1. (10 pts) Suppose we would like to compare a new treatment (treatment 1) to the standard treatment (treatment 2) in reducing weight where treatment assignment will be done by permuted block randomization so that the two-sample t-test will be appropriate to compare these two treatments. Assume the population variance of the weight distribution is 100. We wish to detect a 5 unit weight difference between the new treatment and the standard treatment with 80% power at the significance level $\alpha = 0.01$ using a two-sided t-test.

(a) Find the necessary sample size for the study for the given design characteristics assuming equal allocation.

(b) If the size of the treatment effect turned out to be what you expected, what is the p-value?

(c) How large should the estimated treatment effect be to make the p-value significant ($\leq 0.01$)?

2. (10 pts) Suppose we want to compare the response rates of 2 new treatments (treatments 1 and 2) to the standard treatment (treatment 3) in the market in a phase III clinical trial. The best guess of the response rate for treatment 3 is 0.35. We would like to detect a 10% increase in the response rates for either treatment 1 or treatment 2 using the testing procedure(s) developed in class at significance level 0.05 with power 90%. Assume equal allocation. How large should the sample size be for the study?

3. (20 pts) Suppose we use the following test statistic for testing $H_0 : \pi_1 \leq \pi_2$ vs. $H_a : \pi_1 > \pi_2$

$$T = \frac{p_1 - p_2}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}}$$

where $p_1, p_2$ are sample proportions of patients responding to treatment 1 and treatment 2 respectively. Do the following:

(a) Derive the asymptotic distribution of $T$ under $\Delta = \pi_1 - \pi_2 = 0$ and under $H_a : \Delta = \Delta_A$.

(b) Use the result in (a) to derive the sample size formula under equal allocation (assume significance level $\alpha$ and power $1 - \beta$ to detect a clinically important difference $\Delta_A$; use formula (6.1) on slide 216 for one-sided testing problem).
(c) Re-calculate the sample size using your formula for the problem on slides 227-228. Did you get similar sample size?