1. Apply the Continual Reassessment Method (1990) to design a phase I trial with 4 study dose levels for a target toxicity probability 0.17 (i.e., 1/6) and cohorts of size 2, using prior toxicity probabilities (.05, .15, .30, .45) (which is the prior information based on previous study or animal study so-called model skeleton fixed probabilities). Use the computer program "CRMsimulator" available from the online calculator: https://www.trialdesign.org/one-page-shell.html#BMACRM):

   a) Explain the model and method briefly (how to set a model and how to estimate parameters).

   b) Evaluate the CRM design for 3 different scenarios (the table below) based on 10000 simulations. For each scenario, do two different simulations using maximum sample sizes 20 and 36, respectively (here we are doing sensitivity analysis on sample size). Please report (1) mean number of patients and (2) the probability of "selected dose" in each dose level. Please complete the following table to summarize your simulation result:

Scenario	Dose level	True Toxicity Probability	Mean Number of Patients	Probability of Selected Dose
1	1	0.10		
	2	0.20		
	3	0.30		
	4	0.50		
2	1	0.20		
	2	0.30		
	3	0.45		
	4	0.60		
3	1	0.25		
	2	0.35		
	3	0.45		
	4	0.55		

   c) Repeat (b) (with maximum sample size 20 and 36, respectively) using another prior of skeletons (.15, .20, .25, .30). (here we are doing sensitivity analysis on prior toxicity probabilities)

2. Redo part (b) in Question 2 with a "3+3" design based on 10000 simulations. Note that the sample size in "3+3" design is determined by the algorithm automatically.

    a) Please report (i) mean number of patients and (ii) the probability of "exceed MTD" in each dose level. (Note: this is not equal to probability of selected dose, why?)

Scenario	Dose level	True Toxicity Probability	Mean Number of Patients	Probability of Exceeding MTD
1	1	0.10		
	2	0.20		
	3	0.30		
	4	0.50		
2	1	0.20		
	2	0.30		
	3	0.45		
	4	0.60		
3	1	0.25		
	2	0.35		
	3	0.45		
	4	0.55		

    b) How do you like this "3+3" design, in comparison with the "CRM" in Question 2? Discuss the pros and cons between two methods, based on the simulation results.