









```
markov1 <- function(rr = 1) {</pre>
  y0 < -c(1, 0, 0, 0)
  trans mat \leftarrow matrix(0, nrow = 4, ncol = 4)
  trans mat[1, ] \leftarrow c(0.721, 0.202, 0.067, 0.010)
  trans mat[2, 2:4] \leftarrow c(0.581, 0.407, 0.012)
  trans_{mat}[3, 3:4] \leftarrow c(0.750, 0.250)
  trans mat[4, 4] <- 1
  trans_mat[1, 2:4] <- trans_mat[1, 2:4] * rr</pre>
  trans mat[1, 1] <-1 - sum(trans <math>mat[1, 2:4])
  trans mat[2, 3:4] <- trans mat[2, 3:4] * rr</pre>
  trans mat[2, 2] <- 1 - sum(trans_mat[2, 3:4])</pre>
  trans mat[3, 4] \leftarrow trans mat[3, 4] * rr
  trans mat[3, 3] <- 1 - trans mat[3, 4]
  y store \leftarrow matrix(0, nrow = 20, ncol = 4)
  y store[1, ] <- y0 %*% trans mat
  for(i in 2:20){
    y store[i, ] <- y store[i-1, ] %*% trans mat
  sum(y store[, 1:3])
```

Above function is the markov function to multiply the state matrix with the transition matrix and finally calculate the sum of resultant matrix.

- **3a.** The best estimate for the relative risk r is  $\hat{r} = 0.509$ . Using this value, estimate the gain in life years for patients taking combination therapy versus monotherapy.
  - → For this we use the above defined function and calculate markov1(0.509)-markov1(1) which gives the result as 5.885. Thus the gain the life years using combination therapy is 5.88 as compared to monotherapy.
- **3b.** Because it was estimated from a trial containing a limited number of patients, there is considerable uncertainty regarding the estimate of the relative risk r. Briggs et al propose to model this uncertainty by modelling r as a log normal distribution, log r  $\sim$  N(-0.675, 0.16972). Using samples generated from this distribution, compute the expected number of life years gained by patients taking combination therapy versus monotherapy.
  - → For this we execute the below piece of code with the above function rnorm <- rlnorm(1000,meanlog=-0.675,sdlog=0.1697\*0.1697) flag=0 rnorm\_gain1=c() for(i in rnorm){ rnorm gain1[flag]=markov1(i)-markov1(1)</p>

```
flag=flag+1
}
mean(rnorm_gain1)
```

So after calculating the mean of rnorm\_gain, we get the output as **5.883 as the gain in** life (years) when r is modelled as a log normal distribution.

**3c.** Using the samples generated in b), compute lower and upper bounds  $y\alpha$  and  $y\beta$  such that  $P(y\alpha < y < y\beta) = 0.95$ , where y denotes the amount of life years gained by patients taking combination therapy versus monotherapy.

→ For this we use the quantile function

```
quantile(rnorm_gain1,c(0.025,0.975))
```

output:

```
> quantile(rnorm_gain1,c(0.025,0.975))
     2.5%    97.5%
5.434911 6.308285
```

Thus the lower and upper bounds are 5.4 and 6.31 respectively