Homework 3: DATA130048

Biostatistics

Due Thursday, June 18th, 2020

1 Problem 1: 40pt

Assume we are designing a dose finding Phase I study and the outcome is binary with response / no response. We want to use a logistic model and aim to find the maximum tolerable dose (MTD) with $\theta = 0.25$. Using the following prior distribution combinations for γ and ρ_0 to find the next dose for this trial for the following settings. Use the 25th percentile of the posterior distribution as a next dose and round this to the closest 10 mg/m^2 dose.

- The first two doses are 50 mg/m^2 and 100 mg/m^2 and you did not observe any toxicity for these two patients.
- You observed following results from the first 12 patients.

$$x : (50; 100; 150; 200; 225; 250; 275; 300; 325; 325; 325; 350)$$
$$y : (0; 0; 0; 0; 0; 0; 0; 0; 1; 0; 0; 1)$$

  - γ is uniform on [50, 400] mg/m^2, ρ_0 is uniform on [0, 0.2]
  - γ is uniform on [50, 650] mg/m^2, ρ_0 is uniform on [0, 0.2]
  - γ is uniform on [50, 400] mg/m^2, ρ_0 is uniform on [0, 0.25]
  - γ is uniform on [50, 650] mg/m^2, ρ_0 is uniform on [0, 0.25]

Question

- Are the next dose levels for these prior distribution similar or different? Comment on the results whether the posterior 25th percentile of γ is sensitive to the choice of those prior distributions for γ and ρ_0 after 2 patients and after 12 patients. Why do you think they are different or similar?
- Note: You can modify the code provided to solve this problem. Summarizing your results in a table like the following would be helpful.

2 Problem 2: 60 pt

Assume, we want to assess the efficacy of a new drug compared to a standard therapy in a Phase II trial. The success rate with the standard therapy is around 40%. It is expected that the response rate will be around 60% with the new treatment. We want the type I error rate of the study to be at most 10% and reach 90% power.

Prior Dist	Next Dose	
	After 2 patients	After 12 patients
$\gamma \sim Unif[50, 400], \rho_0 \sim Unif[0, 0.2]$		
$\gamma \sim Unif[50, 650], \rho_0 \sim Unif[0, 0.2]$		
$\gamma \sim Unif[50, 400], \rho_0 \sim Unif[0, 0.25]$		
$\gamma \sim Unif[50, 650], \rho_0 \sim Unif[0, 0.25]$		

- What are the stopping rules with the Simon's optimal design?
- Assume, after observing the first 10 patients, we want to monitor the trial continuously for efficacy or futility. Also assume that the prior distribution for the response is Beta(0.3; 0.7): What are the stopping rules with Bayesian predictive probabilities for N_{max} = 41?
- Create a table similar to Table 4.2 on page 45 in lecture notes (Phase II 2) for N_{max} = 41 to 46.
- Compare Simon's optimal design and Bayesian predictive probabilities designs for this setting (p_0 = 0.4, p_1 = 0.6, $\alpha = \beta = 0.1$).