

# Computing assignment 3

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Write code to run simulation for a two-armed trial (A vs B) according to the followings:

Each subject will be evaluated for a binary response, with probability  $p_A$  and  $p_B$  respectively for arm A and arm B;

- The total sample size is  $N = 120$ ;
- The trial enrolls in 4 blocks each with  $n = 30$  subjects in each block;
- In Block 1, subjects are randomized to arms A and B with equal probability.
- At the end of each block, update the randomization probabilities using Thompson's rule with no attenuation (i.e., set  $a = 1$ ).

1. Run 1,000 simulated trials under Scenario 1:  $p_A = p_B = 0.5$ .

(a) Perform a chi-squared test to compare A and B at the end of each trial. Record the proportion of trials with P-value less than 0.05.

```
simAR = function(pA=0.5, pB=0.5, N=120, n=30){  
  # block 1  
  assignment1 = rbinom(n,1,0.5) #1->A, 0->B  
  resA = rbinom(sum(assignment1), 1, pA)  
  resB = rbinom(n-sum(assignment1), 1, pB)  
  #response and nonresponse numbers  
  A1 = rep(NA, 4)  
  A0 = rep(NA, 4)  
  B1 = rep(NA, 4)  
  B0 = rep(NA, 4)  
  A1[1] = sum(resA)  
  A0[1] = length(resA)-A1[1]  
  B1[1] = sum(resB)  
  B0[1] = length(resB)-B1[1]  
  #pA, pB follows Beta(1,1)  
  alphaA = 1  
  betaA = 1  
  alphaB = 1  
  betaB = 1  
  # block 2-4  
  for (i in 2:4) {  
    #calcualte rA  
    alphaA = alphaA+sum(resA)  
    betaA = betaA+length(resA)-sum(resA)  
    alphaB = alphaB+sum(resB)  
    betaB = betaB+length(resB)-sum(resB)  
    sim_pA = rbeta(1000, alphaA, betaA)  
    sim_pB = rbeta(1000, alphaB, betaB)  
    rA = sum(sim_pA>sim_pB)/1000  
  }  
}
```

```

    #get simulation results
    assignment = rbinom(n,1,rA)
    resA = rbinom(sum.assignment), 1, pA)
    resB = rbinom(n-sum.assignment), 1, pB)
    #response and nonresponse numbers
    A1[i] = sum(resA)
    A0[i] = length(resA)-A1[i]
    B1[i] = sum(resB)
    B0[i] = length(resB)-B1[i]
  }
  res = rbind(A1,A0,B1,B0)
  return(res)
}

```

```

set.seed(123)
chi_res = rep(NA, 1000)
for (i in 1:1000) {
  res = simAR()
  sum_A1 = sum(res[1,])
  sum_A0 = sum(res[2,])
  sum_B1 = sum(res[3,])
  sum_B0 = sum(res[4,])
  sum_res = matrix(c(sum_A1, sum_B1, sum_A0, sum_B0), ncol = 2)
  chi_res[i] = chisq.test(sum_res)$p.value
}
mean(chi_res<0.05)

```

```
## [1] 0.035
```

The proportion of trials with P-value less than 0.05 is 0.035.

2. Run 1,000 simulated trials under Scenario 2:  $p_A = 0.3$  and  $p_B = 0.6$ .

(a) Perform a chi-squared test to compare A and B at the end of the each trial. Record the proportion of trials with P-value less than 0.05.

```

set.seed(123)
chi_res = rep(NA, 1000)
for (i in 1:1000) {
  res = simAR(pA=0.3, pB=0.6)
  sum_A1 = sum(res[1,])
  sum_A0 = sum(res[2,])
  sum_B1 = sum(res[3,])
  sum_B0 = sum(res[4,])
  sum_res = matrix(c(sum_A1, sum_B1, sum_A0, sum_B0), ncol = 2)
  chi_res[i] = chisq.test(sum_res)$p.value
}
mean(chi_res<0.05)

```

```
## [1] 0.677
```

The proportion of trials with P-value less than 0.05 is 0.677.

(b) For a non-adaptive, 1:1 randomized two-armed trial with  $n = 60$  in each arm, what is the power of a chi-squared test under Scenario B?

Power is the probability to accept alternative hypothesis when alternative hypothesis is true. In scenario 2, the null hypothesis is  $p_A = p_B$  and the alternative hypothesis is true. So the power is the probability to reject the null hypothesis.

```
non_ada = function(n = 60, pA = 0.3, pB = 0.6){
  # arm A
  resA = rbinom(n, 1, pA)
  resB = rbinom(n, 1, pB)
  A1 = sum(resA)
  A0 = n-A1
  B1 = sum(resB)
  B0 = n-B1
  res = c(A1, B1, A0, B0)
  return(res)
}
```

```
set.seed(123)
chi_res = rep(NA, 1000)
for (i in 1:1000) {
  res = non_ada()
  sum_res = matrix(res, ncol = 2)
  chi_res[i] = chisq.test(sum_res)$p.value
}
mean(chi_res<0.05)
```

```
## [1] 0.899
```

3. Perform Mantel Haenzel test to the data in Lecture 06 Adaptive randomization, slide #30.

```
data30 <- array(c(3, 1, 7, 9,
                  8, 1, 15, 6,
                  16, 2, 10, 2,
                  33, 1, 6, 0),
               dim = c(2, 2, 4),
               dimnames = list(ARM = c("ARM0", "ARM1"),
                               Response = c("R1", "R0"),
                               Block = 1:4))
mantelhaen.test(data30)
```

```
##
## Mantel-Haenszel chi-squared test with continuity correction
##
## data: data30
## Mantel-Haenszel X-squared = 1.1423, df = 1, p-value = 0.2852
## alternative hypothesis: true common odds ratio is not equal to 1
## 95 percent confidence interval:
## 0.6953671 8.3525664
## sample estimates:
## common odds ratio
## 2.41
```

As p-value is 0.2852 which is larger than 0.05, we cannot reject the null hypothesis and conclude that there is no association between trials and outcomes.

4. Run 1,000 simulated trials under Scenario 3:  $p_A = p_B = 0.3$  in Blocks 1 and 2, and improved response rate  $p_A = p_B = 0.6$  in Blocks 3 and 4.

(a) Perform a chi-squared test to compare A and B at the end of each trial. Record the proportion of trials with P-value less than 0.05.

```
simAR3 = function(N=120, n=30){
  # block 1
  assignment1 = rbinom(n,1,0.5) #1->A, 0->B
  resA = rbinom(sum(assignment1), 1, 0.3)
  resB = rbinom(n-sum(assignment1), 1, 0.3)
  #response and nonresponse numbers
  A1 = rep(NA, 4)
  A0 = rep(NA, 4)
  B1 = rep(NA, 4)
  B0 = rep(NA, 4)
  A1[1] = sum(resA)
  A0[1] = length(resA)-A1[1]
  B1[1] = sum(resB)
  B0[1] = length(resB)-B1[1]
  #pA, pB follows Beta(1,1)
  alphaA = 1
  betaA = 1
  alphaB = 1
  betaB = 1
  #calcualte rA
  alphaA = alphaA+sum(resA)
  betaA = betaA+length(resA)-sum(resA)
  alphaB = alphaB+sum(resB)
  betaB = betaB+length(resB)-sum(resB)
  sim_pA = rbeta(1000, alphaA, betaA)
  sim_pB = rbeta(1000, alphaB, betaB)
  rA = sum(sim_pA>sim_pB)/1000
  #get simulation results
  assignment = rbinom(n,1,rA)
  resA = rbinom(sum(assignment), 1, 0.3)
  resB = rbinom(n-sum(assignment), 1, 0.3)
  #response and nonresponse numbers
  A1[2] = sum(resA)
  A0[2] = length(resA)-A1[2]
  B1[2] = sum(resB)
  B0[2] = length(resB)-B1[2]
  # block 3-4
  for (i in 3:4) {
    #calcualte rA
    alphaA = alphaA+sum(resA)
    betaA = betaA+length(resA)-sum(resA)
    alphaB = alphaB+sum(resB)
    betaB = betaB+length(resB)-sum(resB)
    sim_pA = rbeta(1000, alphaA, betaA)
    sim_pB = rbeta(1000, alphaB, betaB)
    rA = sum(sim_pA>sim_pB)/1000
  }
}
```

```

#get simulation results
assignment = rbinom(n,1,rA)
resA = rbinom(sum(assignment), 1, 0.6)
resB = rbinom(n-sum(assignment), 1, 0.6)
#response and nonresponse numbers
A1[i] = sum(resA)
A0[i] = length(resA)-A1[i]
B1[i] = sum(resB)
B0[i] = length(resB)-B1[i]
}
res = rbind(A1,A0,B1,B0)
return(res)
}

```

```

set.seed(123)
chi_res = rep(NA, 1000)
for (i in 1:1000) {
  res = simAR3()
  sum_A1 = sum(res[1,])
  sum_A0 = sum(res[2,])
  sum_B1 = sum(res[3,])
  sum_B0 = sum(res[4,])
  sum_res = matrix(c(sum_A1, sum_B1, sum_A0, sum_B0), ncol = 2)
  chi_res[i] = chisq.test(sum_res)$p.value
}
mean(chi_res<0.05)

```

```
## [1] 0.308
```

The proportion of trials with P-value less than 0.05 is 0.308.

(b) Perform Mantel Haenzel test to compare A and B at the end of each trial. Record the proportion of trials with P-value less than 0.05.

```

set.seed(123)
ManH_res = rep(NA, 1000)
for (i in 1:1000) {
  res = simAR3()
  simAR3_data <- array(c(res[1,1], res[3,1], res[2,1], res[4,1],
                        res[1,2], res[3,2], res[2,2], res[4,2],
                        res[1,3], res[3,3], res[2,3], res[4,3],
                        res[1,4], res[3,4], res[2,4], res[4,4]),
                      dim = c(2, 2, 4),
                      dimnames = list(ARM = c("ARM0", "ARM1"),
                                       Response = c("R1", "R0"),
                                       Block = 1:4))
  ManH_res[i] = mantelhaen.test(simAR3_data)$p.value
}
mean(ManH_res<0.05)

```

```
## [1] 0.037
```

The proportion of trials with P-value less than 0.05 in Mantel Haenzel test is 0.037.