# Homework3

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## Part I. K-stage design

### i) What is the goal for Simon's two-stage design? (10%)

- minimize the number of patients exposed to a possibly ineffective therapy.
- minimize the sample size under the constraint imposed by the operating characteristics of the design

### ii) What is the null and alternative hypothesis for Simon's two-stage design? (10%)

$H_0$: the true response rate is less than or equal to some pre-specified value

$H_\alpha$: the true response rate is greater than some pre-specified value

### iii) How do you determine the sample size for Simon's two-stage design? (10%)

Two strategy:

- optimal design
- minimax design

### iv) What is the difference between minmax and optimal design for Simon's two-stage procedure? (10%)

Optimal design aim to minimize the expected number of patients treated under $H_0$, while minimax design aim to minimize the total number of patients enrolled in the study.

### v) What are the drawbacks for Simon's two-stage design? (10%)

May not allow early termination even if there is a long run of failures for $p_0 = 0.10$ and above

### vi) How can you overcome the drawbacks? (10%)

Using k-stage designs.

## Part II. Write the statistical section of a protocol for a non-superiority trial comparing a testing drug to an placebo control using a continuous outcome.

We set the hypothesis as $H_0$: $p_T - p_C \geq \Delta$, $H_1$: $p_T - p_C < \Delta$. And choose type I error 0.2 and type II error 0.05, and choose superior threshold $\Delta = 0.1$, where we got all them from corresponding superiority trial.

And we will be using one-sided t test, where $t_0 = \frac{\hat{p}_T - \hat{p}_C - \Delta_0}{\sigma\sqrt{1/n_T + 1/n_C}}$. And $\Delta_0 = (Z_\alpha + Z_\beta)\sigma\sqrt{\frac{1}{n_T} - \frac{1}{n_C}}$.

Given that we could calculate the sample size as $N = (Z_\alpha + Z_\beta)^2 \times [p_T(1-p_T) + p_C(1-p_C)]/\Delta^2$. Therefore the necessary number of patients would be 2N.

- If we reject $H_0$, we could state that there is sufficient evidence to support that treatment is not much better than placebo, so we should stop trial.
- If we fail to reject $H_0$, we cannot rule out that treatment is much better than placebo, so we can move forward to next stage.