

Simple 3-state Partitioned Survival model in R

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. *BioRxiv* 670612 2019.<https://www.biorxiv.org/content/10.1101/670612v1>

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Change `eval` to `TRUE` if you want to knit this document.

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

01 Load packages

```
if (!require('pacman')) install.packages('pacman'); library(pacman) # use this package to conveniently
# load (install if required) packages from CRAN
p_load("here", "dplyr", "devtools", "gems", "flexsurv", "survminer", "survHE", "ggplot2", "msm", "igraph")
```

02 Load functions

```
source("survival_functions.R")
```

03 Input model parameters

```
v_n      <- c("healthy", "sick", "dead")  # state names

c_l      <- 1 / 12                        # cycle length (a month)
n_t      <- 30                            # number of years (20 years)
set.seed(2020)                            # set the seed
n_sim    <- 100                           # number of simulations

n_s      <- length(v_n)                   # No of states
times    <- seq(0, n_t, c_l)              # the cycles in years
```

Create a transition probability matrix with all transitions indicated and numbered.

```
tmat <- matrix(NA, n_s, n_s, dimnames = list(v_n, v_n))
tmat["healthy", "sick"] <- 1
tmat["healthy", "dead"] <- 2
tmat["sick", "dead"] <- 3

layout.fig <- c(2,1)
plotmat(t(tmat), t(layout.fig), self.cex = 0.5, curve = 0, arr.pos = 0.76,
        latex = T, arr.type = "curved", relsize = 0.85, box.prop=0.8,
        cex = 0.1, box.cex = 0.7, lwd = 1)
```

Generate data.

```
source("data.R")
head(true_data)
head(sim_data)
head(status)
head(OS_PFS_data)
```

04 Analysis

Showcasing the use of packages `survival`, `flexsurv`.

```
fit_KM <- survfit(Surv(time = OS_time, event = OS_status) ~ 1, data = OS_PFS_data)
plot(fit_KM, mark.time = T)

# a prettier way of plotting!!

ggsurvplot(
  fit_KM,
  data = OS_PFS_data,
  size = 1,                      # change line size
  palette = c("orange2"),        # custom color palettes
  conf.int = TRUE,               # Add confidence interval
  pval = TRUE,                   # Add p-value
  risk.table = TRUE,             # Add risk table
  risk.table.height = 0.25,      # Useful to change when you have multiple groups
  ggtheme = theme_bw(),          # Change ggplot2 theme
  xlab = 'Time in days',         # Change X-axis label
  title = "Survival curve for Progression-Free Survival (PFS)",
  subtitle = "Based on Kaplan-Meier estimates"
)
```

04.1 Partitioned Survival model

```
# R package flexsurv allows parametric fitting of curves
fit_weib <- flexsurvreg(Surv(time = OS_time, event = OS_status) ~ 1, data = OS_PFS_data,
  dist = "weibull")
plot(fit_weib)

# fit all parametric models to the data and extract the AIC/BIC.
# Select the one with the most appropriate fit
# Repeat for PFS and OS
fit_PFS <- fit.fun(time = "PFS_time", status = "PFS_status", data = OS_PFS_data,
  extrapolate = TRUE, times = times)
fit_OS <- fit.fun(time = "OS_time", status = "OS_status", data = OS_PFS_data,
  extrapolate = TRUE, times = times)

# Check AIC of each model to assess goodness-of-fit
GoF_OS <- data.frame(AIC = fit_OS$AIC, BIC = fit_OS$BIC)
GoF_PFS <- data.frame(AIC = fit_PFS$AIC, BIC = fit_PFS$BIC)

# "Exponential", "Weibull (AFT)", "Gamma", "log-Normal", "log-Logistic", "Gen. Gamma"
choose_PFS <- "Weibull (AFT)"
choose_OS <- "Weibull (AFT)"

# construct a partitioned survival model out of the fitted models
m_M_PSM <- partsurv(fit_PFS, fit_OS, time = times, choose_PFS = choose_PFS,
  choose_OS = choose_OS)

# plot the results of PSM and the true data
```

```

m_M_data <- transitionProbabilities(generate$cohort, times = times)@probabilities
matplot(times,m_M_data, type='l', lty = 1, col = 1, ylab= "proportion of cohort", xlab = "Time",
        main = "Trace comparisons",xlim=c(0,25))
matlines(times, m_M_PSM$trace, col = 4, lty = 1)
legend("right", c("True Data","PSM"), col = c(1,4), lty = c(1,1), bty= "n")

# construct a PSA partitioned survival model out of the fitted models
m_M_PSM_psa <- partsurv(fit_PFS, fit_OS, time = times, choose_PFS = choose_PFS,
                       choose_OS = choose_OS, n_sim = 1000)

# plot the results of PSM and the trace
m_M_data <- transitionProbabilities(generate$cohort, times = times)@probabilities
matplot(times,m_M_data, type='l', lty = 1, col = 1, ylab= "proportion of cohort", xlab = "Time", main =
matlines(times, m_M_PSM_psa$Mean, col = 4, lty = 1)
matlines(times, m_M_PSM_psa$CI[,,"low"], col = 4, lty = 2)
matlines(times, m_M_PSM_psa$CI[,,"high"], col = 4, lty = 2)
legend("right", c("True Data","PSM", "Low CI", "High CI"),
      col = c(1,4,4,4), lty = c(1,1,2,2), bty= "n")

```

Let's now assume that we wanted to extract the monthly transition probabilities from the Weibull OS curve: we could use the convenient fact that $tp(t) = 1 - \frac{S(t)}{S(t-1)}$

```

# create survival probabilities using trans_prob
p_death <- trans_prob(fit_OS,choose_dist = "Weibull (AFT)", times=times)
plot(p_death$times, p_death$t.p, type = 'l')

```