Simple 3-state Markov model in R

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

The DARTH workgroup

Developed by the Decision Analysis in R for Technologies in Health (DARTH) workgroup:

Fernando Alarid-Escudero, PhD (1)

Eva A. Enns, MS, PhD (2)

M.G. Myriam Hunink, MD, PhD (3,4)

Hawre J. Jalal, MD, PhD (5)

Eline M. Krijkamp, MSc (3)

Petros Pechlivanoglou, PhD (6,7)

Alan Yang, MSc (7)

In collaboration of:

- 1. Drug Policy Program, Center for Research and Teaching in Economics (CIDE) CONACyT, Aguas-calientes, Mexico
- 2. University of Minnesota School of Public Health, Minneapolis, MN, USA
- 3. Erasmus MC, Rotterdam, The Netherlands
- 4. Harvard T.H. Chan School of Public Health, Boston, USA
- 5. University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA
- 6. University of Toronto, Toronto ON, Canada
- 7. The Hospital for Sick Children, Toronto ON, Canada

Please cite our publications when using this code:

- 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

Copyright 2017, THE HOSPITAL FOR SICK CHILDREN AND THE COLLABORATING INSTITUTIONS. All rights reserved in Canada, the United States and worldwide. Copyright, trademarks, trade names and any and all associated intellectual property are exclusively owned by THE HOSPITAL FOR Sick CHILDREN and the collaborating institutions. These materials may be used, reproduced, modified, distributed and adapted with proper attribution.

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

01 Load packages

```
# no packages required
```

02 Load functions

```
# no functions required
```

03 Input model parameters

```
# Strategy names
v_names_str <- c("Base Case")</pre>
# Number of strategies
n_str <- length(v_names_str)</pre>
# 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</pre>
# Sick state
v_Sick_tunnels <- paste("Sick_", seq(1, n_tunnel_size), "Yr", sep = "")</pre>
# Create variables for time-dependent model
v_n_tunnels <- c("Healthy", v_Sick_tunnels, "Dead") # state names</pre>
n_states_tunnels <- length(v_n_tunnels)</pre>
                                                       # number of states
p_HD <- seq(0.003, 0.01, length.out = n_t) # probability to die when sick (aqe-dependent) - this is a
p_{HS} < -0.05
                                             # probability to become sick when healthy
p_SD <- 0.1
                                             # probability to die when sick
# Weibull parameters
1 <- 0.08
g <- 1.1
p_SD <- l*g*(1:n_tunnel_size)^{g-1}</pre>
                                            # probability to die when sick (time-dependent)
# Costs and utilities
c_H <- 400
                                             # cost of remaining one cycle healthy
c_S <- 1000
                                             # cost of remaining one cycle sick
c_D <- 0
                                             # cost of remaining one cycle dead
u_H < 0.8
                                             # utility when healthy
u_S <- 0.5
                                             # utility when sick
u_D <- 0
                                             # utility when dead
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
```

```
 \begin{array}{l} v\_dwc <-\ 1\ /\ (1\ +\ d\_e)\ ^\smallfrown\ (0:n\_t) \\ \#\ calculate\ discount\ weights\ for\ effectiveness\ for\ each\ cycle\ based\ on\ discount\ rate\ d\_e \\ v\_dwe <-\ 1\ /\ (1\ +\ d\_c)\ ^\smallfrown\ (0:n\_t) \\ \end{array}
```

04 Define and initialize matrices and vectors

04.1 Cohort trace

04.2 Transition probability array

```
# 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)))</pre>
```

Fill in the transition probability array:

```
# 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</pre>
```

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")
}</pre>
```

05 Run Markov model

```
for (t in 1:n_t) {
                                 # loop through the number of cycles
 m_M[t + 1, ] \leftarrow 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, n = 30)
##
              Sick_1Yr
                      Sick_2Yr
                               Sick_3Yr
      Healthy
                                         {\tt Sick\_4Yr}
    ## 0
    0.8489589 0.04483483 0.04318320 0.041299187 0.000000000 0.000000000
    0.8036620 0.04244795 0.04088937 0.039110331 0.037242829 0.000000000
    0.7606865 0.04018310 0.03871253 0.037032843 0.035268959 0.033478121
   0.7199188 0.03803432 0.03664698 0.035061315 0.033395520 0.031703780
    0.6812506 0.03599594 0.03468730 0.033190586 0.031617633 0.030019719
## 8 0.6445786 0.03406253 0.03282830 0.031415733 0.029930645 0.028421550
## 9 0.6098041 0.03222893 0.03106503 0.029732063 0.028330116 0.026905092
## 10 0.5768333 0.03049021 0.02939278 0.028135098 0.026811814 0.025466354
## 11 0.5455768 0.02884167 0.02780707 0.026620572 0.025371702 0.024101530
## 12 0.5159492 0.02727884 0.02630360 0.025184414 0.024005930 0.022806992
## 13 0.4878693 0.02579746 0.02487830 0.023822749 0.022710830 0.021579280
## 14 0.4612598 0.02439347 0.02352728 0.022531879 0.021482906 0.020415096
## 15 0.4360468 0.02306299 0.02224684 0.021308283 0.020318824 0.019311296
## 16 0.4121603 0.02180234 0.02103345 0.020148607 0.019215408 0.018264886
## 17 0.3895334 0.02060802 0.01988374 0.019049654 0.018169634 0.017273010
## 18 0.3681025 0.01947667 0.01879451 0.018008380 0.017178619 0.016332948
## 19 0.3478070 0.01840513 0.01776273 0.017021888 0.016239618 0.015442111
## 20 0.3285891 0.01739035 0.01678547 0.016087415 0.015350017 0.014598029
## 21 0.3103942 0.01642946 0.01586000 0.015202334 0.014507328 0.013798354
## 22 0.2931700 0.01551971 0.01498367 0.014364145 0.013709179 0.013040848
## 23 0.2768667 0.01465850 0.01415398 0.013570465 0.012953315 0.012323380
## 24 0.2614373 0.01384334 0.01336855 0.012819029 0.012237589 0.011643923
## 25 0.2468367 0.01307186 0.01262512 0.012107681 0.011559959 0.011000547
## 26 0.2330222 0.01234183 0.01192154 0.011434371 0.010918479 0.010391415
## 27 0.2199532 0.01165111 0.01125575 0.010797147 0.010311301 0.009814780
## 28 0.2075911 0.01099766 0.01062581 0.010194154 0.009736664 0.009268978
## 29 0.1958991 0.01037955 0.01002987 0.009623627 0.009192896 0.008752429
       Sick 6Yr
                Sick_7Yr
                         Sick_8Yr
                                   Sick_9Yr
                                           Sick 10Yr
   0.026916686 0.025434244 0.023986516 0.000000000 0.000000000 0.000000000
## 9 0.025483715 0.024083211 0.022715231 0.021387800 0.000000000 0.000000000
## 10 0.024124008 0.022801086 0.021508628 0.020254247 0.019043177 0.000000000
## 11 0.022833987 0.021584513 0.020363567 0.019178368 0.018033888 0.016933470
## 12 0.021610240 0.020430291 0.019277050 0.018157364 0.017075953 0.016035996
```

```
## 13 0.020449513 0.019335365 0.018246218 0.017188561 0.016166875 0.015184186
## 14 0.019348706 0.018296827 0.017268345 0.016269410 0.015304277 0.014375821
 15 0.018304859 0.017311899 0.016340830 0.015397480 0.014485887 0.013608786
 16 0.017315156 0.016377937 0.015461194 0.014570453 0.013709542 0.012881062
 17 0.016376909 0.015492418 0.014627076 0.013786118 0.012973177 0.012190724
 18 0.015487560 0.014652939 0.013836222 0.013042368 0.012274824 0.011535938
 19 0.014644669 0.013857210 0.013086487 0.012337196 0.011612608 0.010914952
## 20 0.013845914 0.013103049 0.012375824 0.011668687 0.010984739 0.010326100
## 21 0.013089082 0.012388378 0.011702285 0.011035018 0.010389516 0.009767790
 22 0.012372067 0.011711216 0.011064015 0.010434452 0.009825312 0.009238508
 23 0.011692861 0.011069680 0.010459245 0.009865332 0.009290582 0.008736811
 24 0.011049556 0.010461973 0.009886291 0.009326083 0.008783851 0.008261321
 25 0.010440332 0.009886387 0.009343550 0.008815203 0.008303717 0.007810729
 26 0.009863459 0.009341296 0.008829497 0.008331263 0.007848842 0.007383786
 27 0.009317291 0.008825149 0.008342677 0.007872903 0.007417954 0.006979305
## 28 0.008800261 0.008336475 0.007881709 0.007438826 0.007009841 0.006596153
 29 0.008310877 0.007873872 0.007445276 0.007027799 0.006623349 0.006233253
##
             Sick 13Yr
                     Sick 14Yr
                            Sick 15Yr
                                    Sick 16Yr
     Sick 12Yr
                                            Sick 17Yr
   0
   ## 9
14 0.013485890 0.012635543 0.011825234 0.000000000 0.000000000 0.000000000
 15 0.012767937 0.011964360 0.011198496 0.010470340 0.000000000 0.000000000
 16 0.012086692 0.011327410 0.010603647 0.009915412 0.009262380 0.000000000
 17 0.011440361 0.010723025 0.010039138 0.009388719 0.008771474 0.008186863
## 18 0.010827236 0.010149616 0.009503490 0.008888889 0.008305545 0.007752959
## 19 0.010245685 0.009605666 0.008995295 0.008414614 0.007863380 0.007341132
## 20 0.009694154 0.009089727 0.008513208 0.007964646 0.007443822 0.006950310
## 21 0.009171163 0.008600423 0.008055948 0.007537795 0.007045767 0.006579470
 22 0.008675298 0.008136437 0.007622292 0.007132926 0.006668162 0.006227636
 23 0.008205215 0.007696518 0.007211076 0.006748957 0.006310002 0.005893877
 24 0.007759630 0.007279471 0.006821189 0.006384856 0.005970332 0.005577306
 25 0.007337322 0.006884159 0.006451573 0.006039641 0.005648237 0.005277076
 26 0.006937127 0.006509497 0.006101220 0.005712375 0.005342850 0.004992383
## 27 0.006557937 0.006154454 0.005769169 0.005402164 0.005053340 0.004722456
 28 0.006198695 0.005818045 0.005454505 0.005108158 0.004778918 0.004466562
 29 0.005858397 0.005499335 0.005156356 0.004829547 0.004518831 0.004224005
##
     Sick_18Yr
             Sick_19Yr
                     Sick_20Yr
                            Sick_21Yr
                                    Sick_22Yr
##
 0
```

```
## 20 0.006483521 0.006042738 0.005627152 0.000000000 0.000000000 0.000000000
21 0.006138356 0.005721756 0.005328913 0.004959002 0.000000000 0.000000000
22 0.005810838 0.005417145 0.005045849 0.004696175 0.004367305 0.000000000
23 0.005500106 0.005128109 0.004777221 0.004446720 0.004135838 0.003843779
24 0.005205338 0.004853885 0.004522328 0.004209989 0.003916148 0.003640059
25 0.004925749 0.004593750 0.004280499 0.003985361 0.003707663 0.003446704
26 0.004660594 0.004347011 0.004051093 0.003772245 0.003509837 0.003263211
## 27 0.004409159 0.004113009 0.003833501 0.003570079 0.003322150 0.003089099
28 0.004170765 0.003891116 0.003627142 0.003378323 0.003144105 0.002923911
29 0.003944766 0.003680732 0.003431461 0.003196466 0.002975230 0.002767209
 Sick 24Yr
    Sick 25Yr
       Sick 26Yr
          Sick 27Yr
             Sick 28Yr
0
 ##
 ## 26 0.003031693 0.002814604 0.002611262 0.000000000 0.000000000 0.000000000
## 27 0.002870294 0.002665096 0.002472865 0.002292967 0.000000000 0.000000000
```

##	20	0	0	0	0	0	0	0
##	21	0	0	0	0	0	0	0
##	22	0	0	0	0	0	0	0
##	23	0	0	0	0	0	0	0
##	24	0	0	0	0	0	0	0
## ##	25 26	0	0	0	0	0	0	0
##	27	0	0	0	0	0	0	0
##	28	0	0	0	0	0	0	0
##	29	0	0	0	0	0	0	0
##		Sick_44Yr	Sick_45Yr	Sick_46Yr	Sick_47Yr	Sick_48Yr	Sick_49Yr	Sick_50Yr
##	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 5	0	0	0	0	0	0	0
##	6	0	0	0	0	0	0	0
##	7	0	0	0	0	0	0	0
##	8	0	0	0	0	0	0	0
##	9	0	0	0	0	0	0	0
##	10	0	0	0	0	0	0	0
##	11	0	0	0	0	0	0	0
##	12	0	0	0	0	0	0	0
##	13	0	0	0	0	0	0	0
##	14	0	0	0	0	0	0	0
## ##	15 16	0	0	0	0	0	0	0
##	17	0	0	0	0	0	0	0
##	18	0	0	0	0	0	0	0
##	19	0	0	0	0	0	0	0
##	20	0	0	0	0	0	0	0
##	21	0	0	0	0	0	0	0
	22	0	0	0	0	0	0	0
	23	0	0	0	0	0	0	0
	24	0	0	0	0	0	0	0
## ##		0	0	0	0	0	0	0
##		0	0	0	0	0	0	0
##		0	0	0	0	0	0	0
##		0	0	0	0	0	0	0
##		Sick_51Yr	Sick_52Yr	Sick_53Yr	Sick_54Yr	Sick_55Yr	Sick_56Yr	Sick_57Yr
##		0	0	0	0	0	0	0
##		0	0	0	0	0	0	0
##		0	0	0	0	0	0	0
## ##	3 4	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0
##	8	0	0	0	0	0	0	0
##	9	0	0	0	0	0	0	0
##		0	0	0	0	0	0	0
##	11	0	0	0	0	0	0	0

```
## 12
                                                                                       0
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
## 13
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
                                                               0
##
   14
                0
                            0
                                        0
                                                                           0
                                                                                       0
                0
                                        0
                                                               0
                                                                           0
                                                                                       0
## 15
                            0
                                                   0
## 16
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
## 17
                0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
                            0
## 18
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
                                                               0
                                                                           0
## 19
                0
                            0
                                        0
                                                   0
                                                                                       0
## 20
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
## 21
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
## 22
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
                0
                                        0
                                                               0
                                                                           0
## 23
                            0
                                                   0
                                                                                       0
                0
                                        0
                                                               0
                                                                           0
##
   24
                            0
                                                   0
                                                                                       0
## 25
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
## 26
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
## 27
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
## 28
                0
                            0
                                        0
                                                   0
                                                               0
                                                                           0
                                                                                       0
                0
                                        0
                                                   0
                                                                                       0
##
   29
                            0
                                                               0
                                                                           0
##
       Sick_58Yr Sick_59Yr Sick_60Yr
                                                 Dead
## 0
                0
                            0
                                        0 0.00000000
## 1
                0
                            0
                                        0 0.00300000
## 2
                0
                            0
                                        0 0.01035336
## 3
                                        0 0.02172383
                0
                            0
## 4
                0
                            0
                                        0 0.03664758
## 5
                0
                            0
                                        0 0.05463798
## 6
                0
                            0
                                        0 0.07522164
## 7
                0
                            0
                                        0 0.09795380
## 8
                0
                            0
                                        0 0.12242522
## 9
                0
                            0
                                        0 0.14826470
                0
                                        0 0.17513925
## 10
                            0
## 11
                0
                            0
                                        0 0.20275287
## 12
                0
                            0
                                        0 0.23084460
## 13
                0
                            0
                                        0 0.25918620
## 14
                0
                            0
                                        0 0.28757954
## 15
                0
                            0
                                        0 0.31585404
## 16
                0
                            0
                                        0 0.34386408
## 17
                0
                            0
                                        0 0.37148650
## 18
                0
                            0
                                        0 0.39861833
## 19
                0
                            0
                                        0 0.42517452
## 20
                0
                            0
                                        0 0.45108598
## 21
                0
                            0
                                        0 0.47629765
## 22
                0
                            0
                                        0 0.50076685
## 23
                0
                                        0 0.52446170
                            0
## 24
                0
                            0
                                        0 0.54735973
## 25
                0
                            0
                                        0 0.56944660
## 26
                0
                            0
                                        0 0.59071503
## 27
                0
                                        0 0.61116370
                            0
## 28
                0
                            0
                                        0 0.63079642
                0
## 29
                            0
                                        0 0.64962131
```

Create aggregated trace.

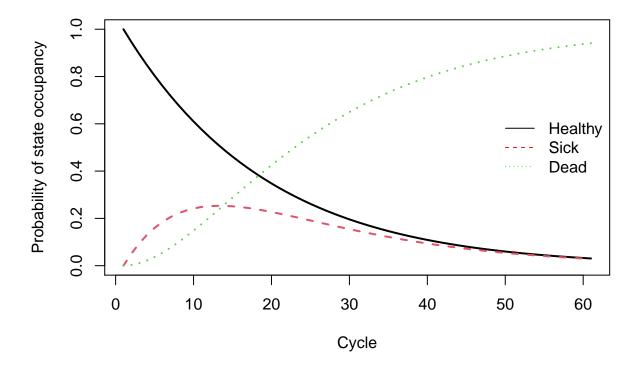
head(m_M_tunnels) # show the first rows of the aggregated Markov trace

```
## 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

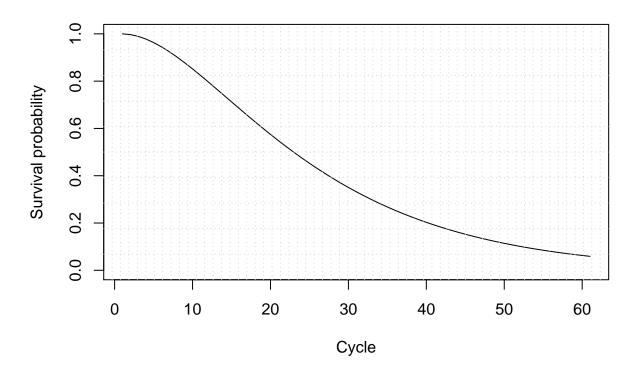
06.1 Cohort trace

Cohort Trace



06.2 Overall Survival (OS)

Overall Survival

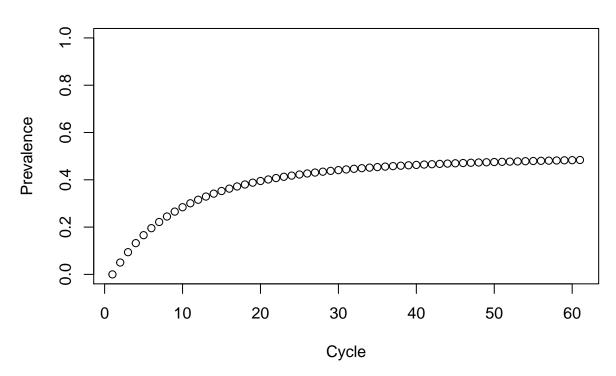


06.2.1 Life Expectancy (LE)

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

06.3 Disease prevalence

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)</pre>
```

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</pre>
```

07.3 Results

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