Biostatistics 140.623
Third Term, 2017-2018

Laboratory Exercise 1
Answer Key

1) Your job is to design a prospective clinical trial to determine whether a new drug reduces the symptoms of schizophrenia more effectively than a placebo. This "Phase III" trial will be used as a key part of a "New Drug Application" (NDA) submitted to the FDA. You will have to show your drug is "statistically significantly" better than placebo with $\alpha = .05$.

   The usual design is to measure the change in PANSS (Positive + Negative Symptoms of Schizophrenia) score (higher is worse symptoms) from baseline to 8 weeks after start of treatment. In past studies with similar patients, the average (std dev) change for placebo was –10 (10) units. You expect the new drug will reduce symptoms by an average value of –12 to –16 units and have a similar standard deviation to that observed for placebo.

   a) How many patients are needed in the placebo group to estimate the mean reduction in symptoms to within ±1 unit on the PANSS scale? ±2 units?

   $$\pm d = \pm 1.96 s / \sqrt{n}$$

   $$n = (1.96)^2 s^2 / d^2$$

   $n = 3.84(10)^2 / 1^2 = 384$ patients if d=1

   $\boldsymbol{n = 3.84(10)^2 / 2^2 = 96}$ patients if d=2

   b) How many patients are needed in each group to estimate the difference in change between the new drug and placebo groups to within ±1 unit on the PANSS scale? ±2 units?

$\pm d = \pm 1.96\sqrt{\frac{s_1^2}{n} + \frac{s_2^2}{n}}$ but we will assume that $s_1 = s_2$

$$\pm d = \pm 1.96 s\sqrt{\frac{2}{n}}$$

$$d^2 = (1.96)^2 s^2 \left(\frac{2}{n}\right)$$

$n = (1.96)^2 s^2 2 / d^2$ = 768 if d=1

$n = (1.96)^2 s^2 2 / d^2$ = 191 if d=2

c) Design a table to show the sample size per group necessary to obtain 90% power to reject the null hypothesis that the two groups have equivalent changes in average PANSS score using a significance level of 0.05. Vary the true difference among 1, 2, and 5 units; vary the standard deviation of a person's change between 10 and 12 units.

True Difference	Standard Deviation	Sample Size per Group
1	10	2102
1	12	3027
2	10	526
2	12	757
5	10	85
5	12	122

d) How might this table be altered to take account of other important events that commonly occur in clinical trials?

One could inflate the sample size for losses-to-follow-up in each treatment group over time. What is the anticipated percentage lost to follow-up? 5 – 15 %?

Also for discussion: What is a clinically meaningful difference? A large sample size may reveal a 1 or 2 unit change as a statistically significant change but is it meaningful?


```
. sampsi 0 1 , p(0.9) r(1) sd1(10) sd2(10)
Estimated sample size for two-sample comparison of means

Test Ho: m1 = m2, where m1 is the mean in population 1
                    and m2 is the mean in population 2
Assumptions:
         alpha =   0.0500  (two-sided)
         power =   0.9000
            m1 =        0
            m2 =        1
           sd1 =       10
           sd2 =       10
         n2/n1 =     1.00

Estimated required sample sizes:

            n1 =     2102
            n2 =     2102
```

```
. sampsi 0 1 , p(0.9) r(1) sd1(12) sd2(12)
Estimated sample size for two-sample comparison of means

Test Ho: m1 = m2, where m1 is the mean in population 1
                    and m2 is the mean in population 2
Assumptions:
         alpha =   0.0500  (two-sided)
         power =   0.9000
            m1 =        0
            m2 =        1
           sd1 =       12
           sd2 =       12
         n2/n1 =     1.00

Estimated required sample sizes:

            n1 =     3027
            n2 =     3027
```

```
. sampsi 0 2 , p(0.9) r(1) sd1(10) sd2(10)
Estimated sample size for two-sample comparison of means

Test Ho: m1 = m2, where m1 is the mean in population 1
                    and m2 is the mean in population 2
Assumptions:
         alpha =   0.0500  (two-sided)
         power =   0.9000
            m1 =        0
            m2 =        2
           sd1 =       10
           sd2 =       10
         n2/n1 =     1.00
Estimated required sample sizes:

            n1 =      526
            n2 =      526
```



```
. sampsi 0 2 , p(0.9) r(1) sd1(12) sd2(12)
Estimated sample size for two-sample comparison of means
Test Ho: m1 = m2, where m1 is the mean in population 1
                    and m2 is the mean in population 2
Assumptions:
         alpha =   0.0500  (two-sided)
         power =   0.9000
            m1 =        0
            m2 =        2
           sd1 =       12
           sd2 =       12
         n2/n1 =     1.00

Estimated required sample sizes:

            n1 =      757
            n2 =      757
```

```
. sampsi 0 5 , p(0.9) r(1) sd1(10) sd2(10)
Estimated sample size for two-sample comparison of means
Test Ho: m1 = m2, where m1 is the mean in population 1
                    and m2 is the mean in population 2
Assumptions:
         alpha =   0.0500  (two-sided)
         power =   0.9000
            m1 =        0
            m2 =        5
           sd1 =       10
           sd2 =       10
         n2/n1 =     1.00

Estimated required sample sizes:

            n1 =       85
            n2 =       85
```

```
. sampsi 0 5 , p(0.9) r(1) sd1(12) sd2(12)
Estimated sample size for two-sample comparison of means
Test Ho: m1 = m2, where m1 is the mean in population 1
                    and m2 is the mean in population 2
Assumptions:
           alpha =   0.0500  (two-sided)
         power =   0.9000
            m1 =        0
            m2 =        5
           sd1 =       12
           sd2 =       12
         n2/n1 =     1.00

Estimated required sample sizes:
            n1 =      122
            n2 =      122
```