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Statistics in Evidence Based Medicine

Lecture 6: Research Questions for One Group

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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.

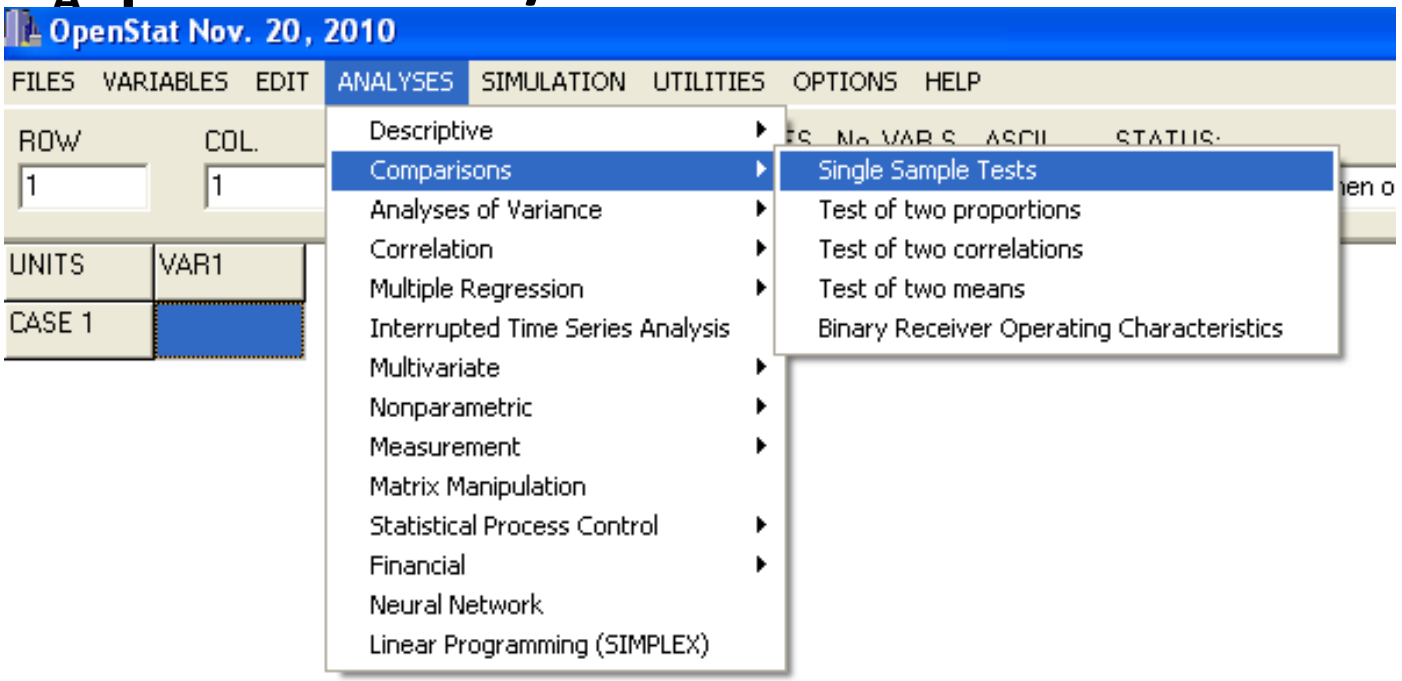
previous studies showed that the mean was commonly close to 2.5 mmol/l in healthy people aged 20-44. Assume that the data are plausibly normally distributed. Is the mean in these patients abnormally high?

Openstat for Everley's Syndrome Example

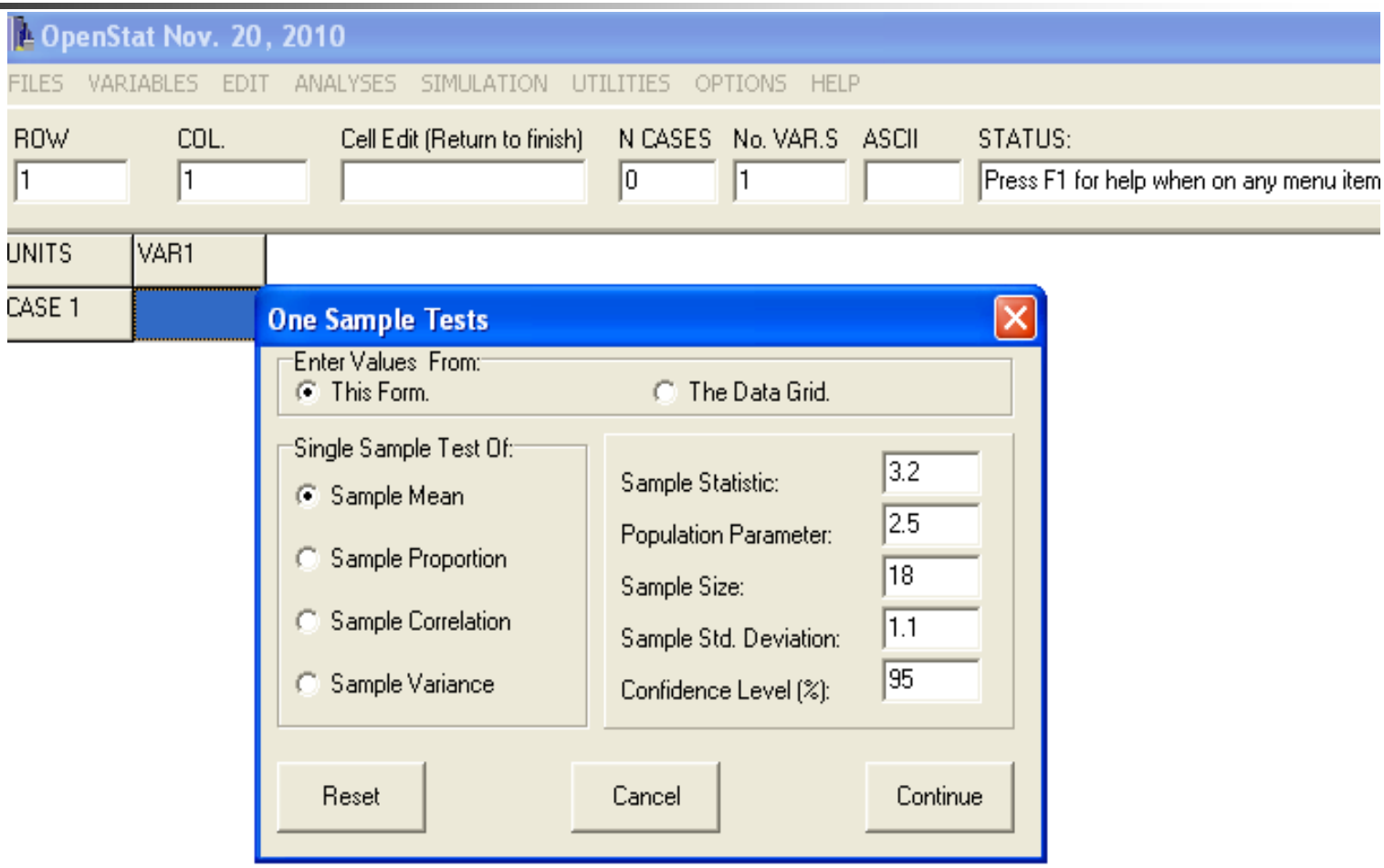
http://www.statprograms4u.com/

H_0: μ = 2.5 mmol/l

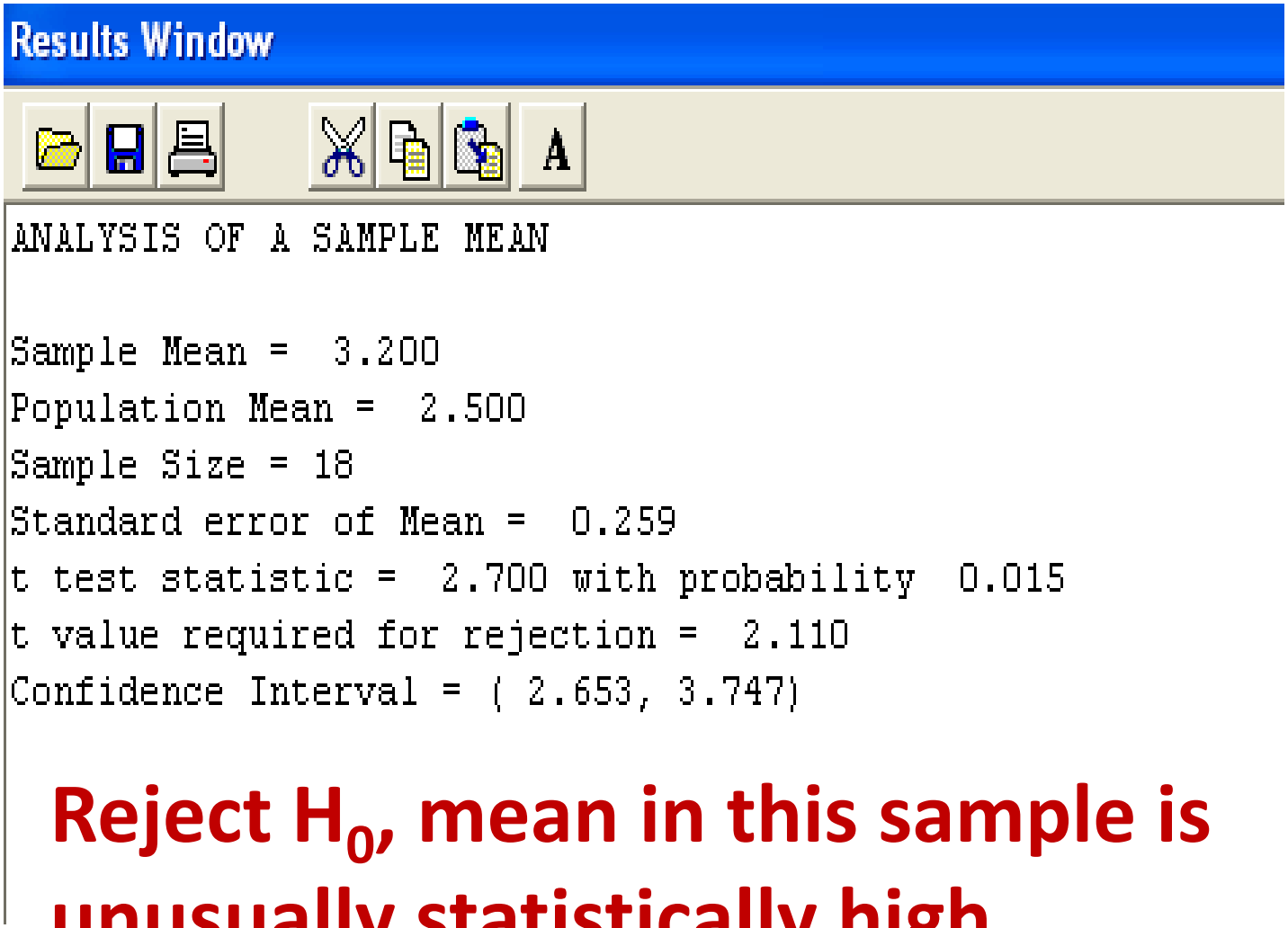
H_A: μ ≠ 2.5 mmol/l



Entering Data in OpenStat



Results from OpenStat



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.

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

Example of Normal Paired Data

FEV_1 from five asthmatics, before and after use of a bronchodilator (liters/sec) with normally distributed data

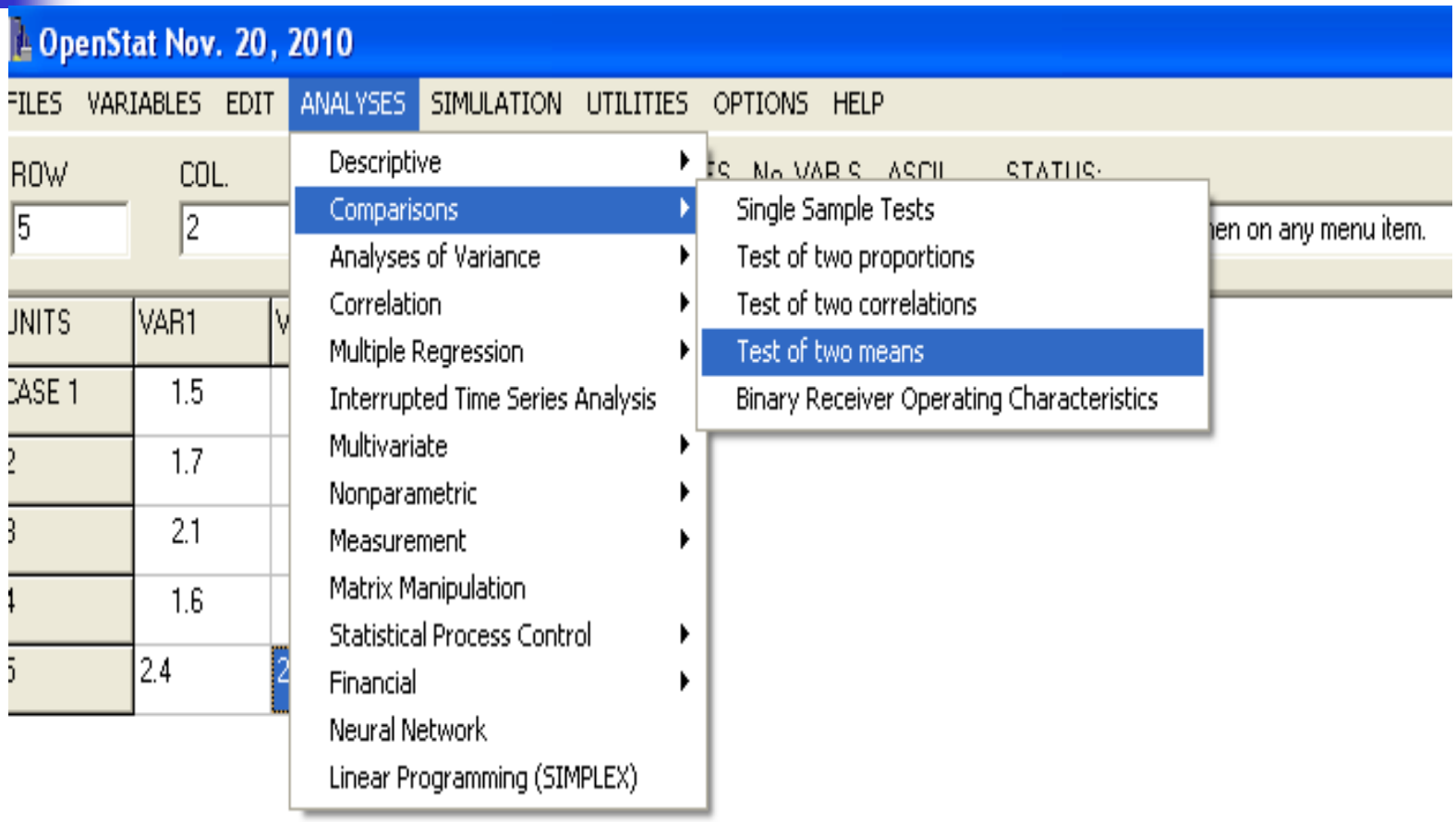
Before	After
1.5	1.7
1.7	1.9
2.1	2.2
1.6	1.9
2.4	2.4

Medical Statistics A Commonsense Approach: Appendix I

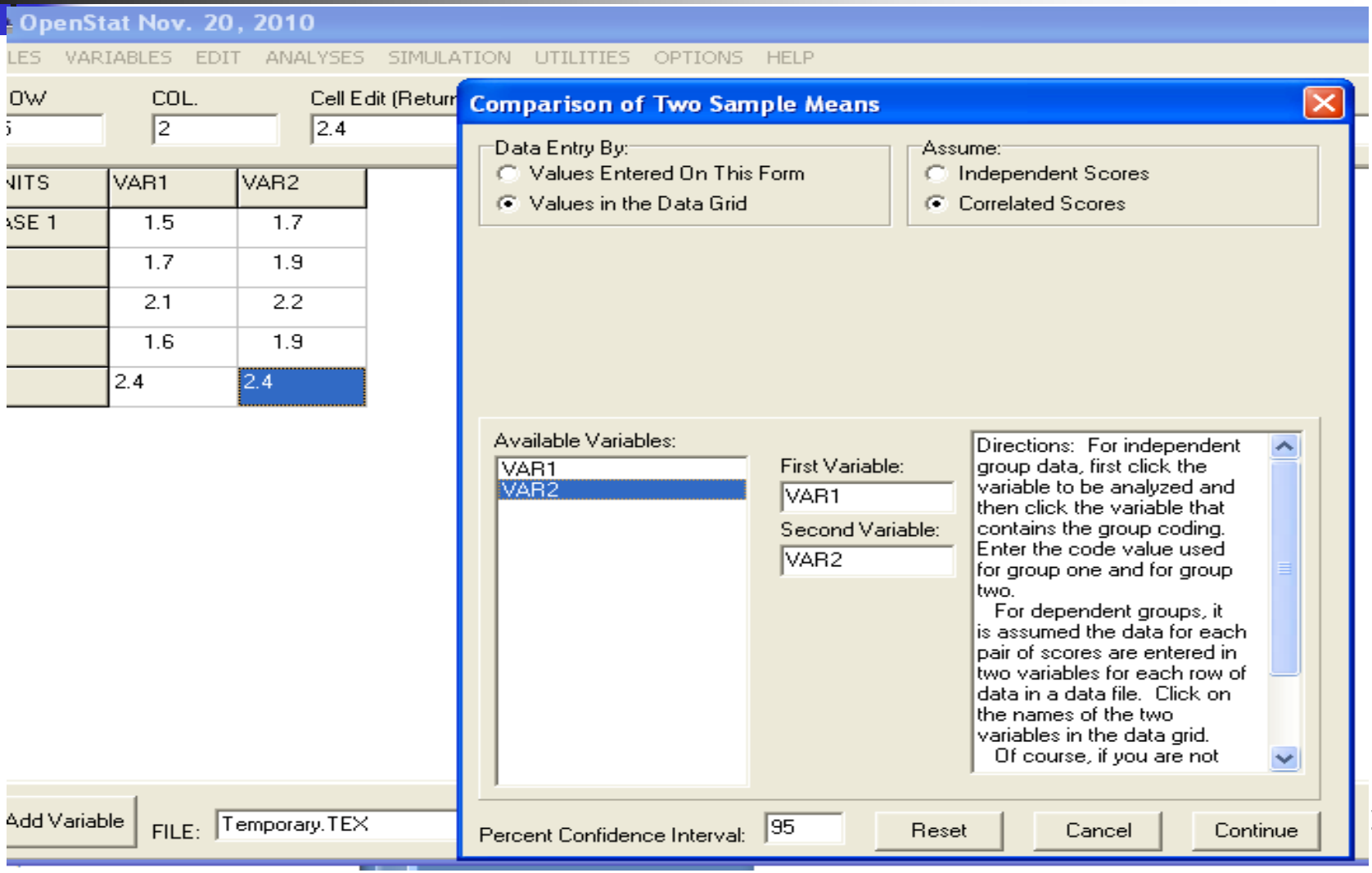
H_0: $\mu_1 - \mu_2 = 0$

H_A: $\mu_1 \neq \mu_2$

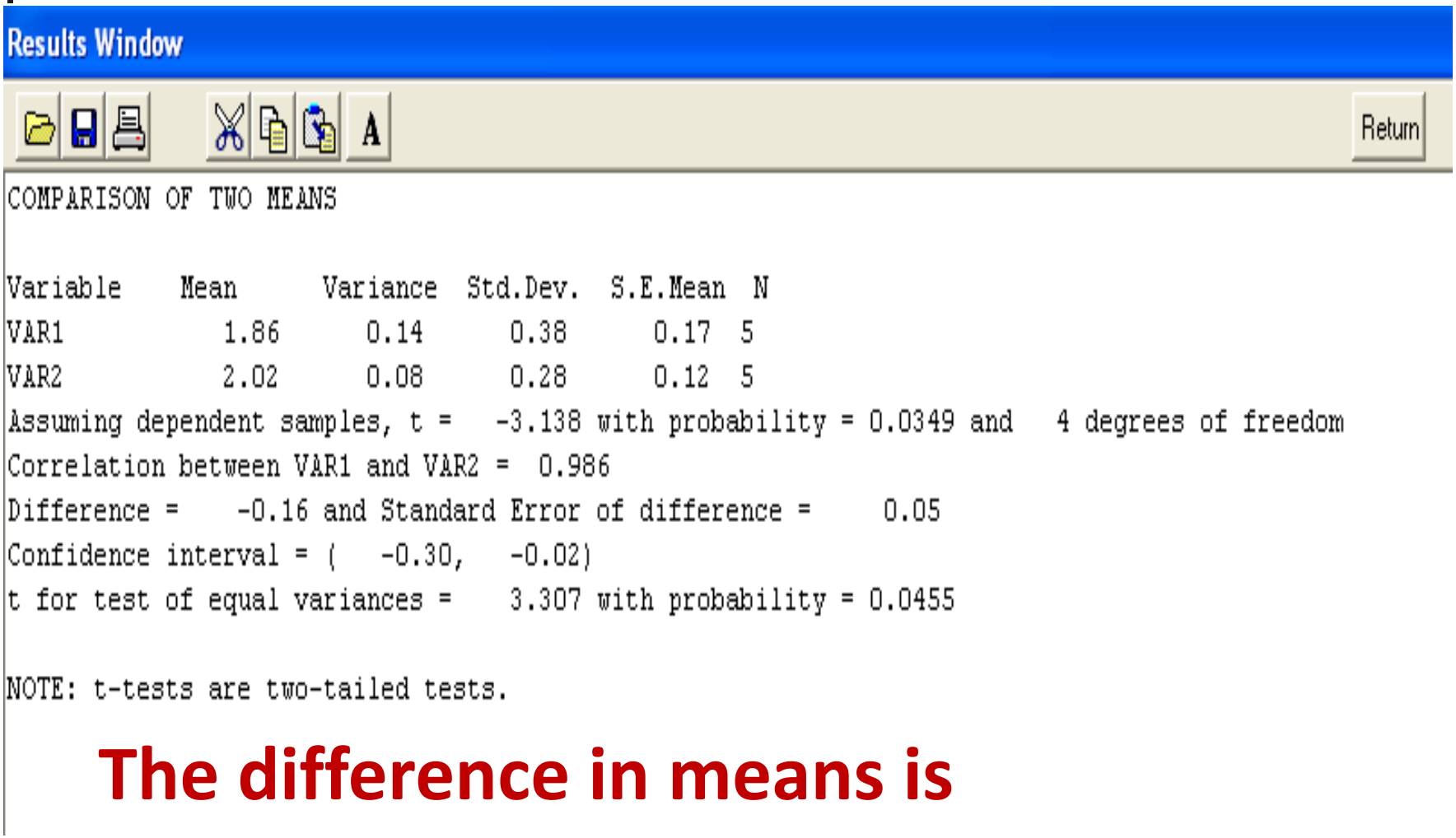
Paired t Test in OpenStat



Entering Data for Analysis



Analysis from OpenStat



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 ≥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

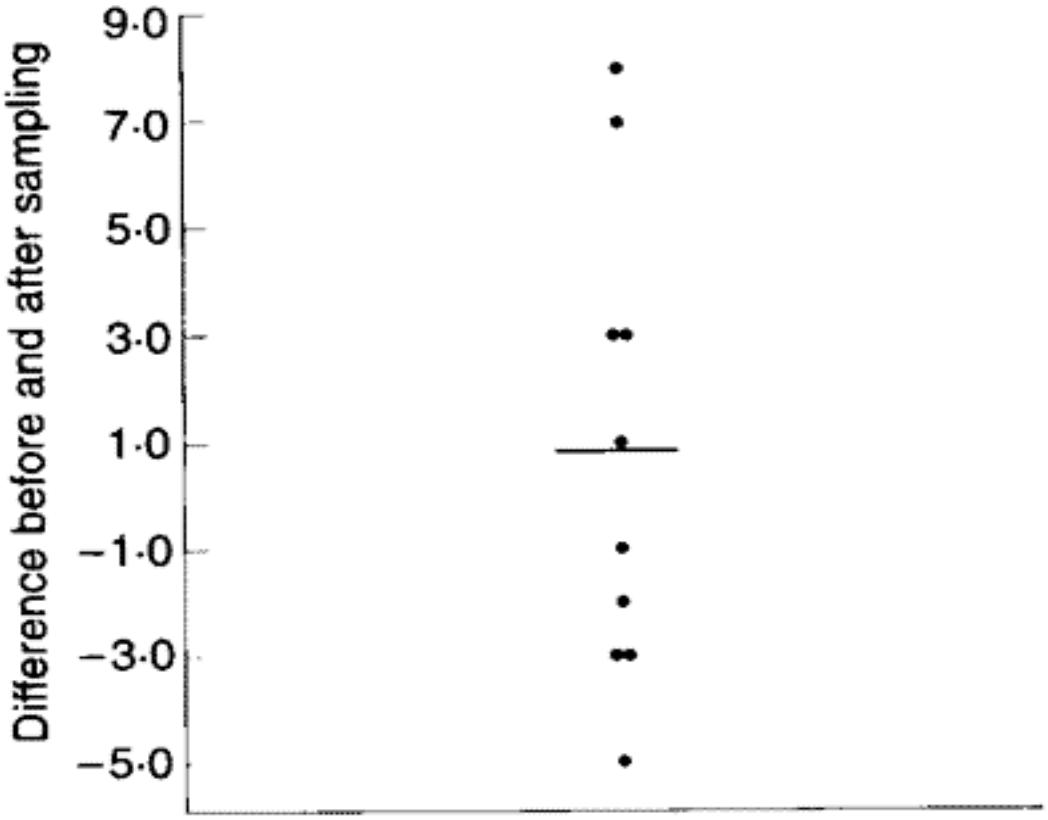
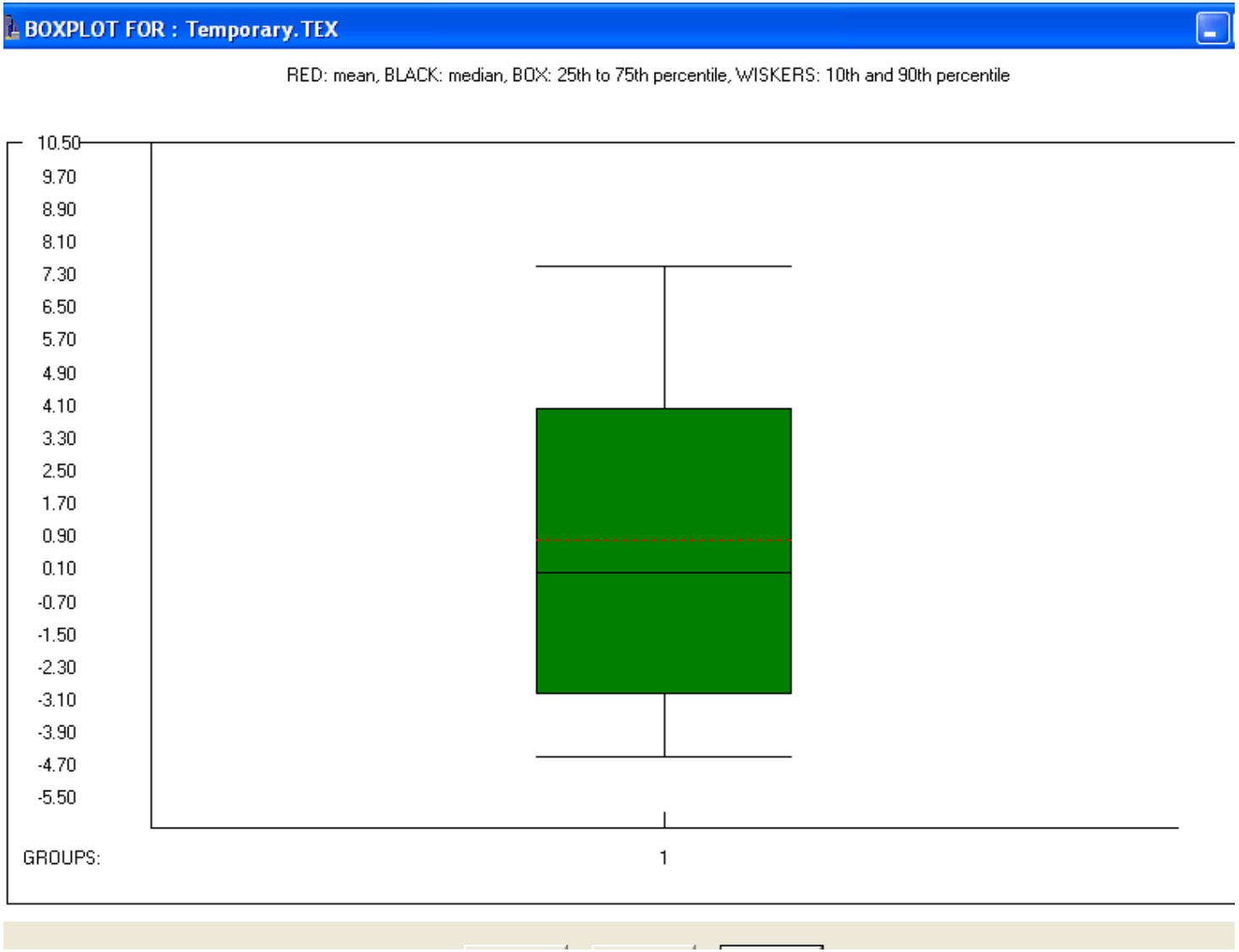
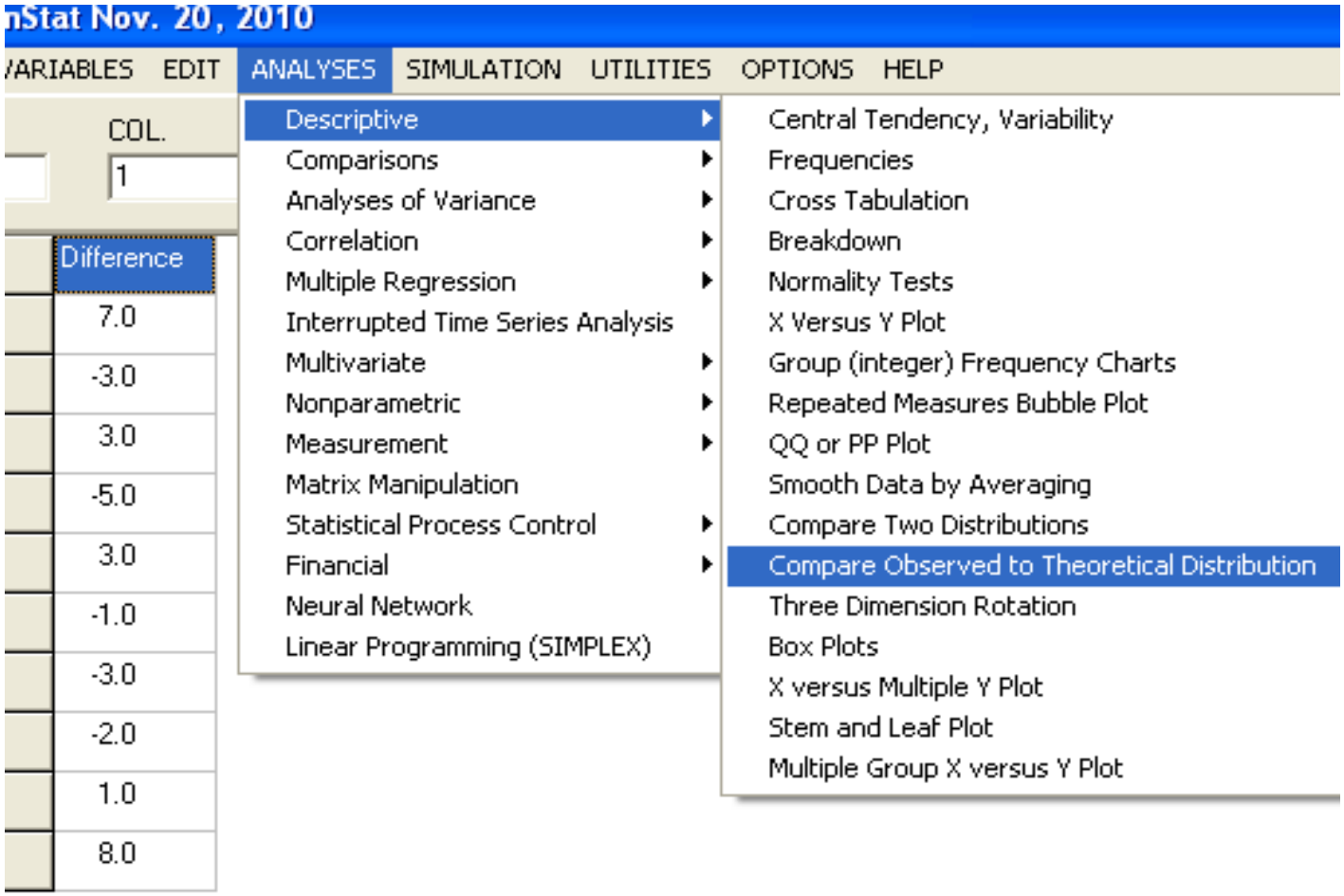


Figure 10.1 Plot of differences in fetal movement with mean value

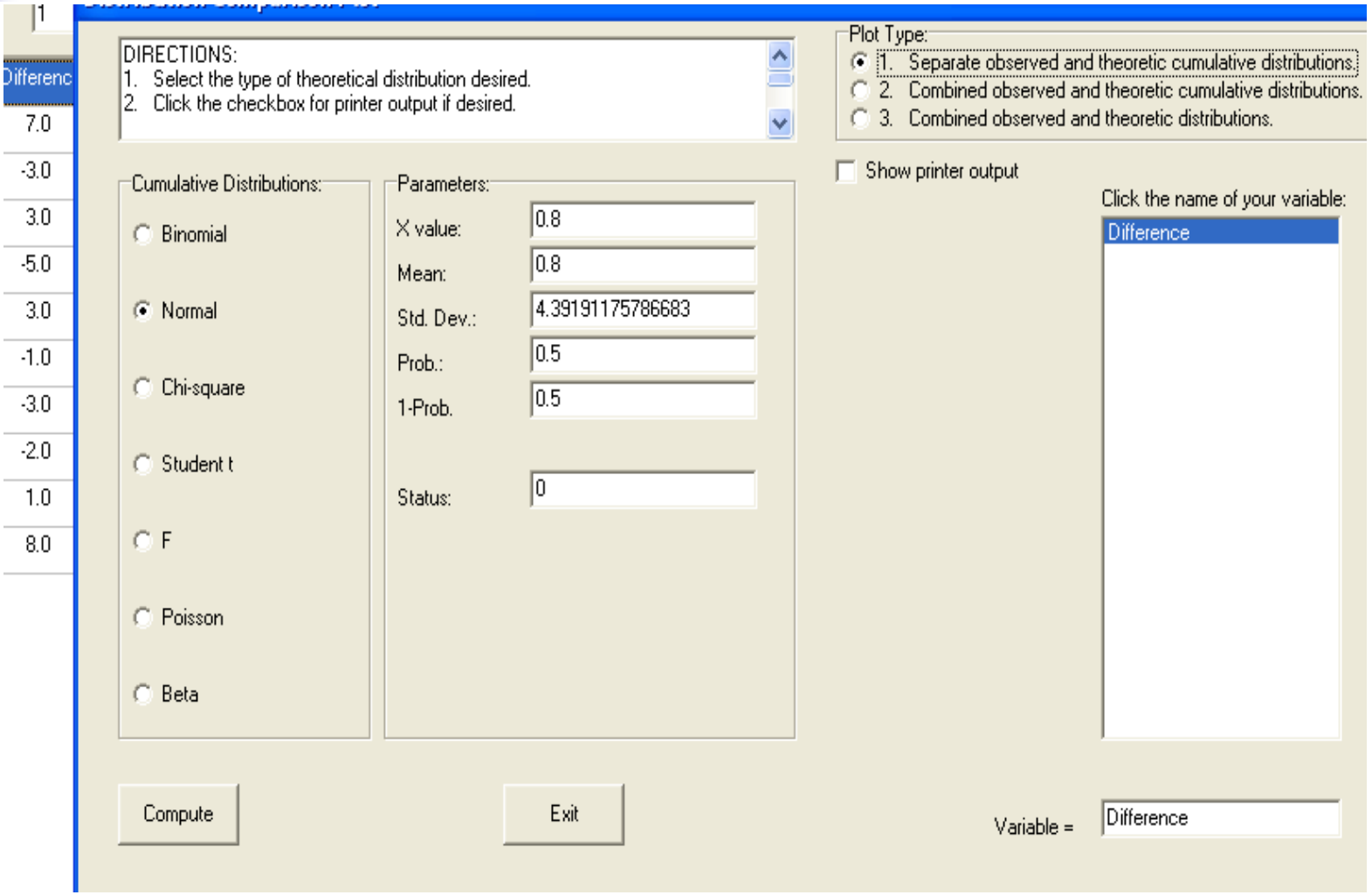
Box Plot of Difference in OpenStat



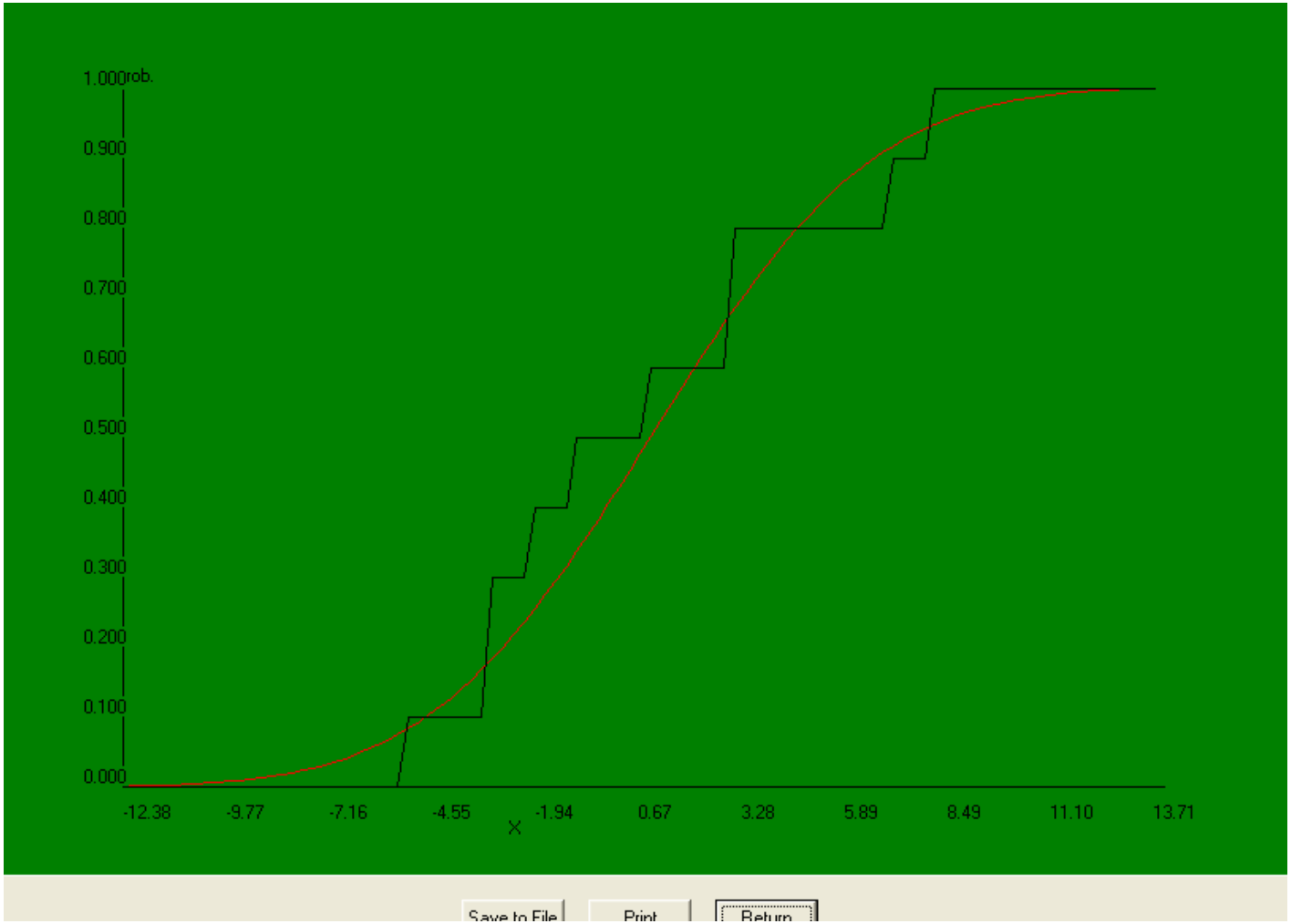
Comparison to Normal Distribution



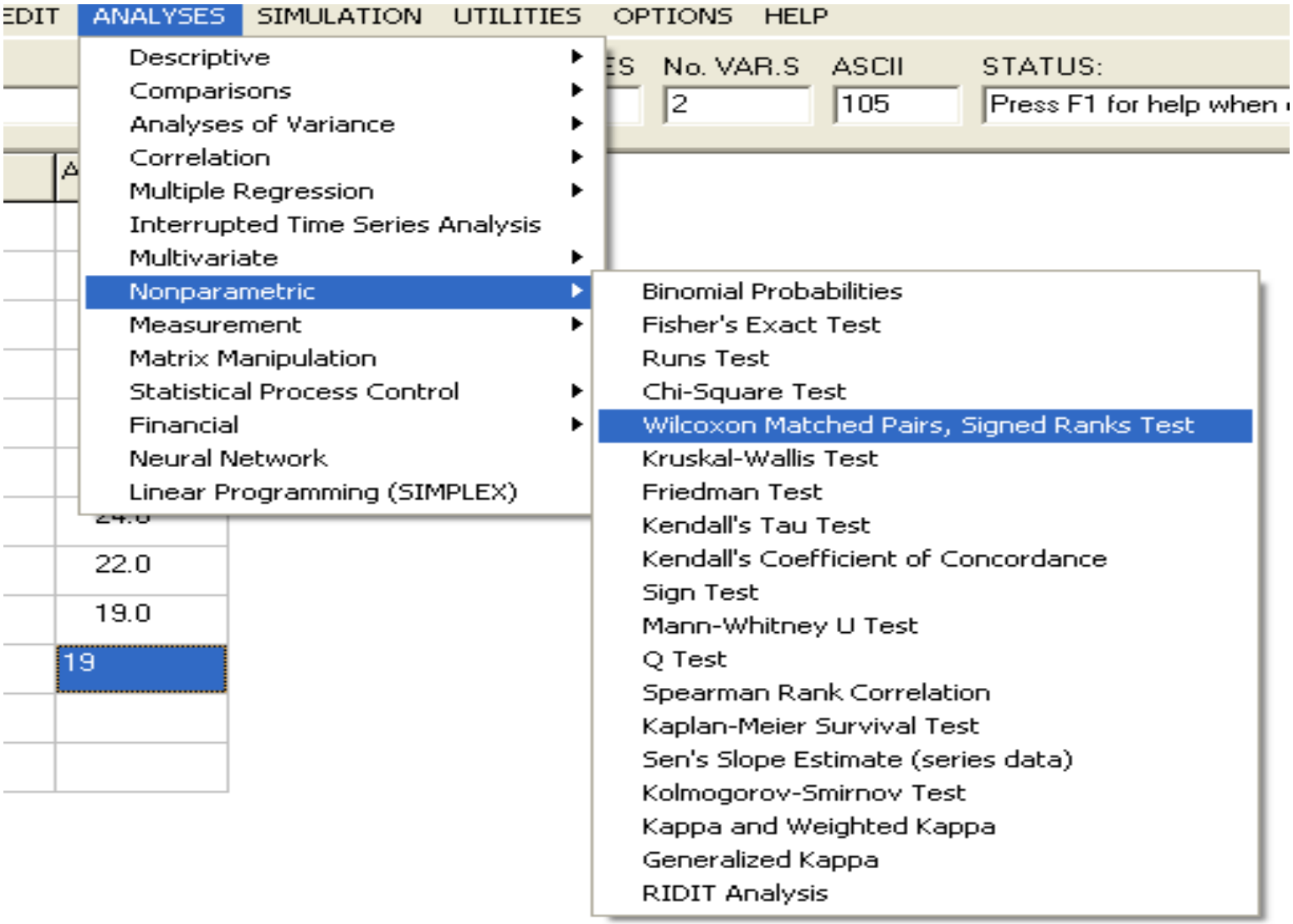
Comparison to Normal Distribution



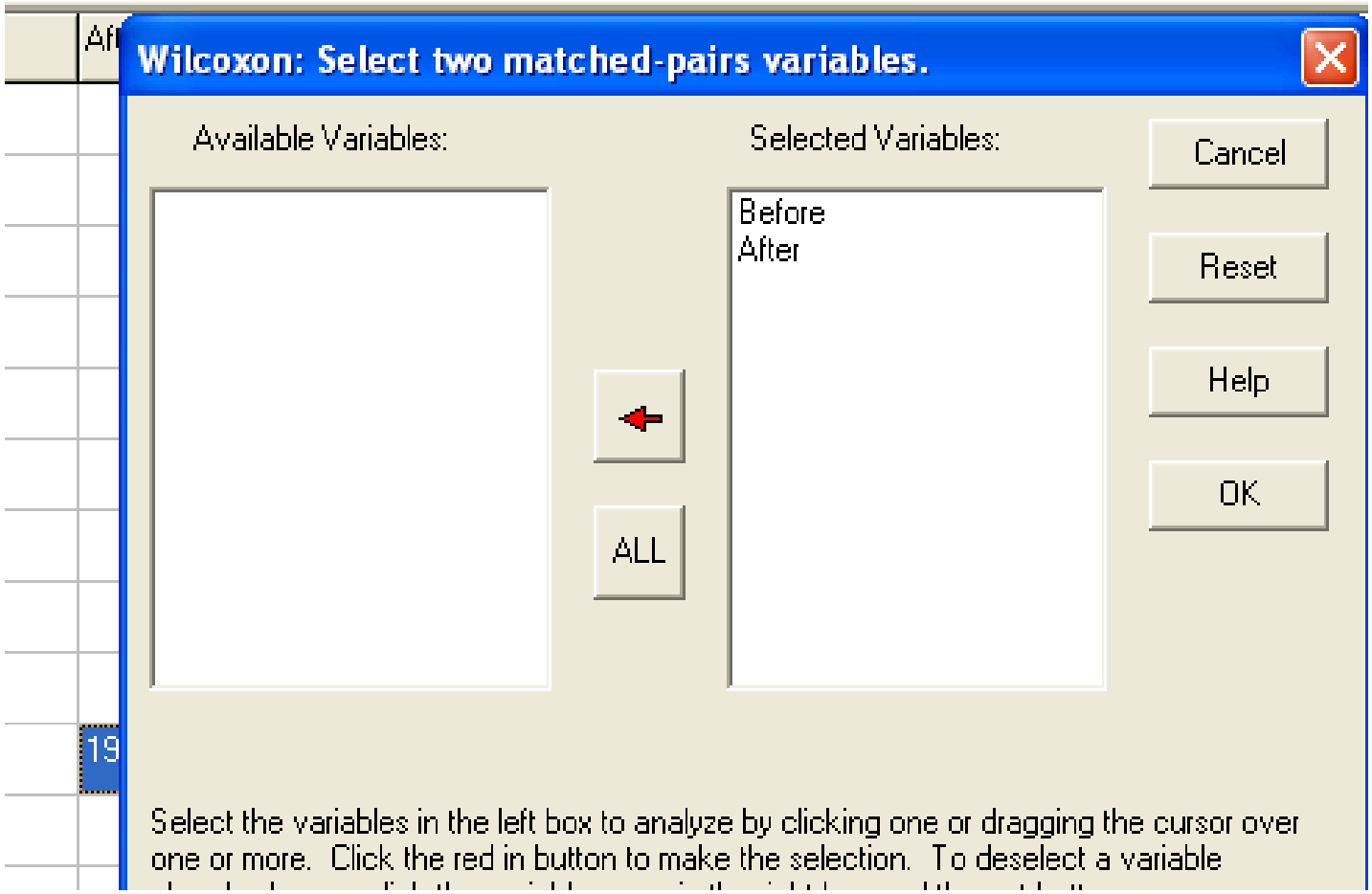
Comparison


1.000rob.
0.900
0.800
0.700
0.600
0.500
0.400
0.300
0.200
0.100
0.000
-12.38
-9.77
-7.16
-4.55
-1.94
0.67
3.28
5.89
8.49
11.10
13.71
X
Save to File
Print
Return

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. Seigel'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

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 tabled values for Wilcoxon Test

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

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.

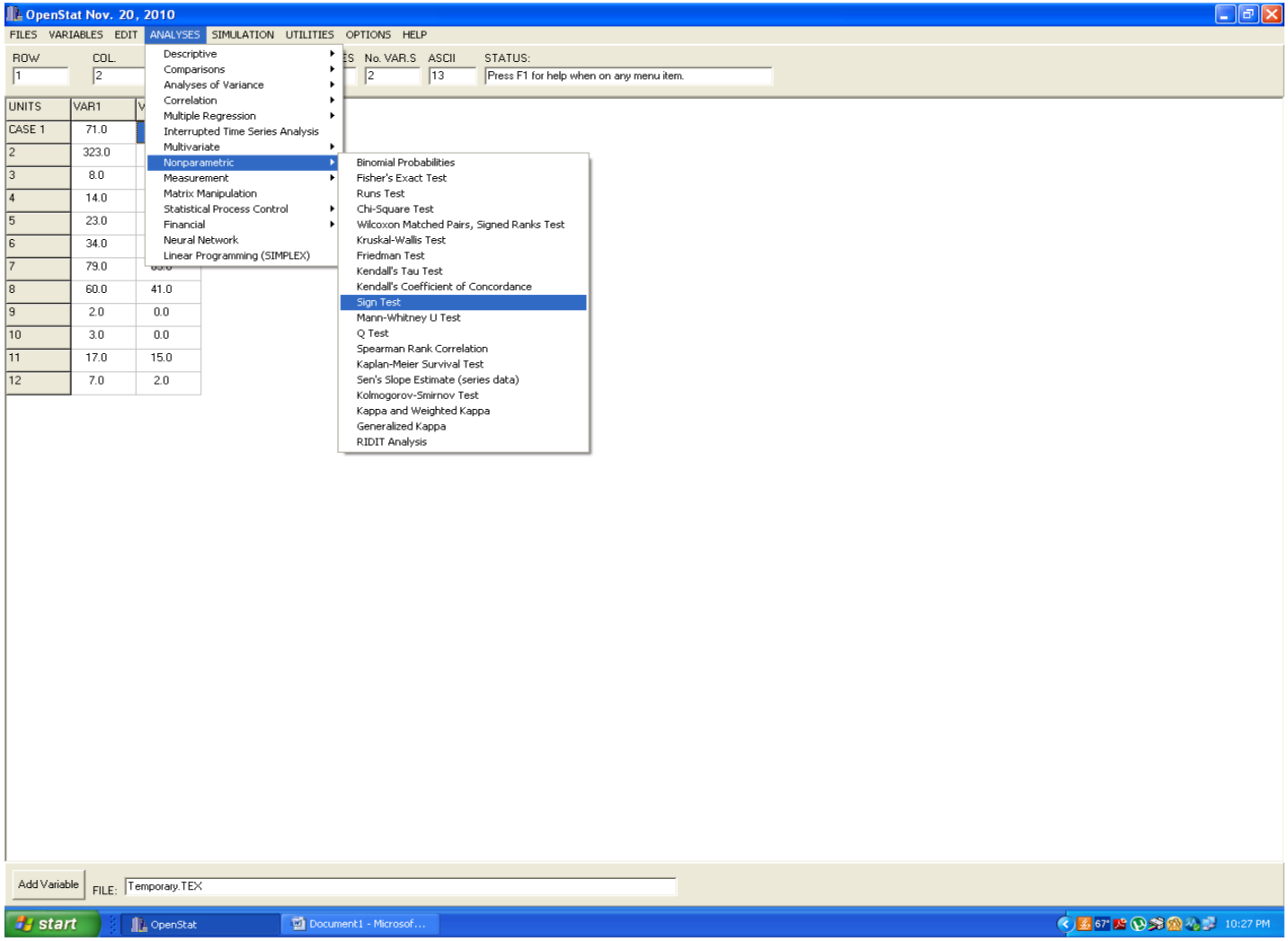
Pronethalol for the Prevention of Angina Pectoris

an introduction to medical statistics by Martin Bland

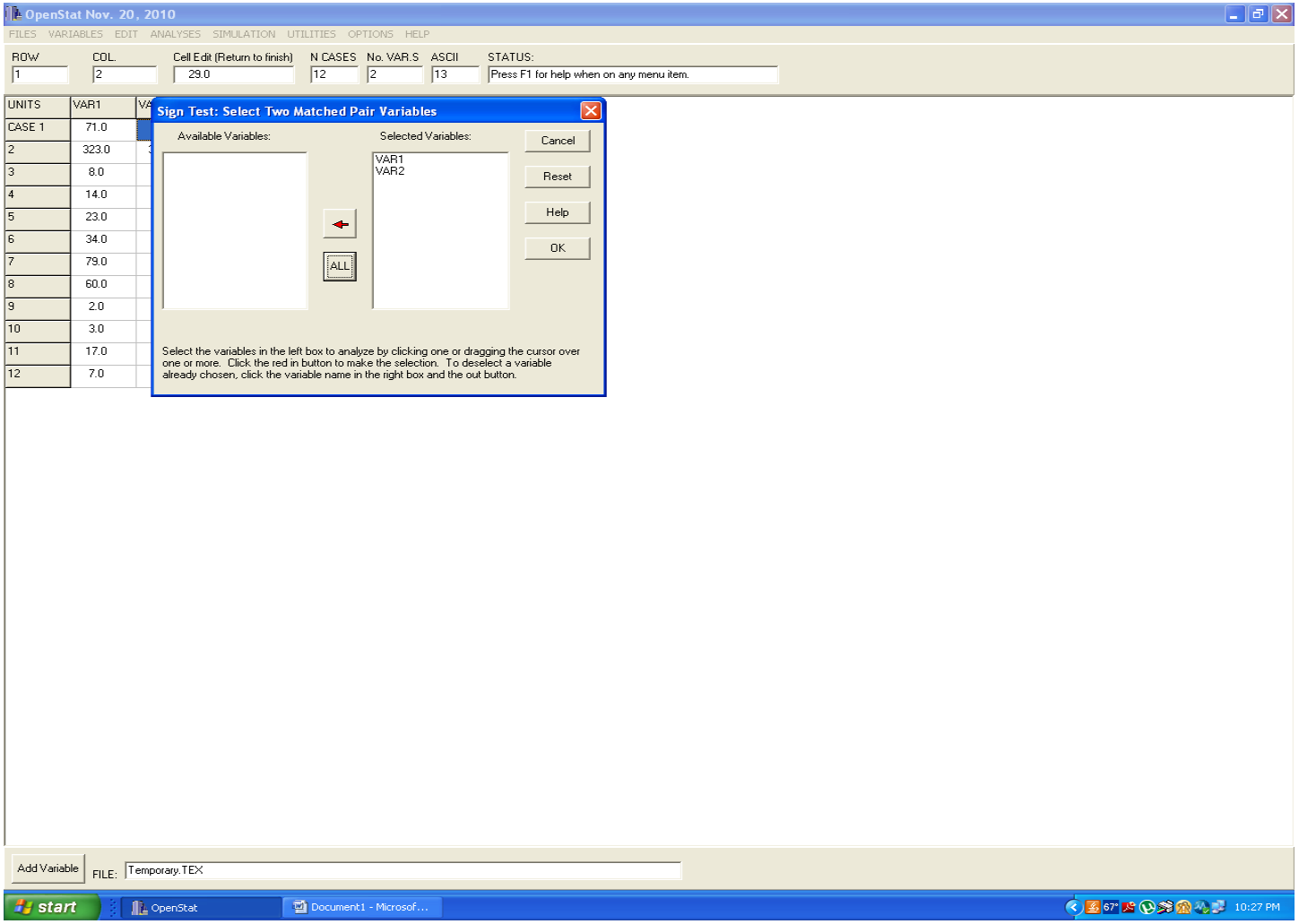
# of Attacks on Placebo	# of Attacks on Pronethalol	Difference	Sign of Difference
71	29	42	+
323	348	-25	-
8	1	7	+
14	7	7	+
23	16	7	+
34	25	9	+
79	65	14	+
60	41	19	+
2	0	2	+
3	0	3	+
17	15	2	+
7	2	5	+

H_0: Placebo and Pronethalol have the same effect on angina

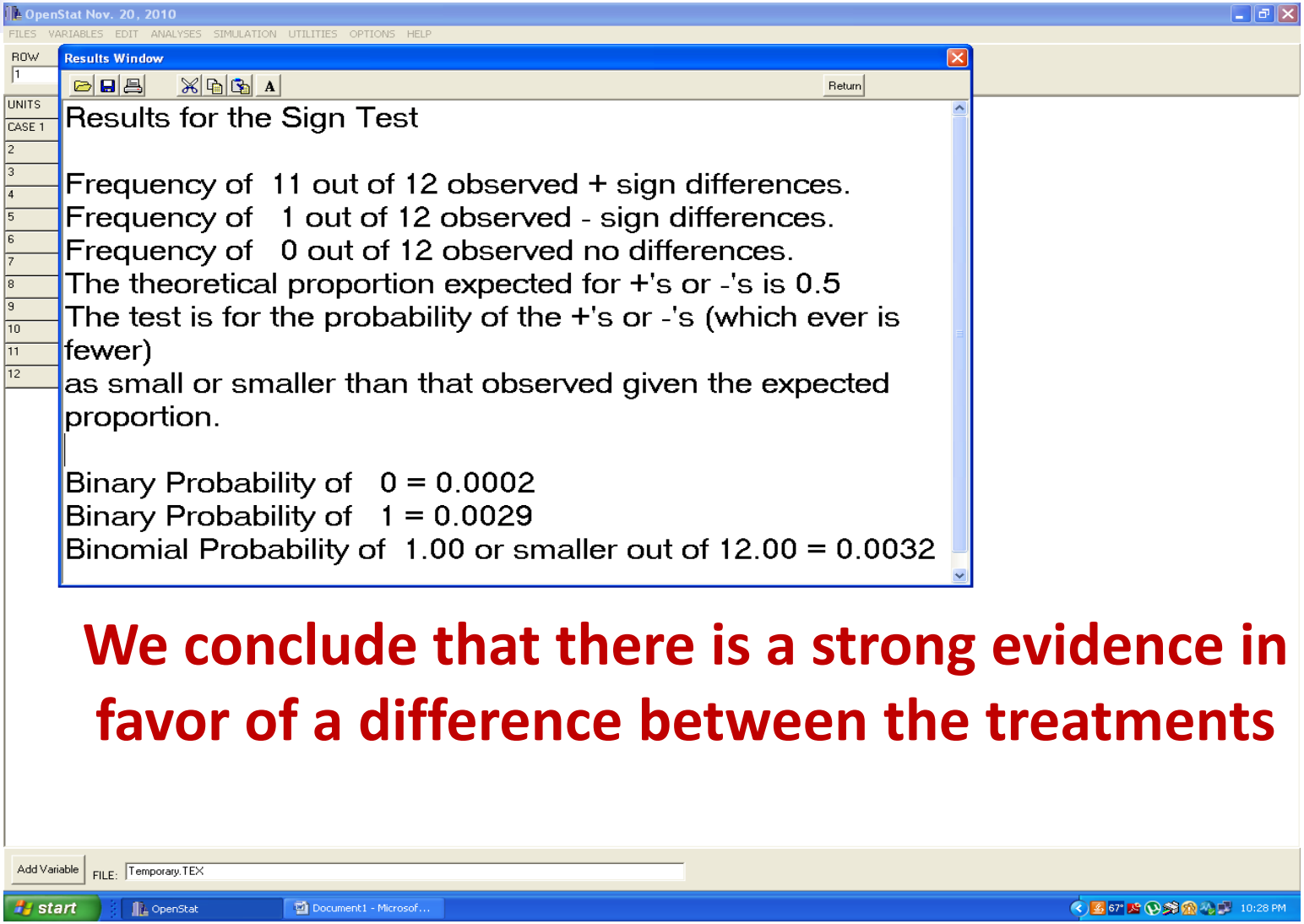
Selecting Sign Test in Openstat



Selecting Variables for Analysis

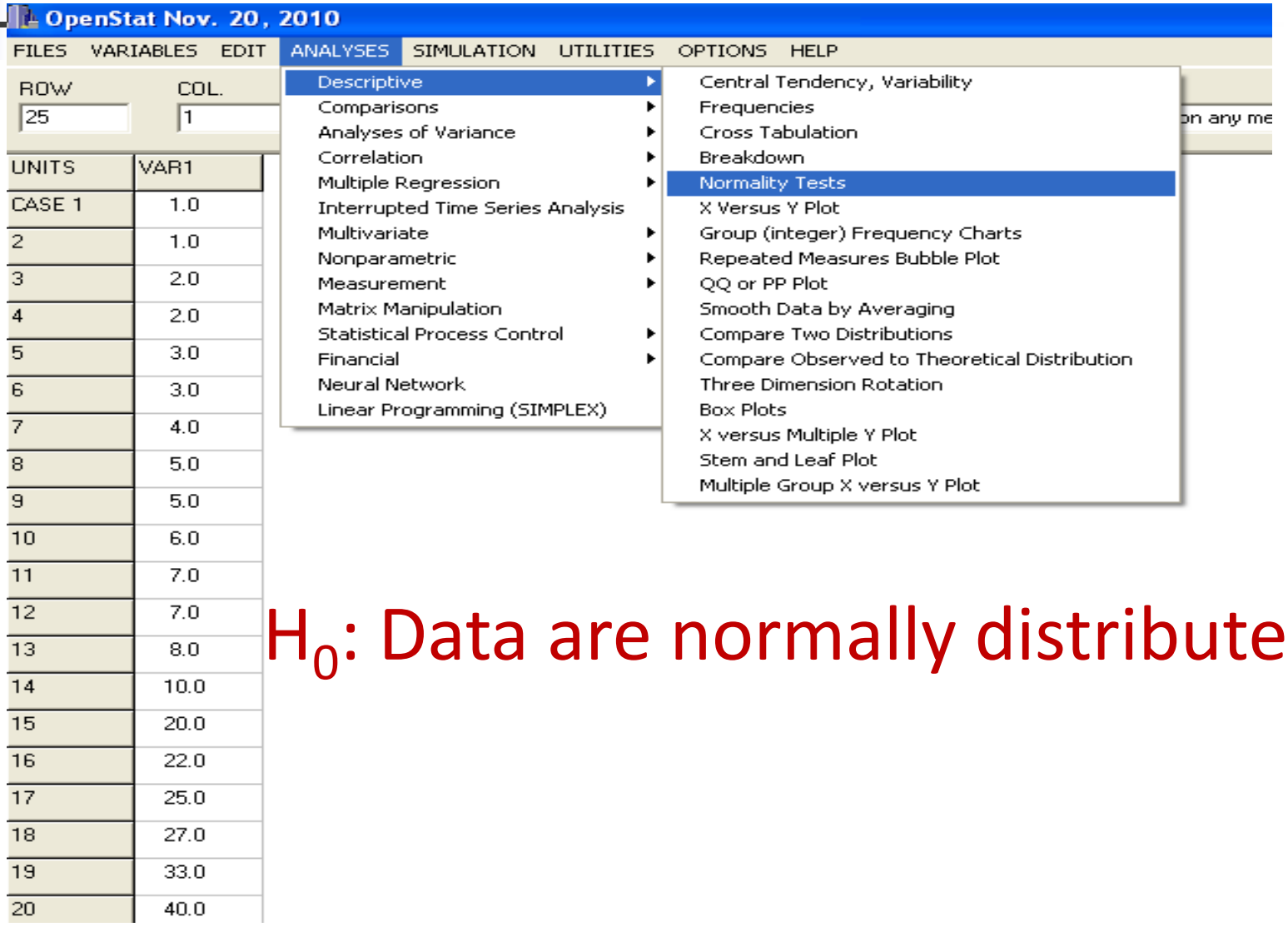


Results



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

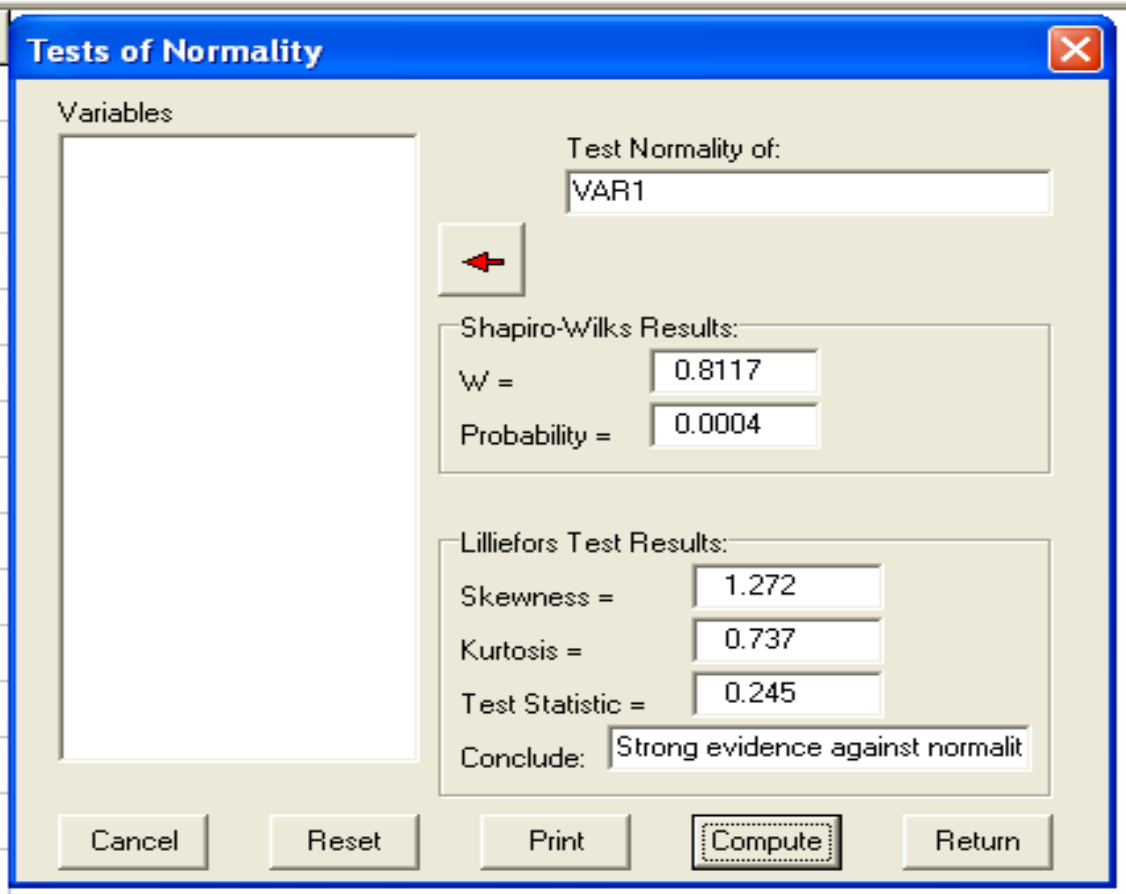
Tests of Normality in OpenStat



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



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

Example of a Proportion

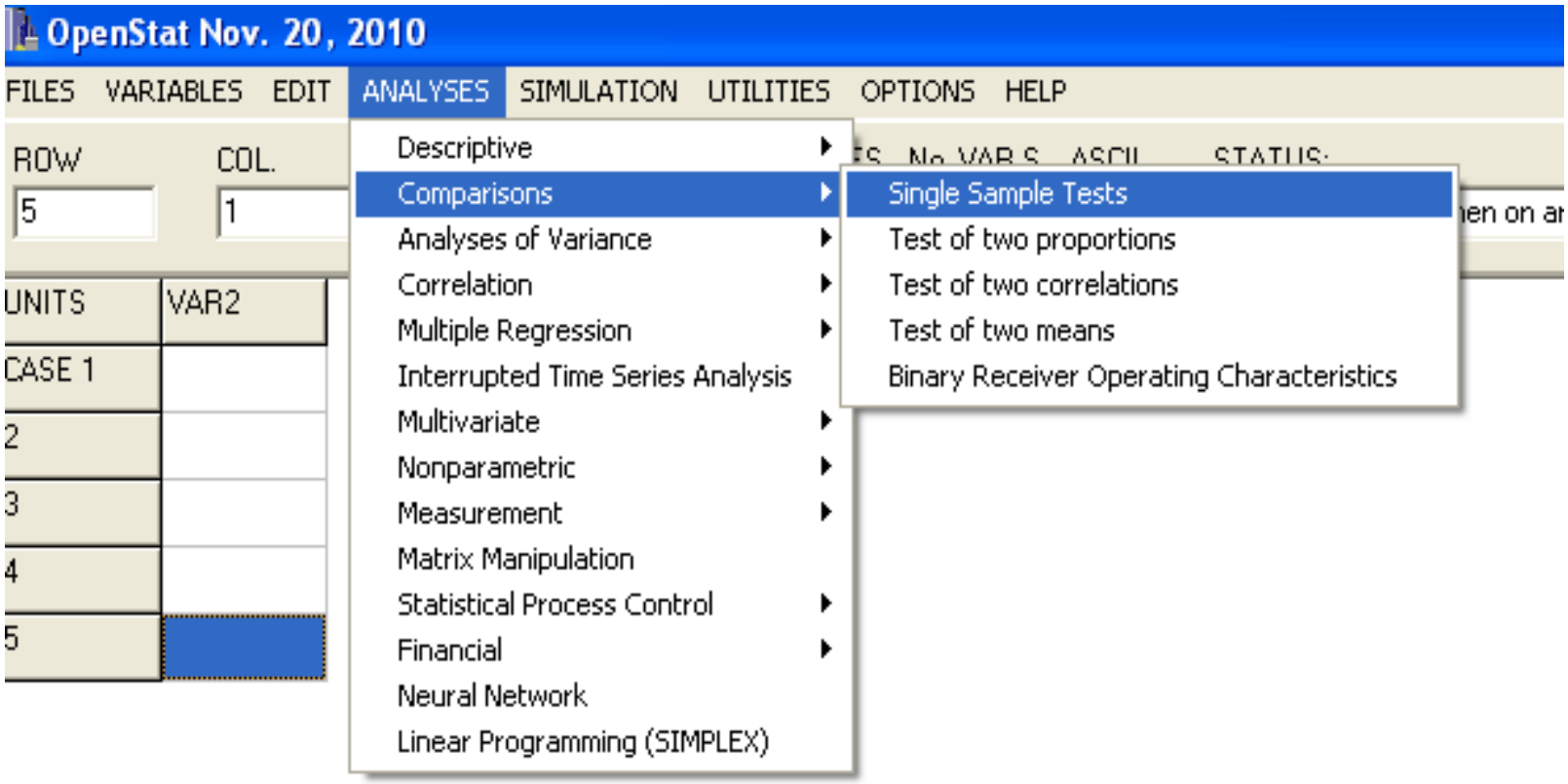
Frey and colleagues wanted to examine the efficacy of different dilutions of smallpox vaccine. The group that received the 1:10 dilution (n=340) had a success rate of 97.1%. Investigators wanted to know if this success rate was greater than 95%.

Basic & Clinical Biostatistics: Chapter 5

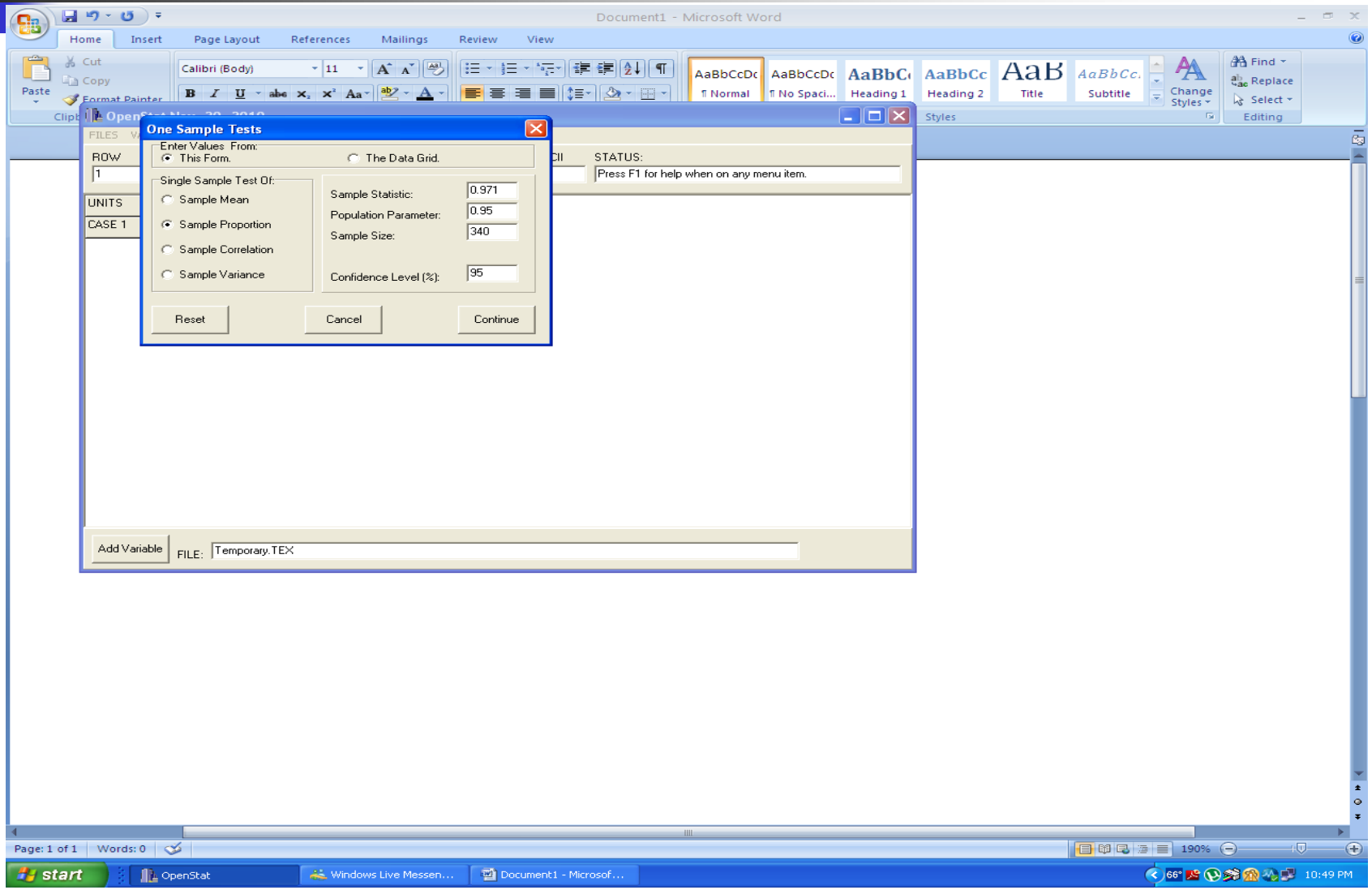
H_0: $\pi \leq 0.95$

H_A: $\pi > 0.95$

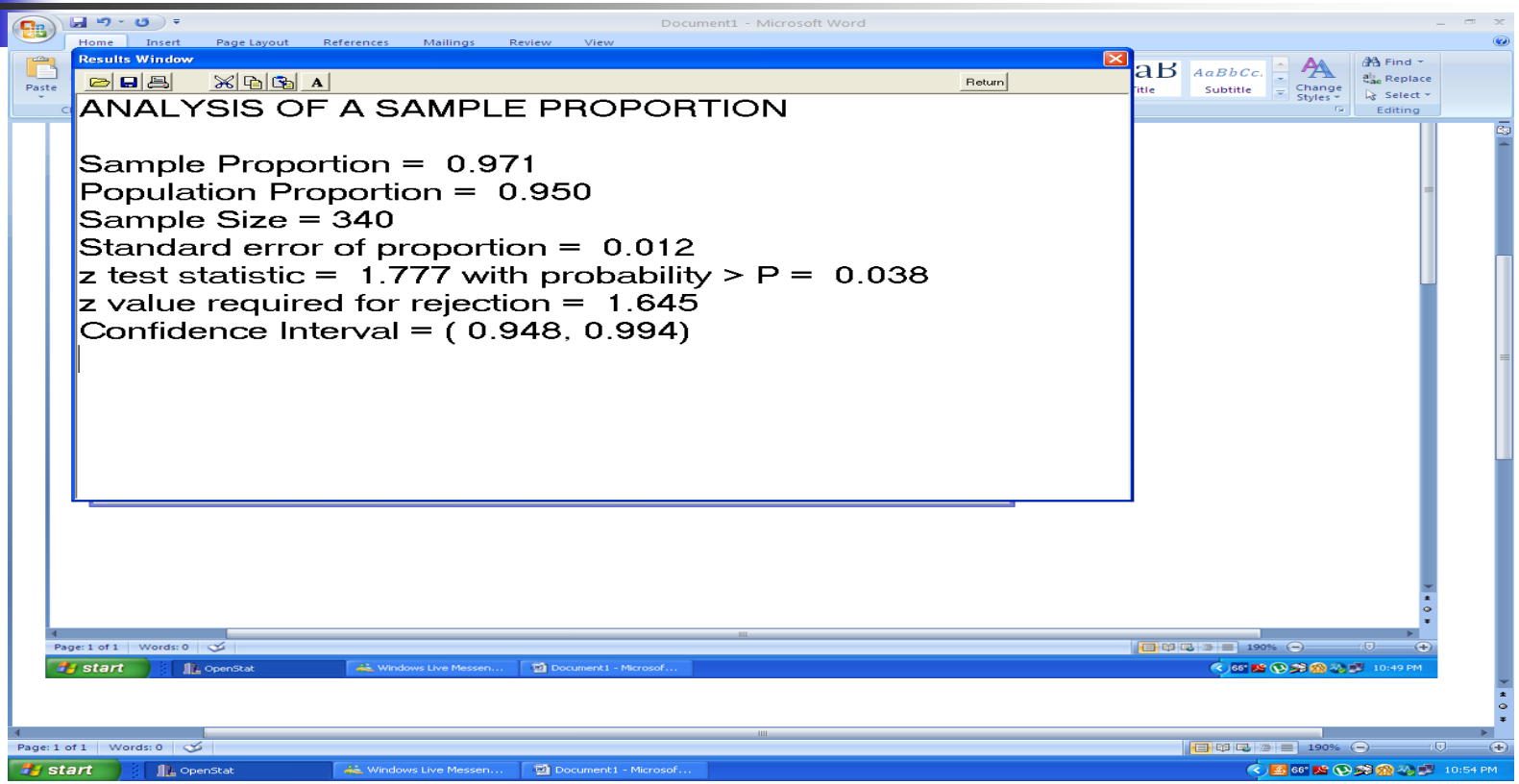
One Proportion Problem in Openstat



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

$\mathbf{H_0}: \pi_1 = \pi_2$

$\mathbf{H_A}: \pi_1 \neq \pi_2$

		After: Bad	After: Good
Before	Bad	a	b
	Good	c	d

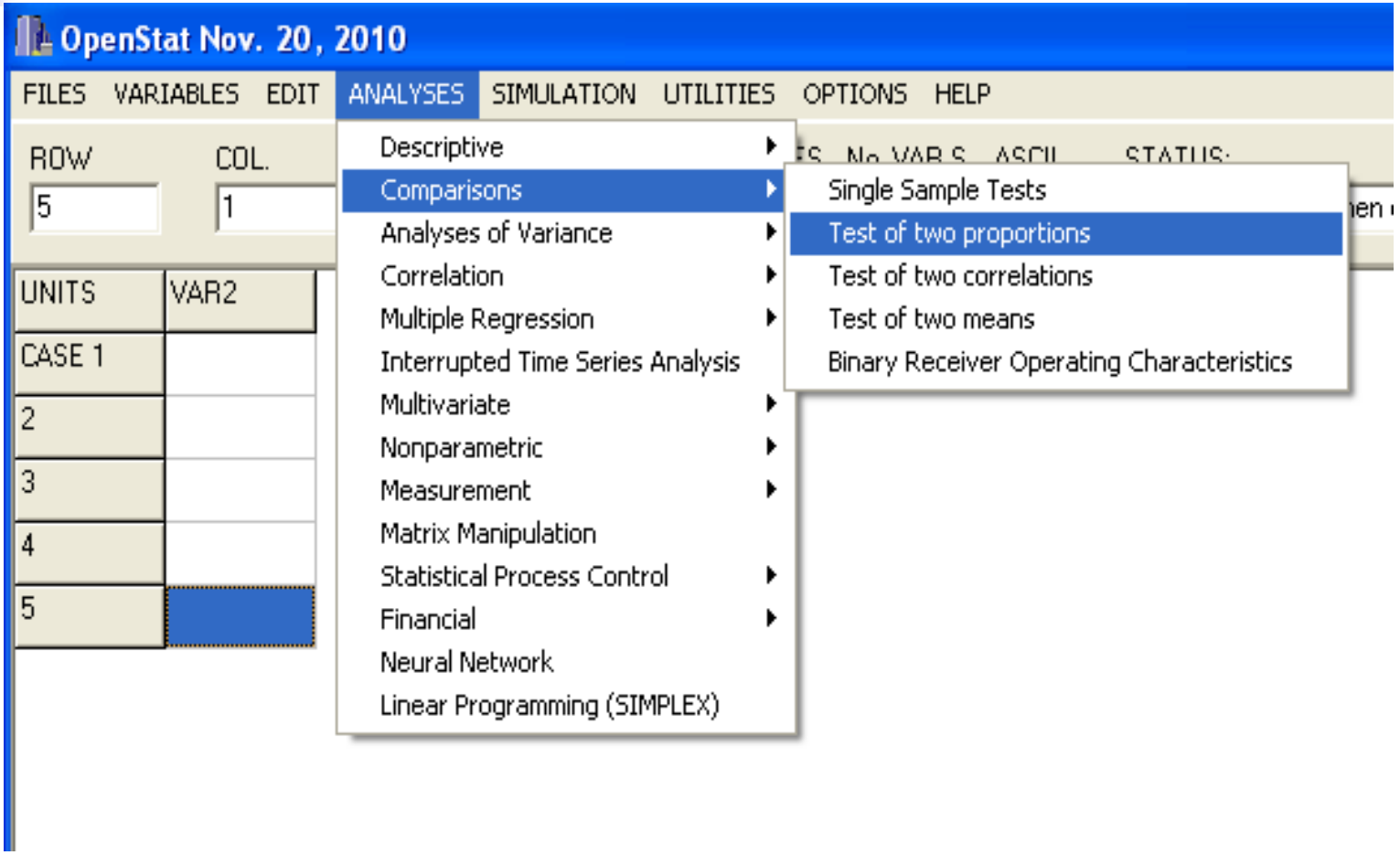
$$McNemar = \frac{(|b - c|)^2}{b + c}$$

Example of Paired Proportions

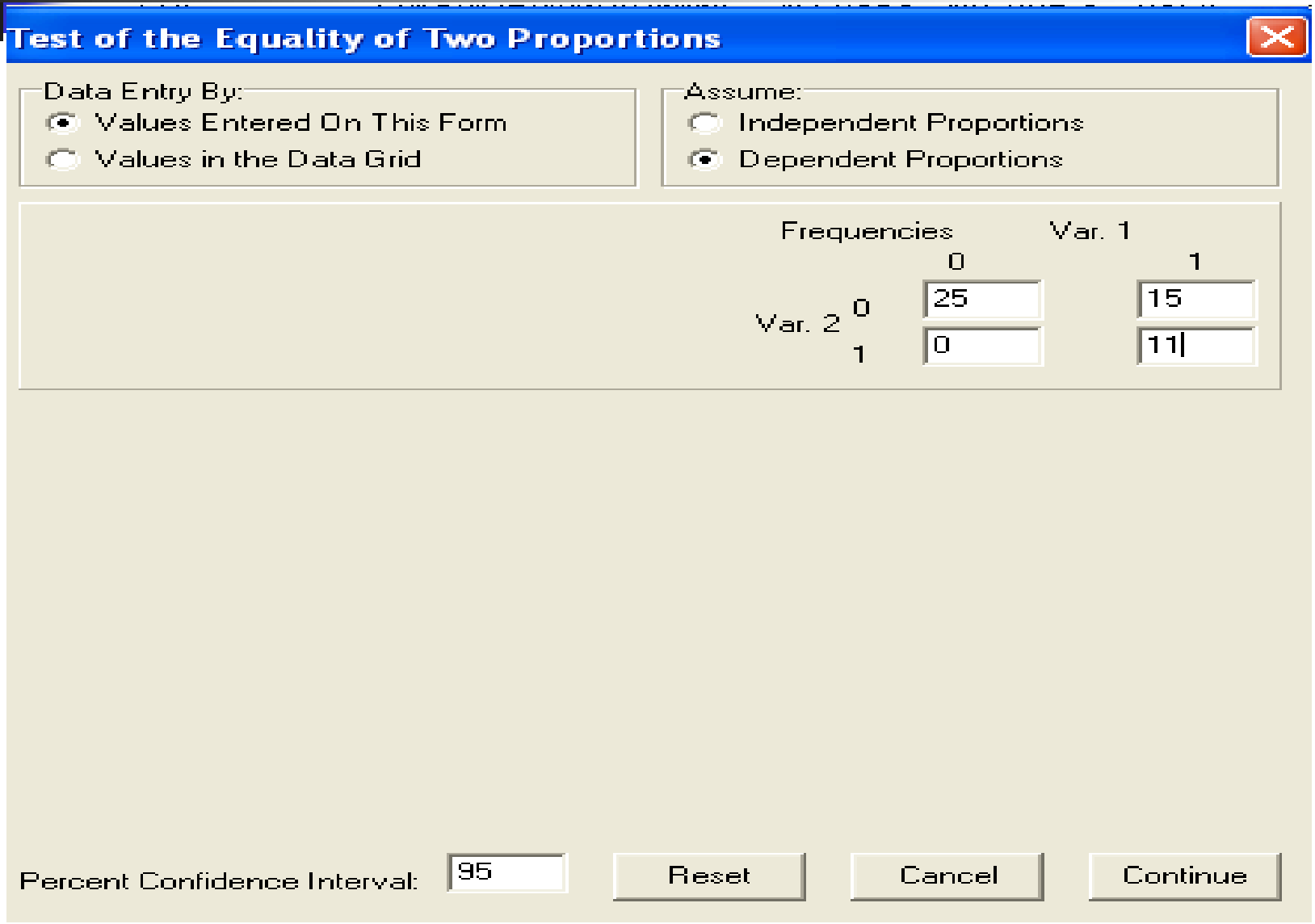
Researches wanted to know whether changes occurred in the bowel function of patients following cholecystectomy. They collected information on # of patients who had one or fewer vs. more than one stool per day.

		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



Results from OpenStat

Results Window

Return

COMPARISON OF TWO PROPORTIONS

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

Sample		2		
		0	1	sum
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

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	0	1	sum
0	25	15	40
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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

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Questions/Comments

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Next lecture's highlights

Research questions about two groups