BIOS 6611

**Biostatistical Methods I**

**Self-assessment Homework #5**

1. Suppose a clinical trial is conducted to test the efficacy of a new drug in the treatment of *Chlamydia* (a sexually transmitted disease that can lead to infertility) in females. Forty patients are given a 4g daily dose of the drug and are seen 1 week later, at which time 4 of the patients still have *Chlamydia*.

a) What is the best point estimate for *p*, the probability of a failure with the drug?

N=40 X=4

**p-hat = 4/40 = 0.10**

**10% probability of drug failure**

b) What is a two-sided 95% confidence interval (CI) for *p* with this drug. Obtain also the respective 90% and 99% CI. Interpret each CI in your own words.

Check: npq > 5

(40)(.10)(.90) = 3.6 < 5

\*Must use exact method for approximating the confidence intervals.

**DATA** hw6;

INPUT fail wt;

CARDS;

1 36

0 4

;

**RUN**;

**PROC** **FORMAT**;

VALUE tx\_fail **0** = 'Yes' **1** = 'No';

**RUN**;

95% CI:

**PROC** **FREQ** DATA=hw6;

TABLES fail / BINOMIAL (LEVEL = 'Yes') ALPHA = **.05**;

WEIGHT wt;

FORMAT fail tx\_fail.;

title '95% Confidence Interval for Failure';

**RUN**;

|  |
| --- |
| ***95% Confidence Interval for Failure*** |

The FREQ Procedure

| **fail** | **Frequency** | **Percent** | **Cumulative Frequency** | **Cumulative Percent** |
| --- | --- | --- | --- | --- |
| **Yes** | 4 | 10.00 | 4 | 10.00 |
| **No** | 36 | 90.00 | 40 | 100.00 |

| **Binomial Proportion for fail = Yes** | |
| --- | --- |
| **Proportion** | 0.1000 |
| **ASE** | 0.0474 |
| **95% Lower Conf Limit** | 0.0070 |
| **95% Upper Conf Limit** | 0.1930 |
|  | |
| **Exact Conf Limits** |  |
| **95% Lower Conf Limit** | 0.0279 |
| **95% Upper Conf Limit** | 0.2366 |

Interpretation: I am 95% confident that the true population proportion of drug failure is between 2.8% and 23.7%.

90% CI:

**PROC** **FREQ** DATA=hw6;

TABLES fail / BINOMIAL (LEVEL = 'No') ALPHA = **.10**;

WEIGHT wt;

FORMAT fail tx\_fail.;

**RUN**;

|  |
| --- |
| ***90% Confidence Interval for Failure*** |

The FREQ Procedure

| **fail** | **Frequency** | **Percent** | **Cumulative Frequency** | **Cumulative Percent** |
| --- | --- | --- | --- | --- |
| **Yes** | 4 | 10.00 | 4 | 10.00 |
| **No** | 36 | 90.00 | 40 | 100.00 |

| **Binomial Proportion for fail = Yes** | |
| --- | --- |
| **Proportion** | 0.1000 |
| **ASE** | 0.0474 |
| **90% Lower Conf Limit** | 0.0220 |
| **90% Upper Conf Limit** | 0.1780 |
|  | |
| **Exact Conf Limits** |  |
| **90% Lower Conf Limit** | 0.0349 |
| **90% Upper Conf Limit** | 0.2144 |

Interpretation: I am 90% confident that the true population proportion of drug failure is between 3.5% and 21.4%.

99% CI:

**PROC** **FREQ** DATA=hw6;

TABLES fail / BINOMIAL (LEVEL = 'Yes') ALPHA = **.01**;

WEIGHT wt;

FORMAT fail tx\_fail.;

title '99% Confidence Interval for Failure';

**RUN**;

|  |
| --- |
| ***99% Confidence Interval for Failure*** |

The FREQ Procedure

| **fail** | **Frequency** | **Percent** | **Cumulative Frequency** | **Cumulative Percent** |
| --- | --- | --- | --- | --- |
| **Yes** | 4 | 10.00 | 4 | 10.00 |
| **No** | 36 | 90.00 | 40 | 100.00 |

| **Binomial Proportion for fail = Yes** | |
| --- | --- |
| **Proportion** | 0.1000 |
| **ASE** | 0.0474 |
| **99% Lower Conf Limit** | 0.0000 |
| **99% Upper Conf Limit** | 0.2222 |
|  | |
| **Exact Conf Limits** |  |
| **99% Lower Conf Limit** | 0.0173 |
| **99% Upper Conf Limit** | 0.2826 |

Interpretation: I am 99% confident that the true population proportion of drug failure is between 1.7% and 28.3%.

c) Suppose we know that the standard drug at a given daily dose for treating *Chlamydia* has an estimated 25% failure rate in treating *Chlamydia* over a large number of patients in several trials. What can be said in comparing the failure rates of the two drugs? Answer this for each level of confidence in (b).

\*To find the lower one-sided CI for failure rates of new drug with p-hat=0.10 I doubled the alpha value so that SAS would give me a confidence interval with the appropriate area in the upper tail. For example, the 90% one-sided CI uses an alpha of 0.20 indicating a total of 20% area in both tails but 10% area in the upper tail so using the upper bound estimate gives me the 90% lower one-sided CI. This could also be done with the nominal alpha levels (0.01, 0.05, 0.10) leading to a more conservative result.

**PROC** **FREQ** DATA=hw6;

TABLES fail / BINOMIAL (LEVEL = 'Yes') ALPHA = **.20**;

WEIGHT wt;

FORMAT fail tx\_fail.;

title '90% Lower One-Sided Confidence Interval for Failure';

**RUN**;

|  |
| --- |
| ***90% Lower One-Sided Confidence Interval for Failure*** |

The FREQ Procedure

| **Binomial Proportion for fail = Yes** | |
| --- | --- |
| **Proportion** | 0.1000 |
| **ASE** | 0.0474 |
| **80% Lower Conf Limit** | 0.0392 |
| **80% Upper Conf Limit** | 0.1608 |
|  |  |
| **Exact Conf Limits** |  |
| **80% Lower Conf Limit** | 0.0443 |
| **80% Upper Conf Limit**  10% area at both tails | 0.1900 |

Interpretation: The one-side confidence interval indicates that I am 90% confident that the new drug’s failure proportion does not exceed 19.0%. Since this is below what is expected with the standard drug, the new drug’s failure rate is an improvement over the old. The same conclusion would be reached if the two-sided 90% CI had been used.

**PROC** **FREQ** DATA=hw6;

TABLES fail / BINOMIAL (LEVEL = 'Yes') ALPHA = **.10**;

WEIGHT wt;

FORMAT fail tx\_fail.;

title '95% Lower One-Sided Confidence Interval for Failure';

**RUN**;

|  |
| --- |
| ***95% Lower One-Sided Confidence Interval for Failure*** |

The FREQ Procedure

| **Binomial Proportion for fail = Yes** | |
| --- | --- |
| **Proportion** | 0.1000 |
| **ASE** | 0.0474 |
| **90% Lower Conf Limit** | 0.0220 |
| **90% Upper Conf Limit** | 0.1780 |
|  |  |
| **Exact Conf Limits**  5% area at both tails |  |
| **90% Lower Conf Limit** | 0.0349 |
| **90% Upper Conf Limit** | 0.2144 |

Interpretation: The one-side confidence interval indicates that I am 95% confident that the new drug’s failure proportion does not exceed 21.4%. Since this is below what is expected with the standard drug, the new drug’s failure rate is an improvement over the old. The same conclusion would be reached if the two-sided 95% CI had been used.

**PROC** **FREQ** DATA=hw6;

TABLES fail / BINOMIAL (LEVEL = 'Yes') ALPHA = **.02**;

WEIGHT wt;

FORMAT fail tx\_fail.;

title '99% Lower One-Sided Confidence Interval for Failure';

**RUN**;

|  |
| --- |
| ***99% Lower One-Sided Confidence Interval for Failure*** |

The FREQ Procedure

| **Binomial Proportion for fail = Yes** | |
| --- | --- |
| **Proportion** | 0.1000 |
| **ASE** | 0.0474 |
| **98% Lower Conf Limit** | 0.0000 |
| **98% Upper Conf Limit** | 0.2103 |
|  |  |
| **Exact Conf Limits**  1% area at both tails |  |
| **98% Lower Conf Limit** | 0.0212 |
| **98% Upper Conf Limit** | 0.2636 |

Interpretation: The one-sided confidence interval indicates that I am 99% confident that the new drug’s failure proportion does not exceed 26.4%. Since this is above what is expected with the standard drug, the new drug’s failure rate is not an improvement over the old. The same conclusion would be reached if the two-sided 99% CI had been used.

2. Intake of high doses of beta carotene in food has been associated in many observational studies with a decreased incidence of cancer. As part of a clinical trial to determine beta carotene’s effect in reducing cancer incidence, a bioavailability comparison was made among 4 preparations of beta carotene taken daily. Levels of serum beta carotene were measured on 23 patients twice at baseline and at 6, 8, and 12 weeks. The Rosner dataset BETACAR.txt contains the data. The data are available on the course website under Files -> Data.

Follow the instructions for the SAS Lab 5 Exercise, p. 2.

1. Average the two baseline serum beta carotene values per subject. Subtract the average baseline value from the Week 12 serum beta-carotene value.

**DATA** beta;

INPUT preparation subject baseline\_1 baseline\_2 week\_6 week\_8 week\_10 week\_12;

CARDS;

1 71 298 116 174 178 218 190

1 73 124 146 294 278 244 262

1 80 176 200 276 286 308 334

1 83 116 180 164 238 308 226

1 90 152 142 290 300 270 268

1 92 106 106 246 206 304 356

2 78 114 110 280 220 178 210

2 82 106 114 114 176 100 104

2 84 100 100 144 114 154 142

2 85 92 92 164 116 140 112

2 87 212 212 354 430 352 382

2 89 92 94 160 200 150 170

3 72 180 162 432 336 440 472

3 79 186 198 242 252 240 336

3 88 202 208 476 408 414 416

3 94 192 160 264 252 320 350

3 95 80 88 160 152 208 226

4 74 174 182 206 268 202 232

4 75 252 234 590 594 522 566

4 76 210 230 474 500 472 444

4 77 162 152 202 204 140 180

4 86 68 64 262 216 214 216

4 93 74 72 218 164 218 184

;

**RUN**;

**PROC** **FORMAT**;

VALUE PREP **1** = 'SOL' **2**= 'ROCHE' **3**= 'BASF-30'

**4**= 'BASF-60';

**RUN**;

**DATA** BETA;

SET BETA;

AVG\_BASELINE = MEAN(BASELINE\_1, BASELINE\_2);

W12\_BASELINE = WEEK\_12 - AVG\_BASELINE;

**RUN**;

1. Use PROC MEANS to generate the 90%, 95%, and 99% confidence intervals of the mean change from baseline to Week 12 for each preparation (use the CLASS statement).

/\*90% CI FOR MEAN CHANGE\*/

**PROC** **MEANS** DATA=beta MEAN STDERR CLM

ALPHA=**0.10**;

VAR W12\_BASELINE;

CLASS PREPARATION;

FORMAT PREPARATION PREP.;

TITLE '90% CONFIDENCE INTERVAL FOR MEAN CHANGE';

**RUN**;

|  |
| --- |
| ***90% CONFIDENCE INTERVAL FOR MEAN CHANGE*** |

The MEANS Procedure

| **Analysis Variable : W12\_BASELINE** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **preparation** | **N Obs** | **Mean** | **Std Error** | **Lower 90% CL for Mean** | **Upper 90% CL for Mean** |
| **SOL** | **6** | 117.5000000 | 35.6471130 | 45.6693429 | 189.3306571 |
| **ROCHE** | **6** | 66.8333333 | 25.7117569 | 15.0228994 | 118.6437673 |
| **BASF-30** | **5** | 194.4000000 | 29.4458826 | 131.6258899 | 257.1741101 |
| **BASF-60** | **6** | 147.5000000 | 45.5461305 | 55.7223439 | 239.2776561 |

/\*95% CI FOR MEAN CHANGE\*/

**PROC** **MEANS** DATA=beta MEAN STDERR CLM

ALPHA=**0.05**;

VAR W12\_BASELINE;

CLASS PREPARATION;

FORMAT PREPARATION PREP.;

TITLE '95% CONFIDENCE INTERVAL FOR MEAN CHANGE';

**RUN**;

|  |
| --- |
| ***95% CONFIDENCE INTERVAL FOR MEAN CHANGE*** |

The MEANS Procedure

| **Analysis Variable : W12\_BASELINE** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **preparation** | **N Obs** | **Mean** | **Std Error** | **Lower 95% CL for Mean** | **Upper 95% CL for Mean** |
| **SOL** | **6** | 117.5000000 | 35.6471130 | 25.8661788 | 209.1338212 |
| **ROCHE** | **6** | 66.8333333 | 25.7117569 | 0.7391580 | 132.9275087 |
| **BASF-30** | **5** | 194.4000000 | 29.4458826 | 112.6451235 | 276.1548765 |
| **BASF-60** | **6** | 147.5000000 | 45.5461305 | 30.4199444 | 264.5800556 |

/\*99% CI FOR MEAN CHANGE\*/

**PROC** **MEANS** DATA=beta MEAN STDERR CLM

ALPHA=**0.01**;

VAR W12\_BASELINE;

CLASS PREPARATION;

FORMAT PREPARATION PREP.;

TITLE '99% CONFIDENCE INTERVAL FOR MEAN CHANGE';

**RUN**;

|  |
| --- |
| ***99% CONFIDENCE INTERVAL FOR MEAN CHANGE*** |

The MEANS Procedure

| **Analysis Variable : W12\_BASELINE** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **preparation** | **N Obs** | **Mean** | **Std Error** | **Lower 99% CL for Mean** | **Upper 99% CL for Mean** |
| **SOL** | **6** | 117.5000000 | 35.6471130 | -26.2342566 | 261.2342566 |
| **ROCHE** | **6** | 66.8333333 | 25.7117569 | -36.8401470 | 170.5068136 |
| **BASF-30** | **5** | 194.4000000 | 29.4458826 | 58.8283631 | 329.9716369 |
| **BASF-60** | **6** | 147.5000000 | 45.5461305 | -36.1485104 | 331.1485104 |

1. Which preparations appear to increase the serum levels of beta carotene? Why or why not? (Justify your answer using the information contained by the confidence limits). Comment on how the conclusions are similar or different, for each of the preparations, according to the level of confidence.

Interpretation: From the 90% CI for mean change in beta carotene levels it appears that all of the preparations increase serum beta carotene levels because the upper and lower limit values of the 90% confidence intervals are both positive indicating change. However, upon further inspection of the 90% CI, BASF-30 appears to have the largest effect on increasing beta carotene levels because the lower limit of its CI is the largest of all the other preparations. This observation is consistent over the 95% and 99% CI’s because BASF-30’s lower confidence limit remains positive and larger than the other preparations.

1. How would these CI differ if we assumed that the standard deviation were known and not estimated from the data, i.e. if we assumed σ known and not estimated by s? (Do not perform any calculations to answer this.)

Interpretation: If we assumed that σ was known we would be able to use Z-values and the standard normal distribution when calculating the CI which would give us narrower confidence intervals. This is because the standard normal distribution has lighter tails that the t-distribution.

1. How comfortable are you with assuming that the sampling distribution of mean change in serum beta carotene follows a normal or a t-distribution, i.e. do you think the conditions for invoking the CLT apply here? Why or why not?

Interpretation: The number of observations (n=23) does not meet the general criteria for applying the CLT (n>30). Although n is small, the distribution appears mostly symmetric (with a slight negative skew) which lends some support for the mean change in beta carotene being normally distributed and that the t-distribution can be used to standardize (because the variance is unknown). (cont’d below)

If the individual groups are examined, because of the small sample sizes it is really too hard to tell one way or another if change in beta carotene is normally distributed within a preparation group.

See code and output below.

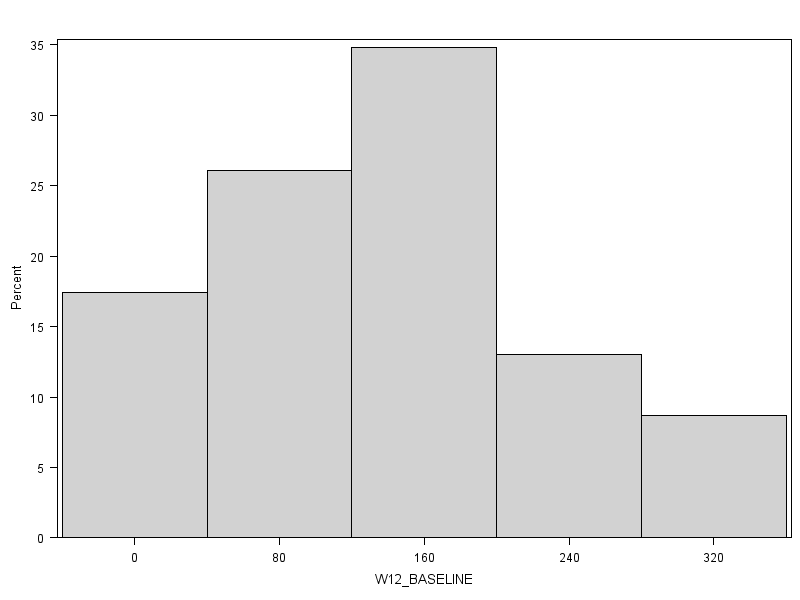
**PROC** **UNIVARIATE** DATA=BETA PLOT;

VAR W12\_BASELINE;

HISTOGRAM W12\_BASELINE;

**RUN**;

| **Location** | |
| --- | --- |
| **Mean** | 128.8261 |
| **Median** | 127.0000 |



1. How would you modify the SAS code to obtain one-sided CI for  = 0.10, 0.05, and 0.01? (Only code is needed to answer this.)

Interpretation: To get one-sided confidence intervals use the option UCLM or LCLM instead of the CLM option in the PROC MEANS statement while keeping the alpha value the same. For example, in the case of mean change, I would want to see at least a minimum value of change so I would calculate an upper one-sided confidence interval as demonstrated below:

/\*99% UPPER ONE-SIDED CI FOR MEAN CHANGE\*/

**PROC** **MEANS** DATA=beta MEAN STDERR LCLM

ALPHA=**0.01**;

VAR W12\_BASELINE;

CLASS PREPARATION;

FORMAT PREPARATION PREP.;

TITLE '99% UPPER ONE-SIDED CONFIDENCE INTERVAL FOR MEAN CHANGE';

**RUN**;

|  |
| --- |
| ***99% UPPER ONE-SIDED CONFIDENCE INTERVAL FOR MEAN CHANGE*** |

The MEANS Procedure

| **Analysis Variable : W12\_BASELINE** | | | | |
| --- | --- | --- | --- | --- |
| **preparation** | **N Obs** | **Mean** | **Std Error** | **Lower 99% CL for Mean** |
| **SOL** | **6** | 117.5000000 | 35.6471130 | -2.4500400 |
| **ROCHE** | **6** | 66.8333333 | 25.7117569 | -19.6849289 |
| **BASF-30** | **5** | 194.4000000 | 29.4458826 | 84.0678272 |
| **BASF-60** | **6** | 147.5000000 | 45.5461305 | -5.7595407 |