Assignment 2

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library(tidyverse)

## Question 1

Let trueDLT = true DLT probability, sp = selection probability, anTreat = average number of patients treated, anDLT = average number of patients with DLT. The table of the 3+3 design is shown below

# Question 1  
get\_res = function(i,p){  
 res = rbinom(3,1,p)  
 res = rbind(rep(i,3),res)  
 return(res)  
}  
dose1 = rbind(c(1:5), c(0.017, 0.043, 0.10, 0.22, 0.41))

sim3p3 = function(dose, N = 1000){  
 mtd\_v = rep(NA,1000)  
 com\_trail = c(0,0)  
 for (j in 1:N) {  
 mtd = 0  
 trail = c(0,0)  
 for (i in 1:5) {  
 res = get\_res(dose[1,i], dose[2,i])  
 trail = cbind(trail, res)  
 if (sum(res[2,])>=2) {  
 mtd = i-1  
 break  
 } else if(sum(res[2,]==1)){  
 ext\_res = get\_res(dose[1,i], dose[2,i])  
 trail= cbind(trail,ext\_res)  
 res = cbind(res, ext\_res)  
 if(sum(res[2,])>=2) {  
 mtd = i-1  
 break  
 }  
 }  
 mtd = i  
 }  
 mtd\_v[j] = mtd  
 com\_trail = cbind(com\_trail, trail[,-1])  
 }  
 trail\_res = t(com\_trail[,-1])  
 colnames(trail\_res) = c("dose", "res")  
 return(list(mtd = mtd\_v, trail\_res = trail\_res))  
}

show\_table = function(sim3p3, dose){  
 sp = table(sim3p3$mtd)  
 per\_m = sim3p3$trail\_res %>%   
 as.data.frame() %>%   
 group\_by(dose) %>%   
 summarize(n = n(),  
 DLT = sum(res)) %>%   
 mutate(anTreat = n/1000,  
 anDLT = DLT/1000,  
 s = as.numeric(sp[c(2:6)]),  
 sp = s/1000)   
 per\_m$trueDLT = as.numeric(dose[2,])  
 per\_m %>%   
 select(dose, trueDLT, sp, anTreat, anDLT) %>%   
 knitr::kable()  
}

set.seed(123)  
sim3p31 = sim3p3(dose1)  
show\_table(sim3p31,dose1)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.017 | 0.019 | 3.132 | 0.045 |
| 2 | 0.043 | 0.075 | 3.354 | 0.141 |
| 3 | 0.100 | 0.293 | 3.609 | 0.331 |
| 4 | 0.220 | 0.425 | 3.828 | 0.824 |
| 5 | 0.410 | 0.187 | 2.628 | 1.063 |

## Question 2

set.seed(123)  
# a  
dose2 = rbind(c(1:5), c(0.10, 0.22, 0.41, 0.64, 0.81))  
sim3p32 = sim3p3(dose2)  
show\_table(sim3p32,dose2)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.10 | 0.310 | 3.660 | 0.327 |
| 2 | 0.22 | 0.427 | 3.819 | 0.841 |
| 3 | 0.41 | 0.181 | 2.640 | 1.060 |
| 4 | 0.64 | 0.005 | 0.687 | 0.455 |
| 5 | 0.81 | NA | 0.015 | 0.014 |

# b  
dose3 = rbind(c(1:5), c(0.043, 0.10,0.22, 0.41, 0.64))  
sim3p33 = sim3p3(dose3)  
show\_table(sim3p33, dose3)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.043 | 0.077 | 3.381 | 0.159 |
| 2 | 0.100 | 0.321 | 3.633 | 0.340 |
| 3 | 0.220 | 0.404 | 3.786 | 0.865 |
| 4 | 0.410 | 0.159 | 2.439 | 0.992 |
| 5 | 0.640 | 0.012 | 0.627 | 0.393 |

dose4 = rbind(c(1:5), c(0.007, 0.017, 0.043, 0.10, 0.22))  
sim3p34 = sim3p3(dose4)  
show\_table(sim3p34, dose4)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.007 | 0.003 | 3.045 | 0.016 |
| 2 | 0.017 | 0.023 | 3.153 | 0.056 |
| 3 | 0.043 | 0.113 | 3.306 | 0.136 |
| 4 | 0.100 | 0.251 | 3.624 | 0.400 |
| 5 | 0.220 | 0.609 | 3.585 | 0.728 |

dose5 = rbind(c(1:5), c(0.003, 0.007, 0.017, 0.043, 0.10))  
sim3p35 = sim3p3(dose5)  
show\_table(sim3p35, dose5)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.003 | 0.001 | 3.024 | 0.010 |
| 2 | 0.007 | 0.021 | 3.066 | 0.024 |
| 3 | 0.017 | 0.074 | 3.123 | 0.045 |
| 4 | 0.043 | 0.902 | 3.312 | 0.137 |
| 5 | 0.100 | NA | 3.597 | 0.329 |

## Question 3

### a)

show\_CRM = function(sim, PI){  
 res\_table = data.frame(dose = c(1:5), trueDLT = PI, sp = sim$MTD, anTreat = sim$level, anDLT = sim$tox)  
 res\_table %>%   
 knitr::kable()  
}

Perfomance metrics of 3+3 design and CRM with different does-toxicity curves are shown below.

library(dfcrm)  
set.seed(123)  
p0 = c(0.08, 0.14, 0.25, 0.37, 0.52)  
# 1  
PI1 = c(0.017, 0.043, 0.010, 0.22, 0.41)  
sim1 = crmsim(PI1, p0, 0.1, 31, x0=3, nsim = 1000, count = FALSE)  
show\_CRM(sim1, PI1)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.017 | 0.014 | 1.069 | 0.018 |
| 2 | 0.043 | 0.038 | 2.822 | 0.132 |
| 3 | 0.010 | 0.545 | 16.021 | 0.155 |
| 4 | 0.220 | 0.395 | 9.587 | 2.101 |
| 5 | 0.410 | 0.008 | 1.501 | 0.662 |

show\_table(sim3p31,dose1)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.017 | 0.019 | 3.132 | 0.045 |
| 2 | 0.043 | 0.075 | 3.354 | 0.141 |
| 3 | 0.100 | 0.293 | 3.609 | 0.331 |
| 4 | 0.220 | 0.425 | 3.828 | 0.824 |
| 5 | 0.410 | 0.187 | 2.628 | 1.063 |

# 2  
PI2 = c(0.10, 0.22, 0.41, 0.64, 0.81)  
sim2 = crmsim(PI2, p0, 0.1, 31, x0=3, nsim = 1000, count = FALSE)  
show\_CRM(sim2, PI2)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.10 | 0.859 | 23.800 | 2.395 |
| 2 | 0.22 | 0.139 | 4.599 | 1.041 |
| 3 | 0.41 | 0.002 | 2.291 | 0.957 |
| 4 | 0.64 | 0.000 | 0.280 | 0.183 |
| 5 | 0.81 | 0.000 | 0.030 | 0.025 |

show\_table(sim3p32,dose2)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.10 | 0.310 | 3.660 | 0.327 |
| 2 | 0.22 | 0.427 | 3.819 | 0.841 |
| 3 | 0.41 | 0.181 | 2.640 | 1.060 |
| 4 | 0.64 | 0.005 | 0.687 | 0.455 |
| 5 | 0.81 | NA | 0.015 | 0.014 |

# 3  
PI3 = c(0.043, 0.10, 0.22, 0.41, 0.64)  
sim3 = crmsim(PI3, p0, 0.1, 31, x0=3, nsim = 1000, count = FALSE)  
show\_CRM(sim3, PI3)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.043 | 0.317 | 11.956 | 0.516 |
| 2 | 0.100 | 0.545 | 11.075 | 1.135 |
| 3 | 0.220 | 0.135 | 6.579 | 1.423 |
| 4 | 0.410 | 0.003 | 1.104 | 0.453 |
| 5 | 0.640 | 0.000 | 0.286 | 0.185 |

show\_table(sim3p33,dose3)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.043 | 0.077 | 3.381 | 0.159 |
| 2 | 0.100 | 0.321 | 3.633 | 0.340 |
| 3 | 0.220 | 0.404 | 3.786 | 0.865 |
| 4 | 0.410 | 0.159 | 2.439 | 0.992 |
| 5 | 0.640 | 0.012 | 0.627 | 0.393 |

# 4  
PI4 = c(0.007, 0.017, 0.043, 0.10, 0.22)  
sim4 = crmsim(PI4, p0, 0.1, 31, x0=3, nsim = 1000, count = FALSE)  
show\_CRM(sim4, PI4)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.007 | 0.004 | 1.034 | 0.011 |
| 2 | 0.017 | 0.040 | 2.738 | 0.040 |
| 3 | 0.043 | 0.285 | 10.217 | 0.413 |
| 4 | 0.100 | 0.535 | 11.523 | 1.124 |
| 5 | 0.220 | 0.136 | 5.488 | 1.239 |

show\_table(sim3p34,dose4)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.007 | 0.003 | 3.045 | 0.016 |
| 2 | 0.017 | 0.023 | 3.153 | 0.056 |
| 3 | 0.043 | 0.113 | 3.306 | 0.136 |
| 4 | 0.100 | 0.251 | 3.624 | 0.400 |
| 5 | 0.220 | 0.609 | 3.585 | 0.728 |

# 5  
PI5 = c(0.003, 0.007, 0.017, 0.043, 0.10)  
sim5 = crmsim(PI5, p0, 0.1, 31, x0=3, nsim = 1000, count = FALSE)  
show\_CRM(sim5, PI5)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.003 | 0.000 | 0.288 | 0.000 |
| 2 | 0.007 | 0.002 | 0.916 | 0.005 |
| 3 | 0.017 | 0.051 | 5.835 | 0.094 |
| 4 | 0.043 | 0.339 | 9.336 | 0.383 |
| 5 | 0.100 | 0.608 | 14.625 | 1.518 |

show\_table(sim3p35,dose5)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| dose | trueDLT | sp | anTreat | anDLT |
| 1 | 0.003 | 0.001 | 3.024 | 0.010 |
| 2 | 0.007 | 0.021 | 3.066 | 0.024 |
| 3 | 0.017 | 0.074 | 3.123 | 0.045 |
| 4 | 0.043 | 0.902 | 3.312 | 0.137 |
| 5 | 0.100 | NA | 3.597 | 0.329 |

By comparing performance metrics of 3+3 design and CRM design we can find that

1. The selection probability of true MTD in CRM design is always the highest among 5 doses, while the dose with the highest selection probability in 3+3 design is always the dose near MTD.
2. Average numbers of patients treated in 3+3 design is similar among each dose while in CRM, more people treated with MTD.
3. Average numbers of patients with DLT in CRM overall are larger than those in 3+3 design.

### b)

PCS = c(sim1$MTD[3], sim2$MTD[1], sim3$MTD[2], sim4$MTD[4], sim5$MTD[5])  
mean(PCS)

## [1] 0.6184

The probability of correctly selecting(PCS) the MTD average over the five scenarios is 0.6184.