

Cohort state-transition Modeling in R

**Using R for Decision Modeling in Health
Technology Assessment**

CE16

NIHES Erasmus Medical Center Rotterdam
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Cohort State-Transition Models

- Models where proportions of a cohort occupy states at each point in time (e.g., healthy, sick, stable, progressed, dead).
- Transitions allowed between states with some probability.
- Transitions occur in cycles (months, years etc).
- Each state associated with a value associated with a model outcome (\$, utility).
- Markov assumption: no “memory” within states.

Building a cohort State-Transition Model

- Determine health states
- Determine transitions
- Choose cycle length
- Estimate transition probabilities
- Estimate state utilities and costs per cycle
- Calculate
- Sensitivity analyses

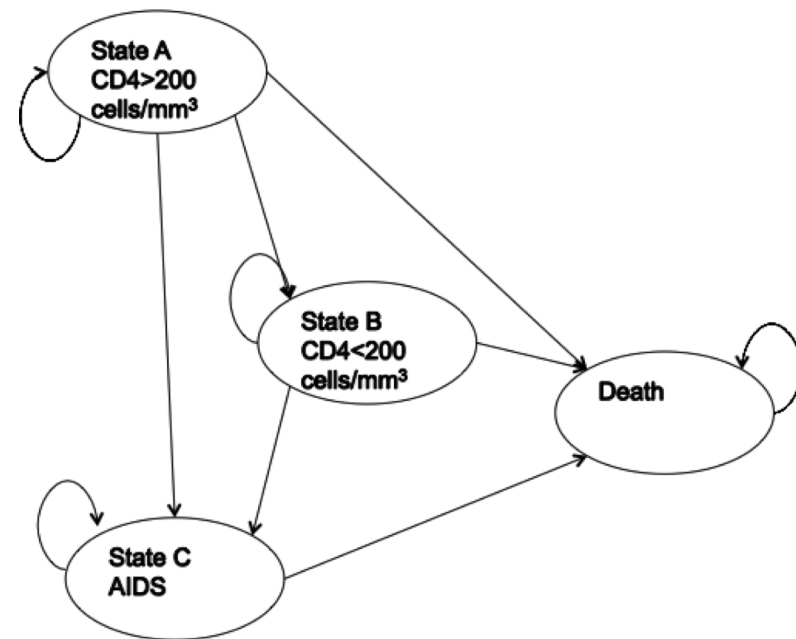
Markov Model of HIV Progression

Transition matrix

Monotherapy

Transition from	Transition to			
	State A	State B	State C	State D
State A	0.721	0.202	0.067	0.01
State B	0	0.581	0.407	0.012
State C	0	0	0.75	0.25
State D	0	0	0	1

State-transition diagram

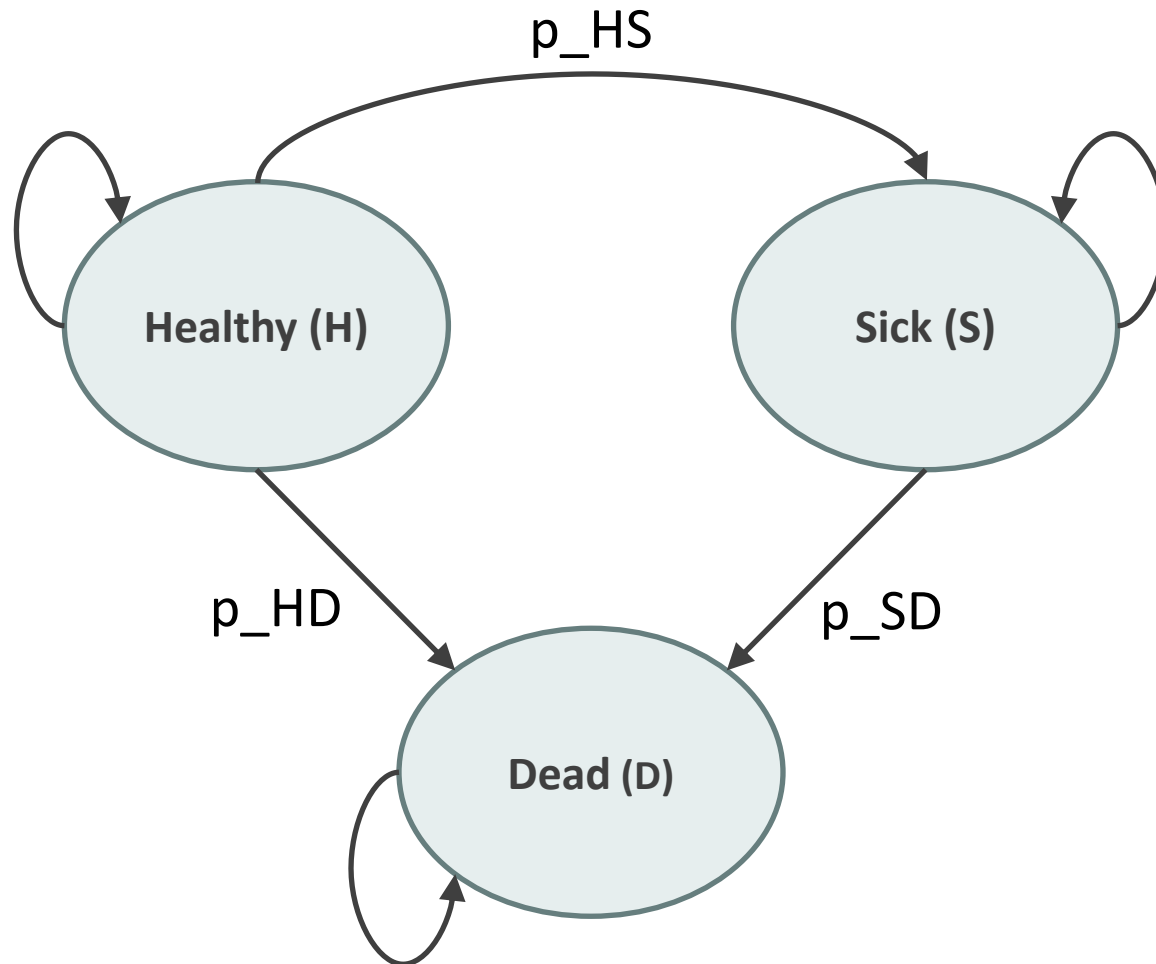


Cycle	State A	State B	State C	State D	Total
0	1000	0	0	0	1000
	1000×0.721	1000×0.202	1000×0.067	1000×0.01	
	↓	↓	↓	↓	
1	721	202	67	10	1000
2	520	263	181	36	1000
3	375	258	277	90	1000
4	270	226	338	166	1000
5	195	186	363	256	1000
6	140	147	361	351	1000
7	101	114	340	445	1000
8	73	87	308	532	1000
9	53	65	271	611	1000
10	38	48	234	680	1000
11	27	36	197	739	1000
12	20	26	164	789	1000
13	14	19	135	831	1000
14	10	14	110	865	1000
15	7	10	89	893	1000
16	5	7	72	916	1000
17	4	5	57	934	1000
18	3	4	45	948	1000
19	2	3	36	959	1000
20	1	2	28	968	1000

Markov Trace

Number or distribution of individuals at each cycle

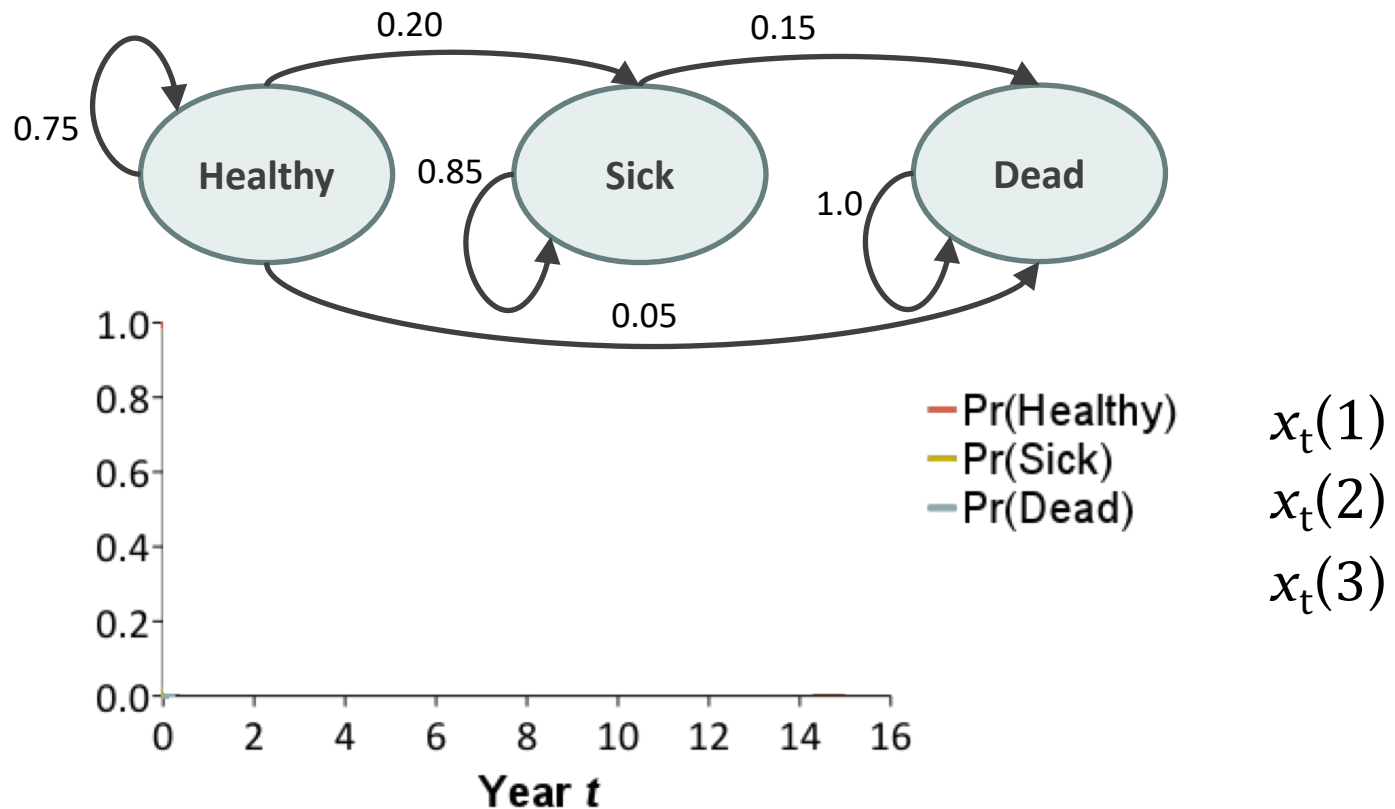
Three-State Model



Trace the Cohort Through Time

- Reflects the distribution of a cohort of patients over a set of health states over time

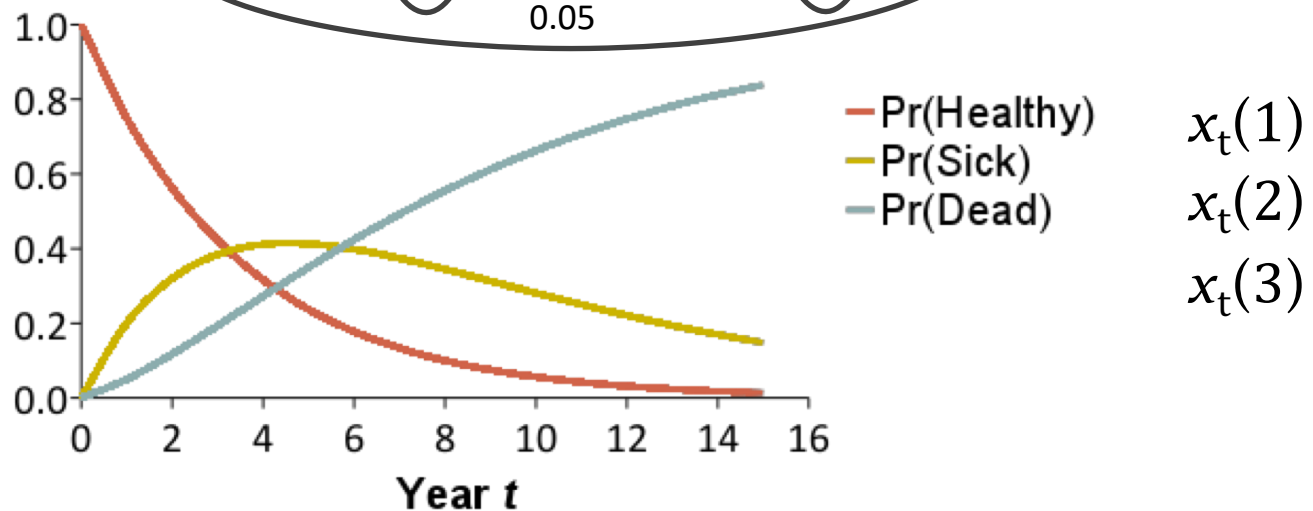
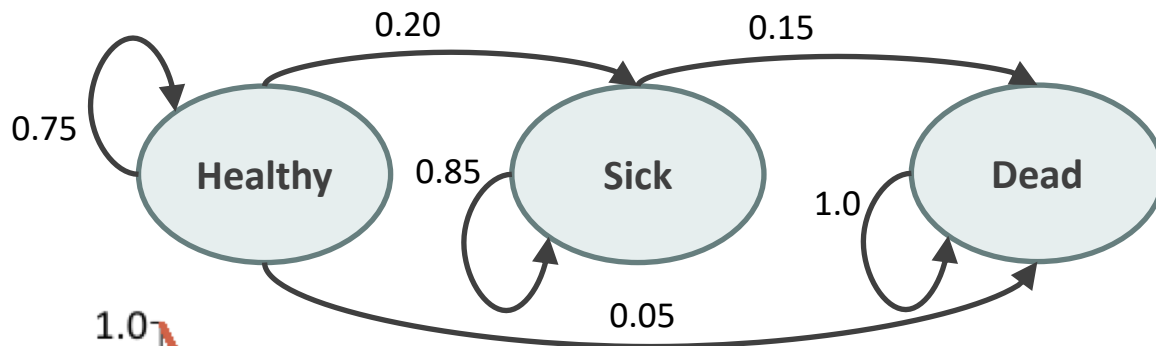
$$x_{10} = [0.06 \quad 0.28 \quad 0.66]$$



Trace the Cohort Through Time

- Reflects the distribution of a cohort of patients over a set of health states over time

$$x_{15} = [0.01 \quad 0.15 \quad 0.84]$$



Model as a Transition Matrix

- Summarize transition probabilities as a matrix

		To:				
		Healthy	Sick	Dead		
From:	Healthy	0.75	0.20	0.05	=	A
	Sick	0	0.85	0.15		
	Dead	0	0	1.0		

- Cohort distribution at next time step calculated through matrix multiplication

$$\begin{bmatrix} \text{Healthy} & x_{t+1} & \text{Sick} & \text{Dead} \end{bmatrix} = \begin{bmatrix} \text{Healthy} & x_t & \text{Sick} & \text{Dead} \end{bmatrix} \begin{bmatrix} A \end{bmatrix}$$

“Running” the Model

- Summarize transition probabilities as a matrix

		To:			=	A
		Healthy	Sick	Dead		
From:	Healthy	0.75	0.20	0.05		
	Sick	0	0.85	0.15		
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“Running” the Model

- Summarize transition probabilities as a matrix

		To:			
		Healthy	Sick	Dead	
From:	Healthy	0.75	0.20	0.05	= A
	Sick	0	0.85	0.15	
	Dead	0	0	1.0	

- Cohort distribution at next time step calculated through matrix multiplication

$$\begin{matrix} & x_1 \\ \begin{bmatrix} 0.75 & 0.20 & 0.05 \end{bmatrix} & = & \begin{bmatrix} \textcircled{1.0} & 0.0 & 0.0 \end{bmatrix} & \begin{matrix} A \\ \begin{bmatrix} 0.75 & 0.20 & 0.05 \\ 0 & 0.85 & 0.15 \\ 0 & 0 & 1.0 \end{bmatrix} \end{matrix}
 \end{matrix}$$

Markov Trace (Life-Years)

- Calculate expected remaining LE, QALE, costs
 - Multiply cohort distribution by state-specific values to calculate expected value at each time
 - Sum expected values over time (discount if desired)

Life-Years: 1.0 1.0 0.0

Time	Healthy	Sick	Dead	E[LYs]
0	1.0	0.0	0.0	--
1	0.75	0.20	0.05	
2	0.56	0.32	0.12	
3	0.42	0.38	0.19	
	

Sum
 \downarrow
 * $1/(1+r)$
 * $1/(1+r)^2$
 * $1/(1+r)^3$

Total life years: 6.77 years
 (Remaining life expectancy)

Markov Trace (Costs)

- Calculate expected remaining LE, QALE, costs
 - Multiply cohort distribution by state-specific values to calculate expected value at each time
 - Sum expected values over time (discount if desired)

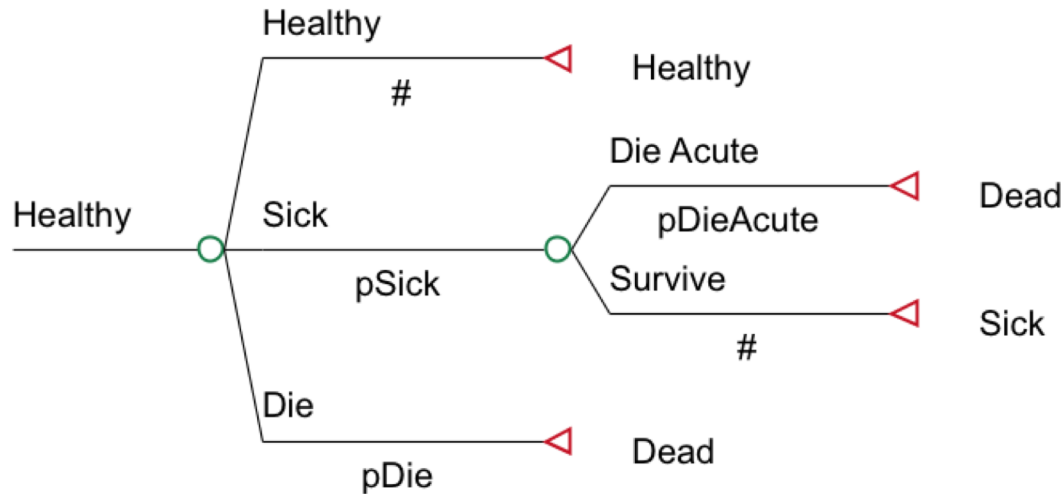
Costs:	\$500	\$2,500	\$0		
Time	Healthy	Sick	Dead	E[Costs]	
0	1.0	0.0	0.0	--	
1	0.75	0.20	0.05		* $1/(1+r)$
2	0.56	0.32	0.12		* $1/(1+r)^2$
3	0.42	0.38	0.19		* $1/(1+r)^3$
		

Sum


Total costs: \$11,557
 (Total remaining lifetime costs)

Transition Probabilities

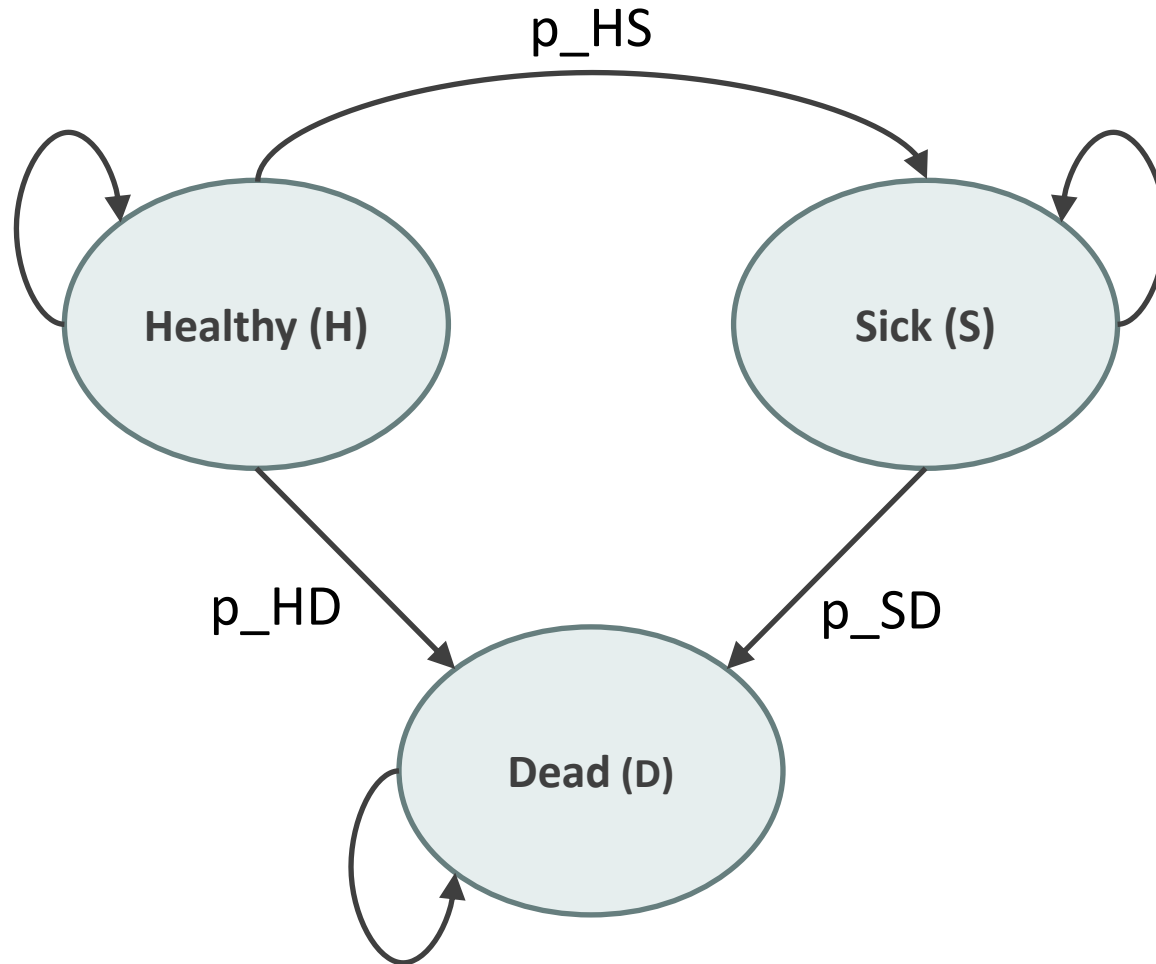
- $\Pr(\text{Healthy} \rightarrow \text{Dead})$ may not be conceptualized as one number



- $p_{\text{HD}} = p_{\text{Die}} + p_{\text{Sick}} * p_{\text{DieAcute}}$

Conceptualizing the Markov model in R

Simple state transition model in R



Simple state transition model

Model input:

p_{HS} : transition probability from *Healthy* to *Sick*

p_{HD} : transition probability *Healthy* to *Dead*

p_{SD} : transition probability *Sick* to *Dead*

c_H : cost of being in state *Healthy*

c_S : cost of being in state *Sick*

e_H : outcomes associated with state *Healthy*

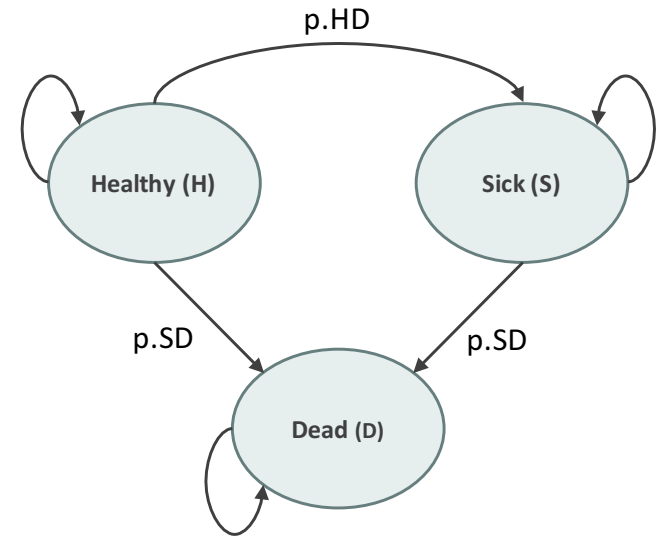
e_S : outcomes associated with state *Sick*

No cost or disutility associated with death

Matrix Implementation of the Markov Model

Transition probability matrix

$$P = \begin{matrix} & \begin{matrix} \mathbf{H} & \mathbf{S} & \mathbf{D} \end{matrix} \\ \begin{matrix} \mathbf{H} \\ \mathbf{S} \\ \mathbf{D} \end{matrix} & \begin{bmatrix} 1 - p_{HS} - p_{HD} & p_{HS} & p_{HD} \\ 0 & 1 - p_{SD} & p_{SD} \\ 0 & 0 & 1 \end{bmatrix} \end{matrix}$$



Vector of cycle's cost/outcomes

$$C = \begin{matrix} & \begin{matrix} \mathbf{H} \\ \mathbf{S} \\ \mathbf{D} \end{matrix} \\ \begin{matrix} c_H \\ c_S \\ 0 \end{matrix} \end{matrix} \quad E = \begin{matrix} & \begin{matrix} \mathbf{H} \\ \mathbf{S} \\ \mathbf{D} \end{matrix} \\ \begin{matrix} e_H \\ e_S \\ 0 \end{matrix} \end{matrix}$$

Matrix Implementation of the Markov Model


Create the $t \times 3$ matrix M that will store the proportion of the cohort at each state and cycle:

At $t = 0$:

$$M_0 = [1, 0, 0]$$

For $t < T$:

$$M_{t+1} = M_t P$$


$$[H_t \quad S_t \quad D_t] \begin{bmatrix} 1 - p_{HS} - p_{HD} & p_{HS} & p_{HD} \\ 0 & 1 - p_{SD} & p_{SD} \\ 0 & 0 & 1 \end{bmatrix}$$

Calculating total costs & effects

Total effects (TE):

$$E = M e$$
$$TE = \mathbf{1}_T E$$

Total costs (TC):

$$C = M c$$
$$TC = \mathbf{1}_T C$$

$\mathbf{1}_T$: $1 \times T$ vector of ones

Calculating total costs & effects (discounted)

Total effects (TE):

$$E = M e$$
$$TE = dw_T E$$

Total costs (TC):

$$C = M c$$
$$TC = dw_T C$$

$$dw_T = \frac{1}{(1 + d)^{0:T}}$$

R Session

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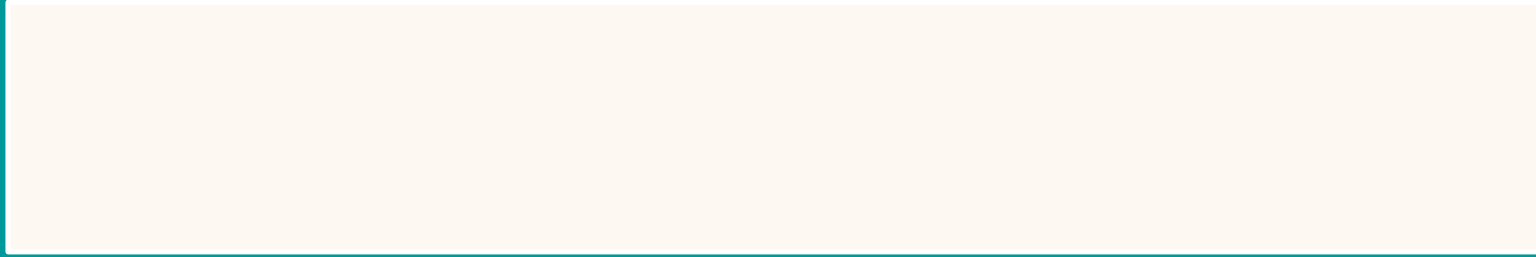


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<http://darthworkgroup.com/>



<https://github.com/organizations/DARTH-git>



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