

# Model B : Estimation Results

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Estimation results of **Model B**, specified by the following input:

```
q <- .01
# transition matrix
Q <- rbind( c(0, q, 0, q),
            c(q, 0, q, q),
            c(0, 0, 0, q),
            c(0, 0, 0, 0))
# misclassification matrix
E <- rbind( c( 0, 0, 0, 0),
            c( 0, 0, .1, 0),
            c( 0, 0, 0, 0),
            c( 0, 0, 0, 0) )
# transition names
qnames = c(
  "Healthy - Mild",    # q12
  # "Healthy - Severe", # q13
  "Healthy - Dead",    # q14
  "Mild - Healthy",    # q21
  "Mild - Severe",     # q23
  "Mild - Dead",       # q24
  # "Severe - Healthy", # q31
  # "Severe - Mild",    # q32
  "Severe - Dead"      # q34
)
```

## Load environmet

Save fitted models here :

```
[1] "./data/shared/derived/models/model-b-mod-1/"
```

## Load data

Before ms encoding:

	id	fu_year	died	age_bl	male	edu	age_death	age_at_visit	mmse	presumed_alive
5120	50402431	0	1	91.41136	FALSE	16	94.82272	91.41136	19	FALSE
5121	50402431	1	1	91.41136	FALSE	16	94.82272	92.33402	12	FALSE
5122	50402431	2	1	91.41136	FALSE	16	94.82272	93.34702	5	FALSE
5123	50402431	3	1	91.41136	FALSE	16	94.82272	94.34634	0	FALSE

After ms encoding

	id	fu_year	died	age_bl	male	edu	age	state	presumed_alive	mmse	firstobs
5120	50402431	0	1	91.41136	FALSE	16	91.41136	3	FALSE	19	1
5121	50402431	1	1	91.41136	FALSE	16	92.33402	3	FALSE	12	0
5122	50402431	2	1	91.41136	FALSE	16	93.34702	3	FALSE	5	0
5123	50402431	3	1	91.41136	FALSE	16	94.34634	3	FALSE	0	0
51201	50402431	NA	1	91.41136	FALSE	16	94.82272	4	FALSE	NA	0

## Remove cases

```
#### 1) Remove observations with missing age
# Initial number of observations with missing age :
sum(is.na(ds_ms$age))
```

```
[1] 1
```

```
ds_clean <- ds_ms %>%
  dplyr::filter(!is.na(age))
# Resultant number of observations with missing age
sum(is.na(ds_clean$age))
```

```
[1] 0
```

```
#### 3) Remove subjects with only ONE observed data point
# Initial number of subjects who have *n* observed data points
ds_clean %>%
  dplyr::group_by(id) %>%
  dplyr::summarize(n_data_points = n()) %>%
  dplyr::group_by(n_data_points) %>%
  dplyr::summarize(n_people=n()) %>%
  print()
```

```
# A tibble: 17 × 2
  n_data_points n_people
    <int>         <int>
1         1         119
```

2	2	205
3	3	184
4	4	180
5	5	190
6	6	104
7	7	108
8	8	113
9	9	127
10	10	116
11	11	110
12	12	71
13	13	21
14	14	14
15	15	13
16	16	17
17	17	3

```
# Determine which ids have only a single observation
```

```
remove_ids <- ds_clean %>%
  dplyr::group_by(id) %>%
  dplyr::summarize(n_data_points = n()) %>%
  dplyr::arrange(n_data_points) %>%
  dplyr::filter(n_data_points==1) %>%
  dplyr::select(id)
```

```
remove_ids <- remove_ids$id
```

```
# How many subjects to be removed from the data set:
```

```
length(remove_ids)
```

```
[1] 119
```

```
ds_clean <- ds_clean %>%
  dplyr::filter(!(id %in% remove_ids))
# Resultant number of subjects who have *n* observed data points
ds_clean %>%
  dplyr::group_by(id) %>%
  dplyr::summarize(n_data_points = n()) %>%
  dplyr::group_by(n_data_points) %>%
  dplyr::summarize(n_people=n()) %>%
  print()
```

```
# A tibble: 16 × 2
```

	n_data_points	n_people
	<int>	<int>
1	2	205
2	3	184
3	4	180
4	5	190
5	6	104
6	7	108
7	8	113
8	9	127
9	10	116
10	11	110
11	12	71
12	13	21

13	14	14
14	15	13
15	16	17
16	17	3

```
#### 3) Remove subjects with IMS at the first observation
# Initial view of subjects with intermediate missing state at first observation:
ids_firstobs_ims <- ds_clean %>%
  dplyr::filter(firstobs == TRUE & state == -1) %>%
  dplyr::select(id) %>% print()
```

```
      id
1 80333458
2 90214403
3 90447310
4 91804757
```

```
ids_firstobs_ims <- ids_firstobs_ims[, "id"]
ds_clean <- ds_clean %>%
  dplyr::filter(!id %in% ids_firstobs_ims)
# Resultant view of subjects with intermediate missing state at first observation:
ds_clean %>%
  dplyr::filter(firstobs == TRUE & state == -1) %>%
  dplyr::select(id) %>% print()
```

```
[1] id
<0 rows> (or 0-length row.names)
```

## Categorize covariates

How education was categorized:

	educatF	edu	n
1	0-9 years	0	4
2	0-9 years	2	6
3	0-9 years	3	10
4	0-9 years	4	17
5	0-9 years	5	20
6	0-9 years	6	48
7	0-9 years	7	27
8	0-9 years	8	178
9	0-9 years	9	76
10	10-11 years	10	167
11	10-11 years	11	225
12	>11 years	12	2400
13	>11 years	13	862
14	>11 years	14	1199
15	>11 years	15	554
16	>11 years	16	2132
17	>11 years	17	486
18	>11 years	18	942
19	>11 years	19	255
20	>11 years	20	286

21	>11 years	21	207
22	>11 years	22	61
23	>11 years	23	37
24	>11 years	24	26
25	>11 years	25	11
26	>11 years	28	21

Frequencies of categorized education :

```
# A tibble: 3 × 2
  educatF      n
  <fctr> <int>
1 0-9 years   386
2 10-11 years 392
3 >11 years  9479
```

## Age diagnostic

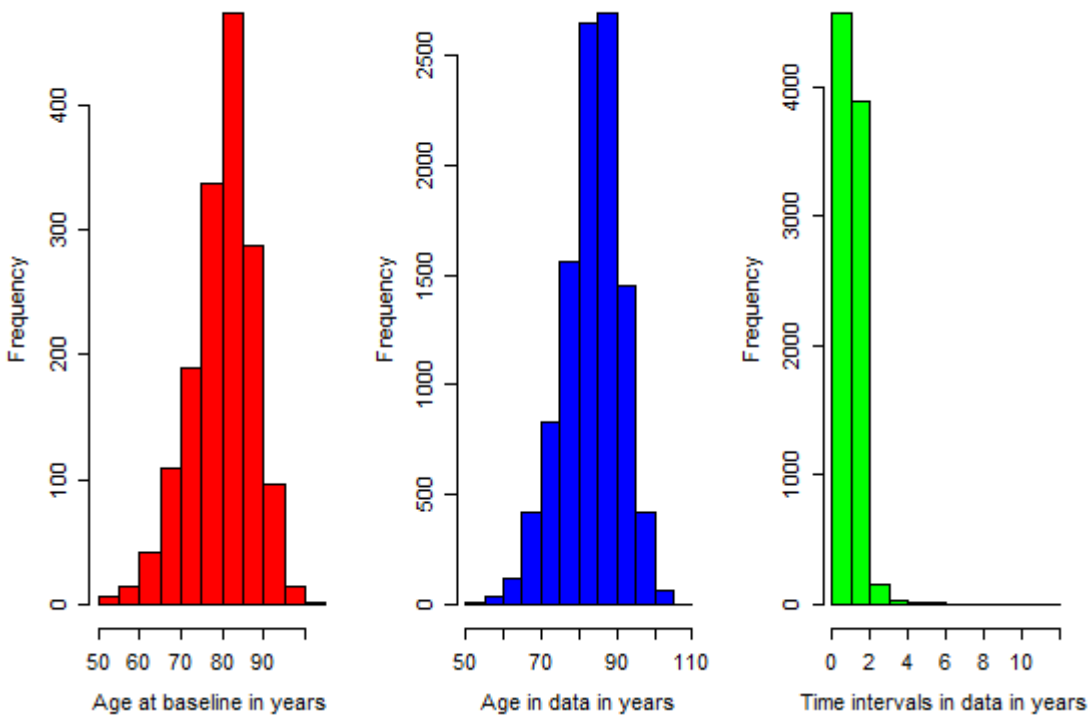
Minimum interval length : 0.00273785

Maximum interval length : 11.86858

Time intervals between observations within individuals:

	0%	25%	50%	75%	100%
0.00	0.96	1.00	1.03	11.87	

Graphs of age distribution :



## Estimation prep

Number of subjects with intermediate missing state (-1) : 104

Number of subjects with right censored state (-2) : 46

Number of subjects with either IMS or RC state(s) : 149

Number of subjects with both IMS and RC state(s) : 1

Centering decisions :

The variable `age` is centered at : 75

The variable `age\_bl` is centered at : 75

The following dataset will be passed to msm call (view for one person):

	id	age_bl	male	edu	educat	educatF	firstobs	fu_year	age	state
1	90544686	7.696783	0	12	1	>11 years	1	0	7.696783	1
2	90544686	7.696783	0	12	1	>11 years	0	1	8.682409	1

3	90544686	7.696783	0	12	1 >11 years	0	2	9.731006	1
4	90544686	7.696783	0	12	1 >11 years	0	3	10.689254	1
5	90544686	7.696783	0	12	1 >11 years	0	4	11.691307	1
6	90544686	7.696783	0	12	1 >11 years	0	5	12.709788	1
7	90544686	7.696783	0	12	1 >11 years	0	6	13.665298	1
8	90544686	7.696783	0	12	1 >11 years	0	7	14.678303	2
9	90544686	7.696783	0	12	1 >11 years	0	8	15.680356	1
10	90544686	7.696783	0	12	1 >11 years	0	9	16.709788	1

Subject count : 1572

Frequency of states at baseline

```
# A tibble: 3 × 3
  state count  pct
  <dbl> <int> <dbl>
1     1  1189  0.76
2     2   281  0.18
3     3   102  0.06
```

State table:

	to					
from	-2	-1	1	2	3	4
-2	32	0	0	0	0	0
-1	0	25	27	13	26	47
1	32	59	4855	715	120	251
2	8	20	534	478	256	146
3	6	34	24	96	649	232

The initial values for estimation : 0.76 0.18 0.06 0

## Specifications

### Fitting functions

```
estimate_multistate <- function(
  model_name
  ,ds                # data object
  ,Q                 # Q-matrix of transitions
  ,E                 # misspecification matrix
  ,qnames            # names of the rows in the Q matrix
  ,cf                # string with covariate names for forward transitions
  ,cb                # string with covariate names for backward transitions
  ,cd                # string with covariate names for death transitions
){
  cov_forward <- as.formula(paste0("~",cf))
  cov_backward <- as.formula(paste0("~",cb))
  cov_death <- as.formula(paste0("~",cd))
  # covariates_ <- as.formula(paste0("~",cov_names))
  covariates_ = list(
```

```

    "1-2"      = cov_forward,
    "2-3"      = cov_forward,
    "2-1"      = cov_backward,
    "1-4"      = cov_death,
    "2-4"      = cov_death,
    "3-4"      = cov_death
  )
  model <- msm(
    formula      = state ~ age,
    subject      = id,
    data         = ds,
    center       = FALSE,
    qmatrix      = Q,
    ematrix      = E,
    death        = TRUE,
    covariates   = covariates_,
    censor       = c(-1,-2),
    censor.states = list(c(1,2,3), c(1,2,3)),
    method       = method_,
    constraint    = constraint_,
    fixedpars    = fixedpars_,
    initprobs    = initprobs_,
    est.initprobs = TRUE,
    control      = list(trace=0,REPORT=1,maxit=1000,fnscale=10000)
  )
  # model <- paste0("test", covariates_)
  saveRDS(model, paste0(pathSaveFolder,model_name,".rds"))
  return(model)
}

```

## Support functions

```

get_crude_Q <- function(ds, Q, cov_names){
  formula_ <- as.formula(paste0("state ~ ",cov_names))
  Q_crude <- crudeinits.msm(
    formula = formula_,
    subject = id,
    qmatrix = Q,
    data = ds,
    censor      = c(-1,-2),
    censor.states = list(c(1,2,3), c(1,2,3))
  )
  return(Q_crude)
}

msm_summary <- function(model){
  cat("\n-2loglik =", model$minus2loglik,"\n")
  cat("Convergence code =", model$opt$convergence,"\n")
  p <- model$opt$par
  p.se <- sqrt(diag(solve(1/2*model$opt$hessian)))
  print(cbind(p=round(p,digits),
              se=round(p.se,digits),"Wald ChiSq"=round((p/p.se)^2,digits),

```



```

        "Pr>ChiSq"=round(1-pchisq((p/p.se)^2,df=1),digits)),
        quote=FALSE)
}

msm_details <- function(model){
  # intensity matrix
  cat("\n Intensity matrix : \n")
  print(qmatrix.msm(model))
  # qmatrix.msm(model, covariates = list(male = 0))
  # transition probability matrix
  t_ <- 2
  cat("\n Transition probability matrix for t = ", t_," : \n")
  print(pmatrix.msm(model, t = t_)) # t = time, in original metric
  # misclassification matrix
  cat("\n Misclassification matrix : \n")
  suppressWarnings(print(ematrix.msm(model), warnings=F))
  # mean sojourn times
  cat("\n Mean sojourn times : \n")
  print(sojourn.msm(model))
  # probability that each state is next
  cat("\n Probability that each state is next : \n")
  suppressWarnings(print(pnext.msm(model)))
  # total length of stay
  cat("\n Total length of stay : \n")
  print(totlos.msm(model))
  # expected number of visits to the state
  cat("\n Expected number of visits to the state : \n")
  suppressWarnings(print(envisits.msm(model)))
  # ratio of transition intensities
  # qratio.msm(model, ind1 = c(2,1), ind2 = c(1,2))
}

```

## Model

```

q <- .01
# transition matrix
Q <- rbind( c(0, q, 0, q),
            c(q, 0, q, q),
            c(0, 0, 0, q),
            c(0, 0, 0, 0))
# misclassification matrix
E <- rbind( c( 0, 0, 0, 0),
            c( 0, 0, .1, 0),
            c( 0, 0, 0, 0),
            c( 0, 0, 0, 0) )
# transition names
qnames = c(
  "Healthy - Mild", # q12
  "Healthy - Severe", # q13
  "Healthy - Dead", # q14
  "Mild - Healthy", # q21

```

```

"Mild - Severe",    # q23
"Mild - Dead",      # q24
# "Severe - Healthy",# q31
# "Severe - Mild",  # q32
"Severe - Dead"     # q34
)

```

## msm options

```

digits = 2
method_ = "BFGS"      # alternatively, if does not converge "Nedler-Mead"
constraint_ = NULL    # additional model constraints
fixedpars_ = NULL     # fixed parameters
initprobs_ = initial_probabilities

```

```

# turn this chunk OFF when printing the report
# compile model objects with msm() call
# each model will be saved in the specified folder, namely pathSaveFolder
(Q_crude <- get_crude_Q(ds, Q, "age"))

```

```

      [,1]      [,2]      [,3]      [,4]
[1,] -0.1569916  0.1141470  0.0000000  0.04284465
[2,]  0.3504402 -0.6212645  0.1696731  0.10115125
[3,]  0.0000000  0.0000000 -0.2434208  0.24342081
[4,]  0.0000000  0.0000000  0.0000000  0.00000000

```

```

# estimate_multistate("mB_mod1_1", ds, Q_crude, E, qnames,
#                    cf = "age + male + educat",
#                    cb = "age",
#                    cd = "age + male")

```

```

# estimate_multistate("mB_mod1_2", ds, Q_crude, E, qnames,
#                    cf = "age + age_bl + male + educat",
#                    cb = "age + age_bl",
#                    cd = "age + age_bl + male")

```

```

# assemble the list object with the results of msm estimation
models <- list()
models[["mB_mod1_1"]][["msm"]] <- readRDS(paste0(pathSaveFolder, 'mB1.rds'))
models[["mB_mod1_2"]][["msm"]] <- readRDS(paste0(pathSaveFolder, 'mB2.rds'))

```

```

alive_states <- c(1,2,3)
ds_alive <- ds[ds$state %in% alive_states,]
fixedpars <- fixedpars_
age_min <- 0
age_max <- 35
age_bl <- 0
male <- 0
educat <- 0

```

```

replication_n <- 1000
time_scale <- "years"
grid_par <- .5

```

```

# turn this chunk OFF when printing the report
# for(model_ in names(models) ){
#   # determine covariate list
#   if(model_=="age"){covar_list = list(age=age_min)}
#   if(model_=="age_bl"){covar_list = list(age=age_min, age_bl=age_bl)}
#   if(model_=="male"){covar_list = list(age=age_min, age_bl=age_bl, male=male)}
#   if(model_=="educat"){covar_list = list(age=age_min, age_bl=age_bl, male=male, educat=educat)}
#   # compute LE
#   models[[model_]][["LE"]] <- elect(
#     model = models[[model_]][["msm"]], # fitted msm model
#     b.covariates = covar_list, # list with specified covarites values
#     statedistdata = ds_alive, # data for distribution of living states
#     time.scale.msm = time_scale, # time scale in multi-state model ("years", ...)
#     h = grid_par, # grid parameter for integration
#     age.max = age_max, # assumed maximum age in years
#     S = replication_n # number of simulation cycles
#   )
# }
# #save models estimated by elect() in a external object for faster access in the future
# saveRDS(models, paste0(pathSaveFolder,"models.rds"))

models <- readRDS(paste0(pathSaveFolder,"models.rds"))
# inspect created object
lapply(models, names)

```

## Model results

### model 1

The model was fitted using the following specification of covariates:

```

# Forward transitions:
"1-2"      = "age + male + educat"
"2-3"      = "age + male + educat"
# Backward transitions:
"2-1"      = "age"
# Death transitions:
"1-4"      = "age + male"
"2-4"      = "age + male"
"3-4"      = "age + male"

```

### summary

```

-2loglik = 15002.69
Convergence code = 0

```

	p	se	Wald	ChiSq	Pr>ChiSq
qbase	-1.94	0.10	343.06		0.00
qbase	-4.21	0.18	525.95		0.00
qbase	-0.27	0.08	10.85		0.00

qbase	-2.07	0.19	122.48	0.00
qbase	-3.44	0.42	65.48	0.00
qbase	-2.28	0.20	131.33	0.00
qcov	0.08	0.01	157.35	0.00
qcov	0.08	0.01	31.04	0.00
qcov	-0.02	0.01	7.72	0.01
qcov	0.05	0.01	23.03	0.00
qcov	0.07	0.03	6.72	0.01
qcov	0.07	0.01	34.90	0.00
qcov	0.29	0.08	13.12	0.00
qcov	0.43	0.22	3.90	0.05
qcov	-0.17	0.16	1.21	0.27
qcov	0.71	0.29	6.28	0.01
qcov	0.35	0.14	6.56	0.01
qcov	-0.28	0.08	12.00	0.00
qcov	-0.08	0.13	0.34	0.56
p	-2.15	0.09	590.86	0.00
initp	-1.33	0.06	432.96	0.00
initp	-2.84	0.13	482.04	0.00

## details

### Intensity matrix :

	State 1	State 2	State 3
State 1	-0.25699 (-0.27607,-0.23923)	0.22528 ( 0.20769, 0.24436)	0
State 2	0.64404 ( 0.58425, 0.70995)	-0.88419 (-0.95762,-0.81639)	0.17404 ( 0.14775, 0.20500)
State 3	0	0	-0.19433 (-0.23957,-0.15763)
State 4	0	0	0

	State 4
State 1	0.03172 ( 0.02584, 0.03893)
State 2	0.06611 ( 0.04269, 0.10237)
State 3	0.19433 ( 0.15763, 0.23957)
State 4	0

### Transition probability matrix for t = 2 :

	State 1	State 2	State 3	State 4
State 1	0.7224876	0.1684461	0.03517298	0.0738933
State 2	0.4815688	0.2535146	0.13991778	0.1249988
State 3	0.0000000	0.0000000	0.67796367	0.3220363
State 4	0.0000000	0.0000000	0.00000000	1.0000000

### Misclassification matrix :

	State 1	State 2	State 3	State 4
State 1	1.0000	0	0	0
State 2	0	0	0.1039 (0.08883,0.1213)	0
State 3	0	0	1.0000	0
State 4	0	0	0	1.0000

### Mean sojourn times :

	estimates	SE	L	U
State 1	3.891149	0.14217843	3.622228	4.180034
State 2	1.130981	0.04603661	1.044256	1.224908

State 3 5.145865 0.54946461 4.174158 6.343777

Probability that each state is next :

	State 1	State 2	State 3	State 4
State 1	0	0.87658 (0.85020,0.8995)	0	0.12342 (0.10053,0.14631)
State 2	0.72840 (0.69041,0.7610)	0	0.19683 (0.16643,0.2266)	0.07477 (0.04868,0.10086)
State 3	0	0	0	1.00000 (1.00000,1.00000)
State 4	0	0	0	0

Total length of stay :

State 1	State 2	State 3	State 4
10.763910	2.742463	2.456092	Inf

Expected number of visits to the state :

State 1	State 2	State 3	State 4
1.7662553	2.4248529	0.4772942	1.0000000

## model 2

The model was fitted using the following specification of covariates:

```
# Forward transitions:
"1-2"      = "age + age_bl + male + educat"
"2-3"      = "age + age_bl + male + educat"
# Backward transitions:
"2-1"      = "age + age_bl"
# Death transitions:
"1-4"      = "age + age_bl + male"
"2-4"      = "age + age_bl + male"
"3-4"      = "age + age_bl + male"
```

## summary

```
-2loglik = 14968.52
Convergence code = 0
```

	p	se	Wald	ChiSq	Pr>ChiSq
qbase	-1.84	0.11	291.66		0.00
qbase	-4.38	0.21	443.15		0.00
qbase	-0.18	0.09	4.20		0.04
qbase	-2.16	0.19	126.47		0.00
qbase	-3.34	0.39	73.46		0.00
qbase	-2.46	0.21	132.02		0.00
qcov	0.03	0.01	6.68		0.01
qcov	0.13	0.03	16.23		0.00
qcov	-0.07	0.02	16.29		0.00
qcov	0.09	0.02	14.56		0.00
qcov	0.09	0.05	4.13		0.04
qcov	0.11	0.02	27.53		0.00
qcov	0.05	0.01	12.83		0.00
qcov	-0.05	0.03	2.30		0.13
qcov	0.06	0.02	10.13		0.00
qcov	-0.04	0.02	2.48		0.12

qcov	-0.04	0.05	0.83	0.36
qcov	-0.05	0.02	5.74	0.02
qcov	0.29	0.08	12.61	0.00
qcov	0.43	0.23	3.66	0.06
qcov	-0.17	0.16	1.18	0.28
qcov	0.67	0.28	5.58	0.02
qcov	0.43	0.14	8.99	0.00
qcov	-0.27	0.08	11.42	0.00
qcov	-0.08	0.13	0.33	0.57
p	-2.15	0.09	589.00	0.00
initp	-1.33	0.06	434.17	0.00
initp	-2.84	0.13	485.99	0.00

## details

### Intensity matrix :

	State 1	State 2	State 3
State 1	-0.25383 (-0.27272,-0.23624)	0.22304 ( 0.20556, 0.24200)	0
State 2	0.62394 ( 0.56441, 0.68975)	-0.87084 (-0.94446,-0.80295)	0.17356 ( 0.14719, 0.20467)
State 3	0	0	-0.18472 (-0.22930,-0.14881)
State 4	0	0	0

	State 4
State 1	0.03079 ( 0.02487, 0.03812)
State 2	0.07333 ( 0.04913, 0.10945)
State 3	0.18472 ( 0.14881, 0.22930)
State 4	0

### Transition probability matrix for t = 2 :

	State 1	State 2	State 3	State 4
State 1	0.7224250	0.1685856	0.03524712	0.07374225
State 2	0.4716115	0.2560511	0.14211103	0.13022640
State 3	0.0000000	0.0000000	0.69111910	0.30888090
State 4	0.0000000	0.0000000	0.00000000	1.00000000

### Misclassification matrix :

	State 1	State 2	State 3	State 4
State 1	1.0000	0	0	0
State 2	0	0	0.1042 (0.08908,0.1216)	0
State 3	0	0	1.0000	0
State 4	0	0	0	1.0000

### Mean sojourn times :

	estimates	SE	L	U
State 1	3.939720	0.14429121	3.666826	4.232923
State 2	1.148322	0.04755186	1.058804	1.245409
State 3	5.413553	0.59714750	4.361037	6.720090

### Probability that each state is next :

	State 1	State 2	State 3	State 4
State 1	0	0.87871 (0.85048,0.9021)	0	0.12129 (0.09790,0.14468)
State 2	0.71648 (0.67781,0.7473)	0	0.19931 (0.17053,0.2309)	0.08421 (0.05815,0.11027)
State 3	0	0	0	1.00000 (1.00000,1.00000)

```
State 4 0 0 0
```

```
Total length of stay :  
State 1 State 2 State 3 State 4  
10.635804 2.724037 2.559504 Inf
```

```
Expected number of visits to the state :  
State 1 State 2 State 3 State 4  
1.6996345 2.3721879 0.4727955 1.0000000
```

## Session Info

```
sessionInfo()
```

```
R version 3.3.1 (2016-06-21)  
Platform: x86_64-w64-mingw32/x64 (64-bit)  
Running under: Windows 10 x64 (build 14393)
```

```
locale:  
[1] LC_COLLATE=English_United States.1252 LC_CTYPE=English_United States.1252 LC_MONETARY=English_United States.1252  
[4] LC_NUMERIC=C LC_TIME=English_United States.1252
```

```
attached base packages:  
[1] stats graphics grDevices utils datasets methods base
```

```
other attached packages:  
[1] msm_1.6.1 magrittr_1.5 nnet_7.3-12 knitr_1.14
```

```
loaded via a namespace (and not attached):  
[1] Rcpp_0.12.6 formatR_1.4 nloptr_1.0.4 plyr_1.8.4 tools_3.3.1 dig  
[7] lme4_1.1-12 evaluate_0.9 tibble_1.2 gtable_0.2.0 nlme_3.1-128 lat  
[13] mgcv_1.8-14 Matrix_1.2-7.1 DBI_0.5 yaml_2.1.13 parallel_3.3.1 Spa  
[19] mvtnorm_1.0-5 expm_0.999-0 dplyr_0.5.0 stringr_1.1.0 MatrixModels_0.4-1 gri  
[25] R6_2.1.3 survival_2.39-5 rmarkdown_1.0 minqa_1.2.4 ggplot2_2.1.0 car  
[31] scales_0.4.0 htmltools_0.3.5 splines_3.3.1 MASS_7.3-45 assertthat_0.1 pbk  
[37] testit_0.5 colorspace_1.2-6 quantreg_5.26 stringi_1.1.1 lazyeval_0.2.0 mun
```