Homework 3 (due Mon, Jan 27):

Download this software program to do this week's homework exercises:
http://biostat.mc.vanderbilt.edu/wiki/Main/PowerSampleSize
Otherwise, use STATA or SAS or SPSS or your own favorite package.

Example 1:

- Outcome: Forced expiratory volume in one second (FEV_1), measured in liters
- Intervention: E = experimental asthma therapy; C = control asthma therapy.
- Design: Use inhaler for 7 days, as needed. Measure the outcome once per participant, at Day 7.

1.1 From the list of outcome types on p.9, what is the likely distribution of this outcome?

1.2 Express the study objective as a two-sided hypothesis using statistical notation (choose from parameters used in class, Lecture 3).

1.3 Calculate the sample size needed to detect a difference between therapies of δ=0.25 L when the standard deviation is σ=0.75 L, the type-1 error rate is α=0.05, the type-2 error rate is β=0.10, and equal allocation to arms is planned ($\gamma = n_E/n_C = 1$). Use the following formula for the control-arm sample size:

$$n_C = \left(\frac{\gamma + 1}{\gamma}\right)\frac{(z_{1-\alpha/2} + z_{1-\beta})^2}{(\delta/\sigma)^2}$$

1.4 What is the combined sample size across arms?

1.5 Repeat this calculation using software, such as STATA (twomeans) or SAS (proc power), and provide a screenshot of your output.

1.6 What statistical summaries of the intervention-outcome relationship are most likely of interest to report?

1.7 Suppose you have funding to study $n_C + n_E = 300$ participants. Use algebra to convert the formula above to enable you to calculate the smallest value of δ that can be detected. Is this a clinically relevant value? Should you proceed with the trial?

Example 2:

- Outcome: Oral candidiasis lesion present after 3 weeks of asthma inhaler use
- Intervention: E = experimental asthma therapy; C = control asthma therapy
- Design: Use inhaler for 3 weeks, as needed. Measure the outcome once per participant, at Day 21.

2.1 From the list of outcome types on p.9, what is the likely distribution of this outcome?

2.2 Express the study objective as a two-sided hypothesis using statistical notation (choose from parameters used in class, Lecture 3).

2.3 If there is no difference between arms, the unbiased estimate of (i) the proportion of participants with a lesion is

$$\bar{p} = \left(\frac{\gamma}{\gamma+1}\right)p_E + \left(\frac{1}{\gamma+1}\right)p_C$$

and (ii) the standard deviation is $\sigma = \sqrt{\bar{p}(1-\bar{p})}$. Calculate the sample size needed to detect a difference between therapies of $\delta = \pi_E - \pi_C$ = 0.25, when $\pi_C = 0.25$, the type-1 error rate is α=0.05, the type-2 error rate is β=0.20, and equal allocation to arms is planned (γ = 1). Use the sample-size formula above to calculate n_C.

2.4 What is the combined sample size across arms?

2.5 Repeat this calculation using software, such as STATA or SAS, and provide a screenshot of your output.

2.5.1 http://www.ats.ucla.edu/stat/stata/dae/proportionpow.htm

2.6 What statistical summaries of the intervention-outcome relationship are most likely of interest to report?

Recommended Reading:

- Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med. 2013 Feb 5;158(3):200-7.
- Chan AW, Tetzlaff JM, Gøtzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ. 2013 Jan 8;346:e7586.