Simple 3-state Markov model in R

with dependency for time-since model start AND with state-residency dependency

The DARTH workgroup

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- Jalal H, Pechlivanoglou P, Krijkamp E, Alarid-Escudero F, Enns E, Hunink MG. An Overview of R in Health Decision Sciences. Med Decis Making. 2017; 37(3): 735-746. https://journals.sagepub.com/doi/abs/10.1177/0272989X16686559
- Krijkamp EM, Alarid-Escudero F, Enns EA, Jalal HJ, Hunink MGM, Pechlivanoglou P. Microsimulation modeling for health decision sciences using R: A tutorial. Med Decis Making. 2018;38(3):400–22. https://journals.sagepub.com/doi/abs/10.1177/0272989X18754513
- Krijkamp EM, Alarid-Escudero F, Enns E, Pechlivanoglou P, Hunink MM, Jalal H. A Multidimensional Array Representation of State-Transition Model Dynamics. Med Decis Making. 2020 Online first. https://doi.org/10.1177/0272989X19893973

```r
rm(list = ls())      # clear memory (removes all the variables from the workspace)
```

01 Load packages

```r
# no packages required
```

02 Load functions

```r
# no functions required
```

03 Input model parameters

```r
# Strategy names
v_names_str <- c("Base Case")

# Number of strategies
n_str <- length(v_names_str)

# Markov model parameters
v_n  <- c("Healthy", "Sick", "Dead")    # state names
n_states  <- length(v_n)                # number of states
n_t  <- 60                              # number of cycles

# Tunnels
n_tunnel_size <- n_t
# Sick state
v_Sick_tunnels <- paste("Sick_", seq(1, n_tunnel_size), "Yr", sep = "")
# Create variables for time-dependent model
v_n_tunnels  <- c("Healthy", v_Sick_tunnels, "Dead")  # state names
n_states_tunnels  <- length(v_n_tunnels)              # number of states

p_HD <- seq(0.003, 0.01, length.out = n_t)  # probability of dying when sick (age-dependent) - this is
p_HS <- 0.05                                # probability of becoming sick when healthy, conditioned on
p_SD <- 0.1                                 # probability of dying when sick

# Weibull parameters
l <- 0.08
g <- 1.1
p_SD <- l*g*(1:n_tunnel_size)^{g-1}         # probability of dying when sick (time-in-state dependent)

# Costs and utilities
c_H  <- 400                                 # cost of one cycle in healthy state
c_S  <- 1000                                # cost of one cycle in sick state
c_D  <- 0                                   # cost of one cycle in dead state
u_H  <- 0.8                                 # utility when healthy
u_S  <- 0.5                                 # utility when sick
u_D  <- 0                                   # utility when dead
```

```r
d_e <- d_c <- 0.03                          # equal discount of costs and QALYs by 3%

# calculate discount weights for costs for each cycle based on discount rate d_c
v_dwc <- 1 / (1 + d_e) ^ (0:n_t)
# calculate discount weights for effectiveness for each cycle based on discount rate d_e
v_dwe <- 1 / (1 + d_c) ^ (0:n_t)
```

04 Define and initialize matrices and vectors

04.1 Cohort trace

```r
m_M <- matrix(NA,
              nrow = n_t + 1,  # create Markov trace (n_t + 1 because R doesn't understand
                               # Cycle 0)
              ncol = n_states_tunnels,
              dimnames = list(0:n_t, v_n_tunnels))

# The cohort starts as healthy
# initialize first cycle of Markov trace accounting for the tunnels
m_M[1, ] <- c(1, rep(0, n_tunnel_size), 0)
```

04.2 Transition probability array

```r
# create the transition probability array
a_P <- array(0,                                          # Create 3-D array
             dim = c(n_states_tunnels, n_states_tunnels, n_t),
             dimnames = list(v_n_tunnels, v_n_tunnels, 0:(n_t-1)))
```

Fill in the transition probability array:

```r
# from Healthy
a_P["Healthy", "Healthy", ]  <- 1 - p_HD - p_HS
a_P["Healthy", "Sick_1Yr", ] <- p_HS
a_P["Healthy", "Dead", ]     <- p_HD

# from Sick
for(i in 1:(n_tunnel_size - 1)){
  a_P[v_Sick_tunnels[i], v_Sick_tunnels[i + 1], ] <- 1 - p_SD[i]
  a_P[v_Sick_tunnels[i], "Dead", ] <- p_SD[i]
}

a_P[v_Sick_tunnels[n_tunnel_size], v_Sick_tunnels[n_tunnel_size], ] <- 1 - p_SD[n_tunnel_size]
a_P[v_Sick_tunnels[n_tunnel_size], "Dead", ] <- p_SD[n_tunnel_size]

# from Dead
a_P["Dead", "Dead", ] <- 1
```

04.3 Check if transition array and probabilities are valid

```
# Check if transition matrix is valid (i.e., each row should add up to 1)
valid <- apply(a_P, 3, function(x) sum(rowSums(x))==n_states_tunnels)
if (!isTRUE(all.equal(as.numeric(sum(valid)), as.numeric(n_t)))) {
  stop("This is not a valid transition Matrix")
}
```

05 Run Markov model

```
for (t in 1:n_t) {                          # loop through the number of cycles
  m_M[t + 1, ] <- m_M[t, ] %*% a_P[, , t]   # estimate the Markov trace for cycle t + 1
                                            # using the t-th matrix from the
                                            # probability array
}
head(m_M)
```

```
##     Healthy   Sick_1Yr   Sick_2Yr   Sick_3Yr   Sick_4Yr   Sick_5Yr
## 0 1.0000000 0.00000000 0.00000000 0.00000000 0.00000000 0.00000000
## 1 0.9470000 0.05000000 0.00000000 0.00000000 0.00000000 0.00000000
## 2 0.8966966 0.04735000 0.04560000 0.00000000 0.00000000 0.00000000
## 3 0.8489589 0.04483483 0.04318320 0.04129919 0.00000000 0.00000000
## 4 0.8036620 0.04244795 0.04088937 0.03911033 0.03724283 0.00000000
## 5 0.7606865 0.04018310 0.03871253 0.03703284 0.03526896 0.03347812
##   Sick_6Yr Sick_7Yr Sick_8Yr Sick_9Yr Sick_10Yr Sick_11Yr Sick_12Yr
## 0        0        0        0        0         0         0         0
## 1        0        0        0        0         0         0         0
## 2        0        0        0        0         0         0         0
## 3        0        0        0        0         0         0         0
## 4        0        0        0        0         0         0         0
## 5        0        0        0        0         0         0         0
##   Sick_13Yr Sick_14Yr Sick_15Yr Sick_16Yr Sick_17Yr Sick_18Yr Sick_19Yr
## 0         0         0         0         0         0         0         0
## 1         0         0         0         0         0         0         0
## 2         0         0         0         0         0         0         0
## 3         0         0         0         0         0         0         0
## 4         0         0         0         0         0         0         0
## 5         0         0         0         0         0         0         0
##   Sick_20Yr Sick_21Yr Sick_22Yr Sick_23Yr Sick_24Yr Sick_25Yr Sick_26Yr
## 0         0         0         0         0         0         0         0
## 1         0         0         0         0         0         0         0
## 2         0         0         0         0         0         0         0
## 3         0         0         0         0         0         0         0
## 4         0         0         0         0         0         0         0
## 5         0         0         0         0         0         0         0
##   Sick_27Yr Sick_28Yr Sick_29Yr Sick_30Yr Sick_31Yr Sick_32Yr Sick_33Yr
## 0         0         0         0         0         0         0         0
## 1         0         0         0         0         0         0         0
## 2         0         0         0         0         0         0         0
## 3         0         0         0         0         0         0         0
## 4         0         0         0         0         0         0         0
```

```
## 5         0         0         0         0         0         0         0
##   Sick_34Yr Sick_35Yr Sick_36Yr Sick_37Yr Sick_38Yr Sick_39Yr Sick_40Yr
## 0         0         0         0         0         0         0         0
## 1         0         0         0         0         0         0         0
## 2         0         0         0         0         0         0         0
## 3         0         0         0         0         0         0         0
## 4         0         0         0         0         0         0         0
## 5         0         0         0         0         0         0         0
##   Sick_41Yr Sick_42Yr Sick_43Yr Sick_44Yr Sick_45Yr Sick_46Yr Sick_47Yr
## 0         0         0         0         0         0         0         0
## 1         0         0         0         0         0         0         0
## 2         0         0         0         0         0         0         0
## 3         0         0         0         0         0         0         0
## 4         0         0         0         0         0         0         0
## 5         0         0         0         0         0         0         0
##   Sick_48Yr Sick_49Yr Sick_50Yr Sick_51Yr Sick_52Yr Sick_53Yr Sick_54Yr
## 0         0         0         0         0         0         0         0
## 1         0         0         0         0         0         0         0
## 2         0         0         0         0         0         0         0
## 3         0         0         0         0         0         0         0
## 4         0         0         0         0         0         0         0
## 5         0         0         0         0         0         0         0
##   Sick_55Yr Sick_56Yr Sick_57Yr Sick_58Yr Sick_59Yr Sick_60Yr       Dead
## 0         0         0         0         0         0         0 0.00000000
## 1         0         0         0         0         0         0 0.00300000
## 2         0         0         0         0         0         0 0.01035336
## 3         0         0         0         0         0         0 0.02172383
## 4         0         0         0         0         0         0 0.03664758
## 5         0         0         0         0         0         0 0.05463798
```

Create aggregated trace.

```
m_M_tunnels <- cbind(Healthy = m_M[, "Healthy"],
                Sick = rowSums(m_M[, 2:(n_tunnel_size + 1)]),
                Dead = m_M[, "Dead"])
head(m_M_tunnels) # show the first rows of the aggregated Markov trace
```

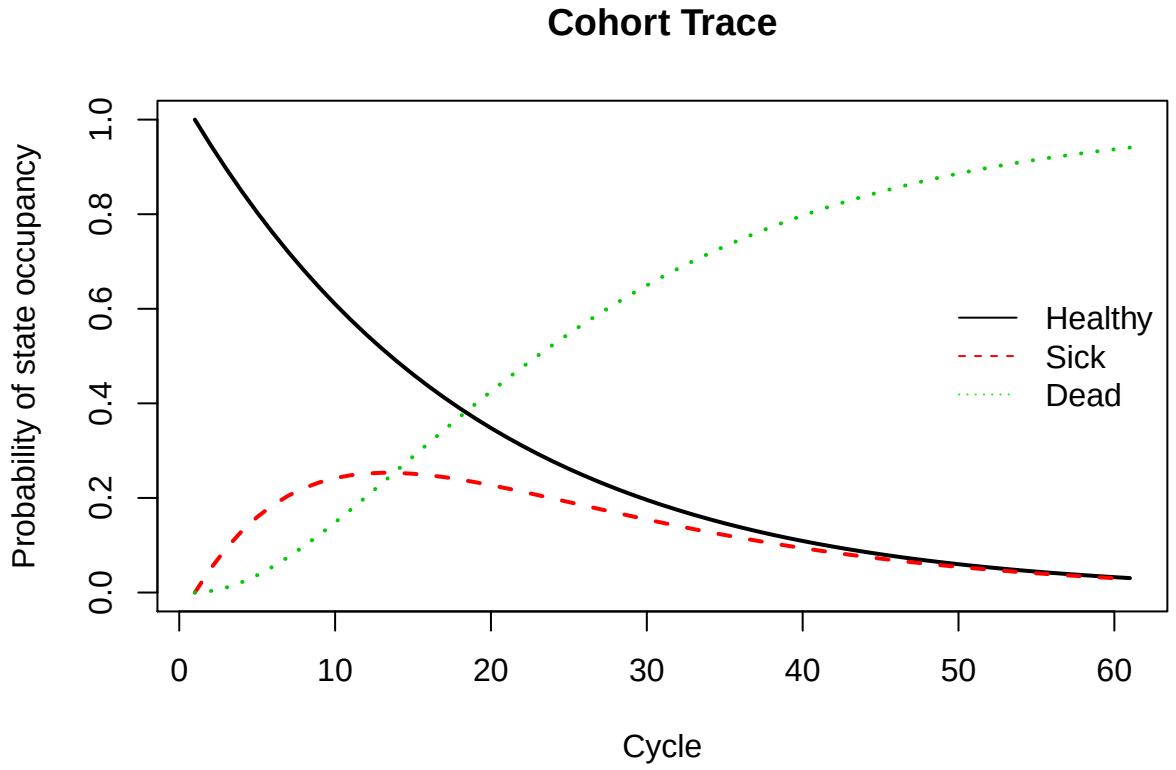
```
##     Healthy      Sick       Dead
## 0 1.0000000 0.0000000 0.00000000
## 1 0.9470000 0.0500000 0.00300000
## 2 0.8966966 0.0929500 0.01035336
## 3 0.8489589 0.1293172 0.02172383
## 4 0.8036620 0.1596905 0.03664758
## 5 0.7606865 0.1846755 0.05463798
```

06 Compute and Plot Epidemiological Outcomes

06.1 Cohort trace

```
# create a plot of the data
matplot(m_M_tunnels, type = 'l',
        ylab = "Probability of state occupancy",
        xlab = "Cycle",
```

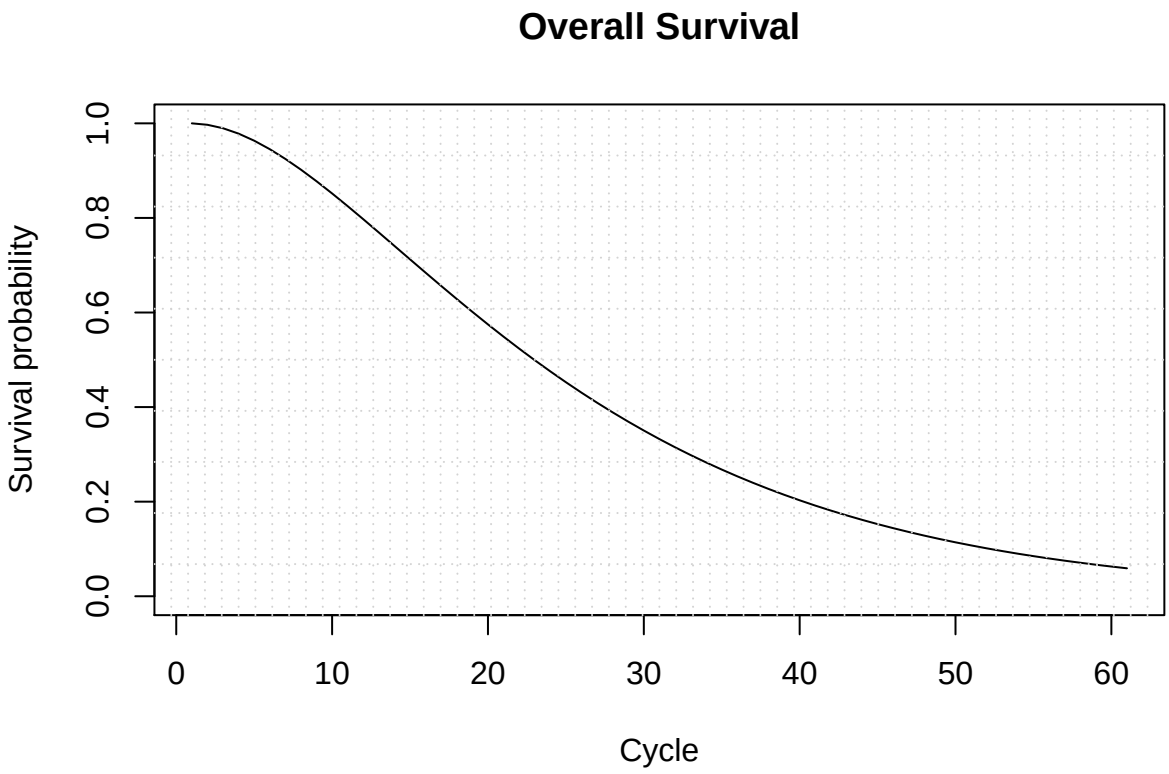
```
       main = "Cohort Trace", lwd = 2)
# add a legend to the graph
legend("right", v_n, col = c("black", "red", "green"), lty = 1:3, bty = "n")
```



06.2 Overall Survival (OS)

```
v_os <- 1 - m_M_tunnels[, "Dead"]    # calculate the overall survival (OS) probability
v_os <- rowSums(m_M_tunnels[, 1:2])  # alternative way of calculating the OS probability

# create a simple plot showing the OS
plot(v_os, type = 'l',
     ylim = c(0, 1),
     ylab = "Survival probability",
     xlab = "Cycle",
     main = "Overall Survival")
# add grid
grid(nx = n_t, ny = 10, col = "lightgray", lty = "dotted", lwd = par("lwd"), equilogs = TRUE)
```

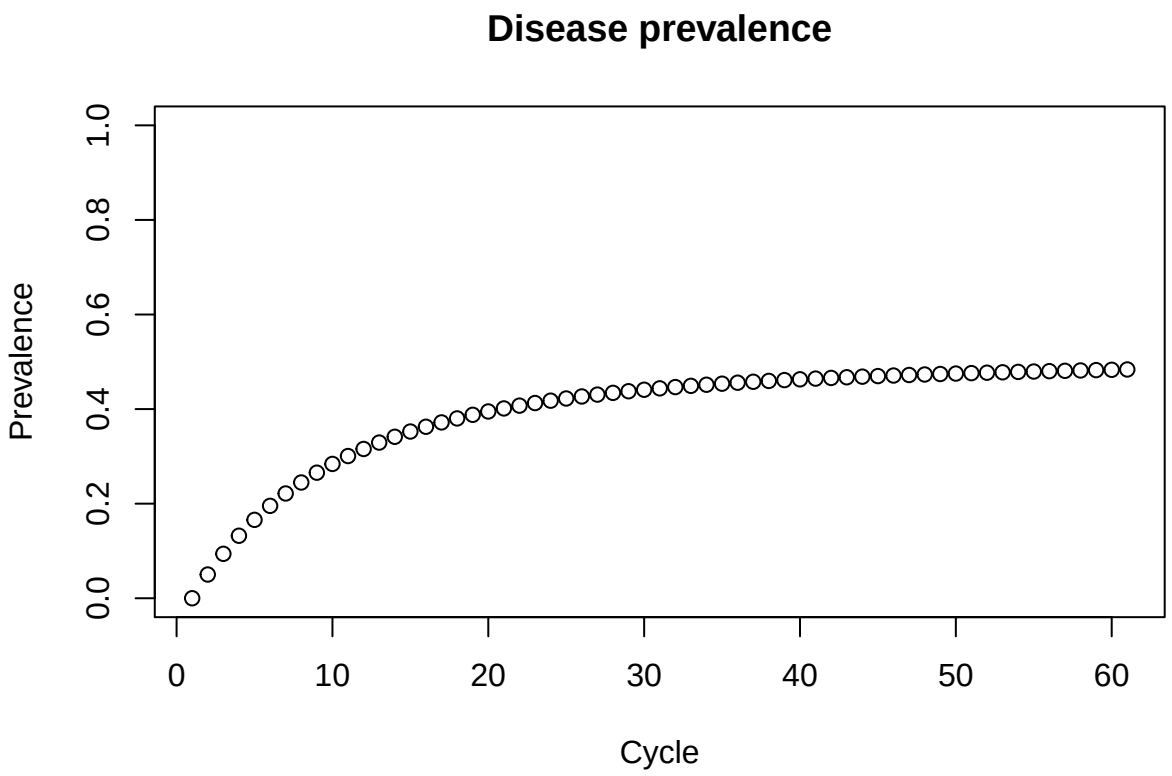


06.2.1 Life Expectancy (LE)

```
v_le <- sum(v_os)           # summing probablity of OS over time  (i.e. life expectancy)
```

06.3 Disease prevalence

```
v_prev <- m_M_tunnels[, "Sick"]/v_os
plot(v_prev,
     ylim = c(0, 1),
     ylab = "Prevalence",
     xlab = "Cycle",
     main = "Disease prevalence")
```



07 Compute Cost-Effectiveness Outcomes

07.1 Mean Costs and QALYs

```
# per cycle
# calculate expected costs by multiplying m_M with the cost vector for the different
# health states
v_tc <- m_M_tunnels %*% c(c_H, c_S, c_D)
# calculate expected QALYs by multiplying m_M with the utilities for the different
# health states
v_tu <- m_M_tunnels %*% c(u_H, u_S, u_D)
```

07.2 Discounted Mean Costs and QALYs

```
# Discount costs  by multiplying the cost vector with discount weights (v_dw)
v_tc_d <-  t(v_tc) %*% v_dwc
# Discount QALYS  by multiplying the QALYs vector with discount weights (v_dw)
v_te_d <-  t(v_tu) %*% v_dwe
```

07.3 Results

```
results <- data.frame( "Total Discounted Cost" = v_tc_d,
                       "Life Expectancy" = v_le,
                       "Total Discounted QALYs" = v_te_d,
```

```
                        check.names = F)
results
```

```
##   Total Discounted Cost Life Expectancy Total Discounted QALYs
## 1              9382.938        25.89709                11.98968
```