapter 5

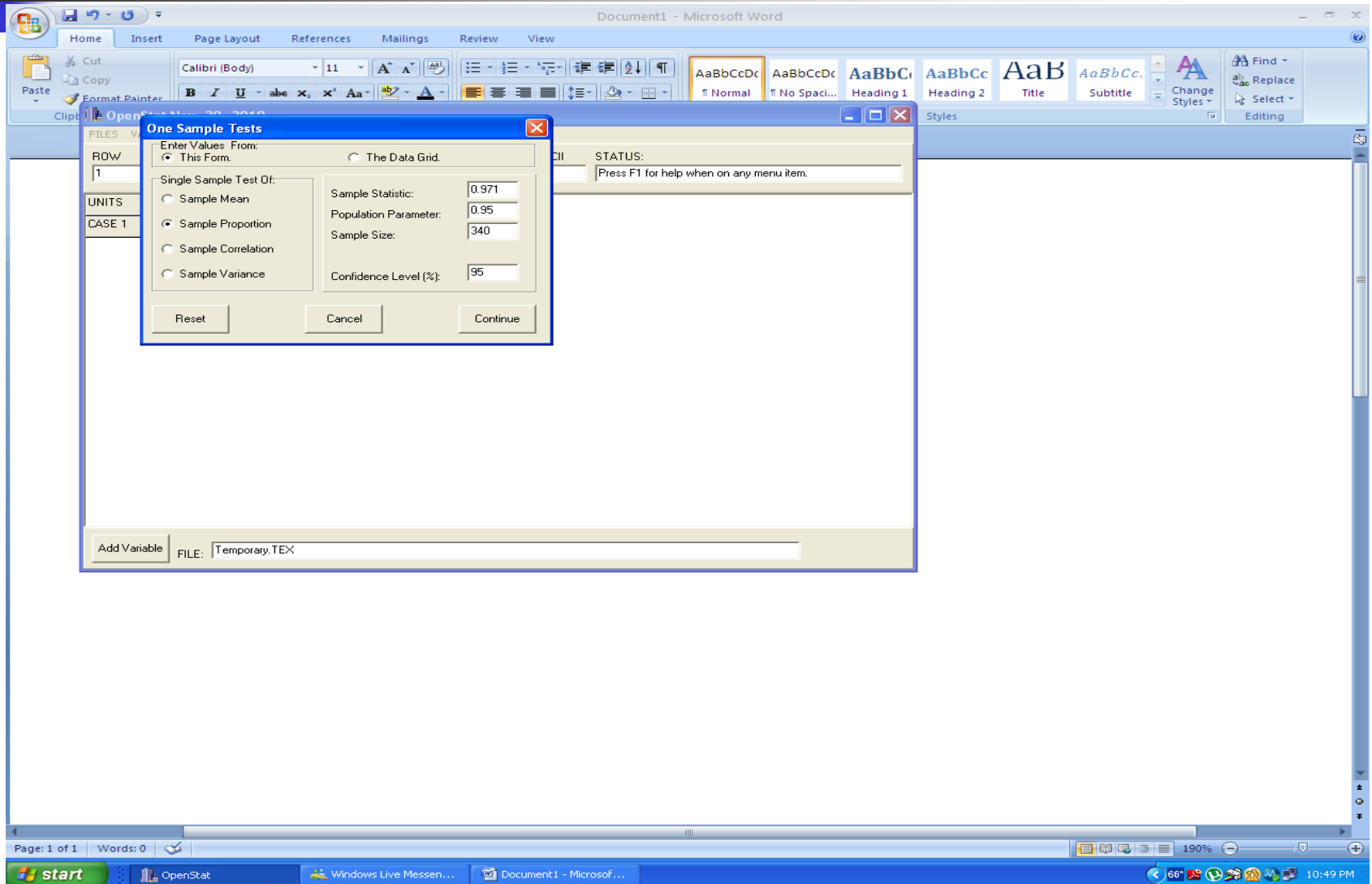
$$H_0: \pi \leq 0.95$$

$$H_A: \pi > 0.95$$

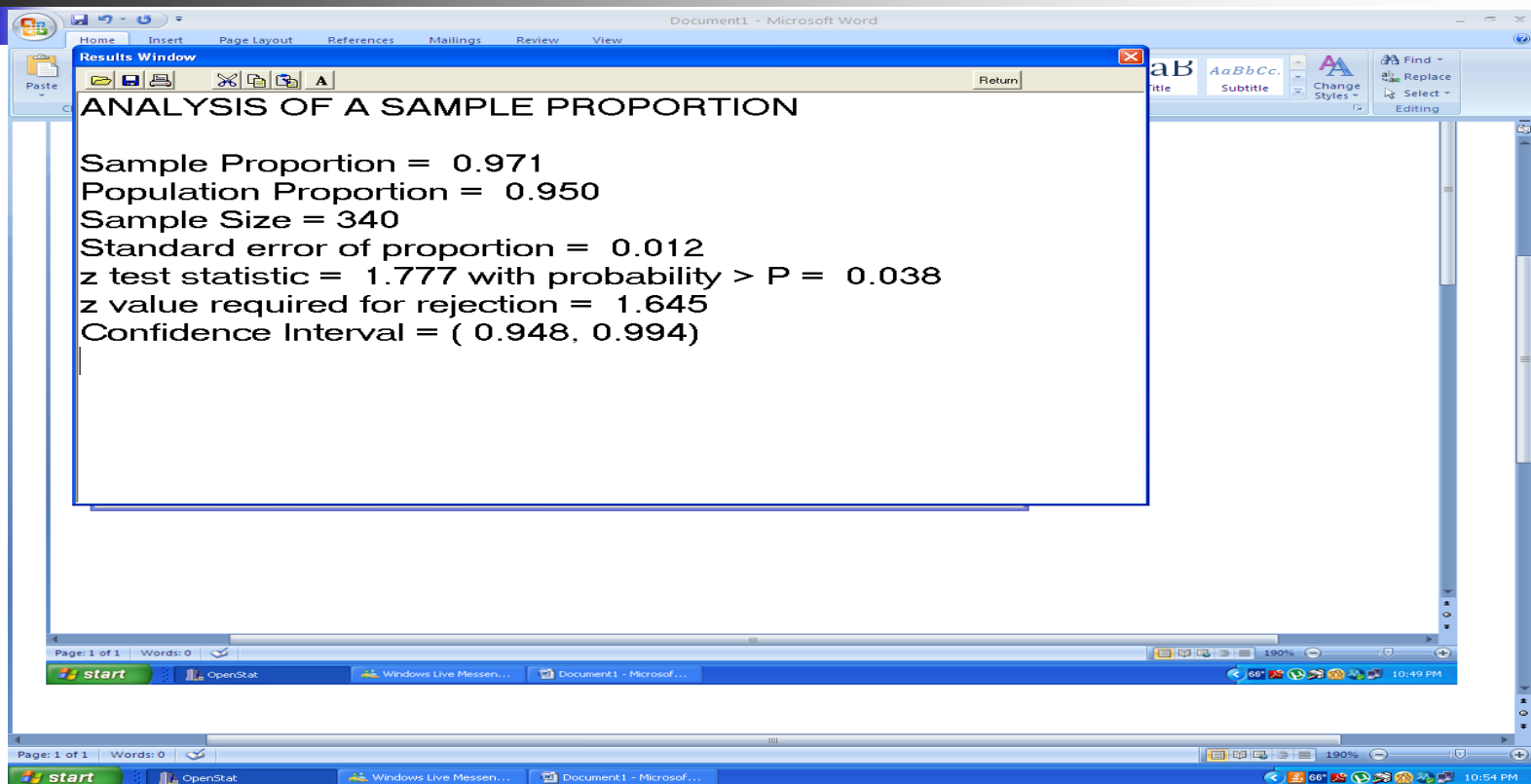
One Proportion Problem in Openstat



Computations



Results



The proportion of patients with a positive vaccination is greater than 95%.

Difference in Proportions of Paired Data

- Use McNemar's test for difference in proportions

$$H_0: \pi_1 = \pi_2$$

$$H_A: \pi_1 \neq \pi_2$$

		After	
		Bad	Good
Before	Bad	a	b
	Good	c	d

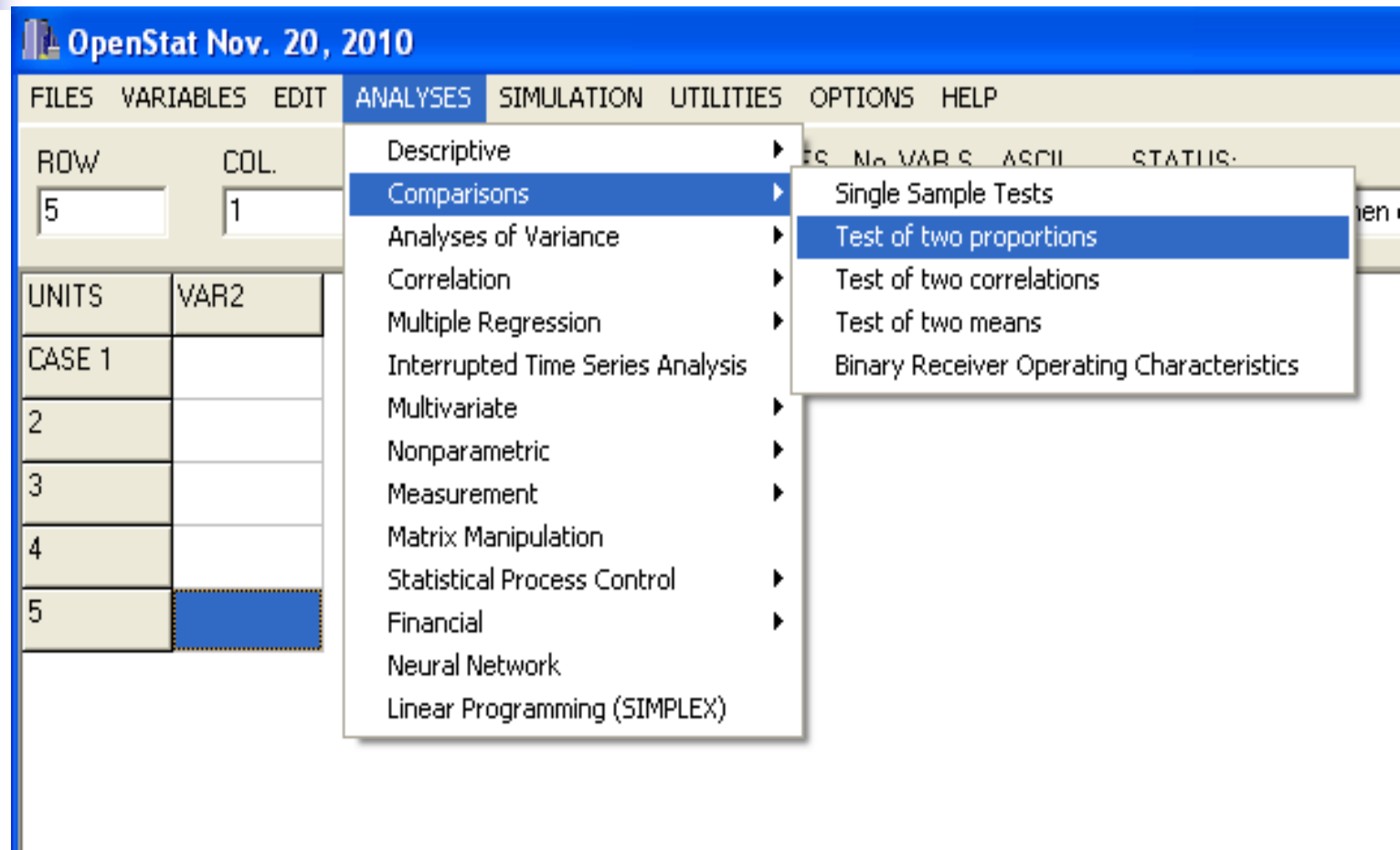
$$\text{McNemar} = \frac{(|b - c|)^2}{b + c}$$

Example of Paired Proportions

Researches wanted to know whether changes occurred in the bowel function of patients following cholecystectomy. They collected information on # of patients who had one or fewer vs. more than one stool per day.

		1 month after CHE		
		≤ 1	> 1	Total
Before CHE	≤ 1	25	15	40
	> 1	0	11	11
Total		25	26	51

OpenStat for McNemar's Test



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

Frequencies		Var. 1	
		0	1
Var. 2	0	25	15
	1	0	11

Percent Confidence Interval:

95

Reset

Cancel

Continue

Results from OpenStat

Results Window



Return

COMPARISON OF TWO PROPORTIONS

--> McNemar Test (Test for the Difference Between two Correlated Proportions)

Sample	2		sum
	0	1	
1	0 25	15	40
	1 0	11	11
sum	25	26	51

Chi-Square statistic = 15.0000 p-value two-tailed =0.0001

Chi-Square statistic with Continuity Correction = 13.0667 p-value two-tailed =0.0003

Binomial p-value for the two-tailed exact test =0.0000

Proportion of zeros in Sample 1 =0.7843 Proportion of zeros in Sample 2 =0.4902 51 cases


Difference in proportions = 0.2941

Standard Error of Difference = 0.0638

z value for confidence interval =1.9600

Confidence Interval 95% = (0.1691,0.4192)

Results in Bigger Font

Results Window				
				Return
COMPARISON OF TWO PROPORTIONS				
--> McNemar Test (Test for the Difference Between two Correlated Proportions)				
Sample	2			
	0	1	sum	
0	25	15	40	
1	0	11	11	
sum	25	26	51	
Chi-Square statistic = 15.0000 p-value two-tailed =0.0001				
Chi-Square statistic with Continuity Correction = 13.0667 p-value two-tailed =0.0003				
Binomial p-value for the two-tailed exact test =0.0000				

Results in Bigger Font (cont'd)

Proportion of zeros in Sample 1 = 0.7843 Proportion of zeros in Sample 2 = 0.490251 cases

Difference in proportions = 0.2941

Standard Error of Difference = 0.0638

z value for confidence interval = 1.9600

Confidence Interval 95% = (0.1691, 0.4192)

There is a significant difference, increase, in the proportion of patients having more than one stool per day before and after CHE.



Reporting Results

- Indicate the software used for analysis.
- Report the results for test statistic, degrees of freedom and p value. Also provide the confidence interval.
- p value for non-parametric tests should be interpreted with caution.



Summary

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
Dependent groups; proportion	McNemar



www.epilepsy.va.gov/Statistics

Questions/Comments

Rizwana.Rehman@va.gov

(919) 286-0411 ext: 5024

Next lecture's highlights

Research questions about two groups