A Tutorial on Time-Dependent Cohort State-Transition Models in R using a Cost-Effectiveness Analysis Example

Appendix

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Cohort tutorial model components

This table contains an overview of the key model components used in the code for the Sick-Sicker example from the DARTH manuscript: "A Tutorial on Time-Dependent Cohort State-Transition Models in R". The first column gives the mathematical notation for some of the model components that are used in the equations in the manuscript. The second column gives a description of the model component with the R name in the third column. The forth gives the data structure, e.g. scalar, list, vector, matrix etc, with the according dimensions of this data structure in the fifth column. The final column indicated the type of data that is stored in the data structure, e.g. numeric (5.2,6.3,7.4), category (A,B,C), integer (5,6,7), logical (TRUE, FALSE).

Element	Description	R name	Data structure	Dimensions	Data type
n_t	Time horizon	`n_t`	scalar		numeric
v_s	Names of the health states	`v_n`	vector	`n_states` x 1	character
n_s	Number of health states	`n_states`	scalar		numeric
$n_{S_{tunnels}}$	Number of health states with tunnels	`n_states_tunnels` scalar		numeric	

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Element	Description	R name	Data structure	Dimensions	Data type
v_{str}	Names of the strategies	`v_names_str`	scalar		character
n_{str}	Number of strategies	`n_str`	scalar		character
$\mathbf{d_c}$	Discount rate for costs	`d_c`	scalar		numeric
$\mathbf{d_e}$	Discount rate for effects	`d_e`	scalar		numeric
	Discount weights for costs	`v_dwc`	vector	(`n_t` x 1) + 1	numeric
	Discount weights for effects	`v_dwe`	vector	(`n_t` x 1) + 1	numeric
$\mathbf{wcc}$	Within-cycle correction weights using Simpson's 1/3 rule	`v_wcc`	vector	(`n_t` x 1) + 1	numeric
age_0	Age at baseline	`n_age_init`	scalar		numeric
age	Maximum age of follow up	`n_age_max`	scalar		numeric
M_{ad}	Cohort trace for age-dependency	`m_M_ad`	matrix	(`n_t` + 1) x `n_states`	numeric
$M_{tunnels}$	Aggregated Cohort trace for state-dependency	`m_M_tunnels`	matrix	(`n_t` + 1) x `n_states`	numeric
m_0	Initial state vector	`v_s_init`	vector	1 x `n_states`	numeric
m_t	State vector in cycle t	`v_mt`	vector	1 x `n_states`	numeric
	Transition probabilities				
$p_{[H,S1]}$	From Healthy to Sick conditional on surviving	`p_HS1`	scalar		numeric
$p_{[S1,H]}$	From Sick to Healthy conditional on surviving	`p_S1H`	scalar		numeric
$p_{[S1,S2]}$	From Sick to Sicker conditional on surviving	`p_S1S2`	scalar		numeric
$r_{[H,D]}$	Constant rate of dying when Healthy (all-cause mortality rate)	`r_HD`	scalar		numeric
$hr_{[S1,H]}$	Hazard ratio of death in Sick vs Healthy	`hr_S1`	scalar		numeric
$hr_{[S2,H]}$	Hazard ratio of death in Sicker vs Healthy	`hr_S2`	scalar		numeric
$hr_{[S1,S2]_{trtB}}$	Hazard ratio of becoming Sicker when Sick under treatment B	`hr_S1S2_trtB`	scalar		numeric
$p_{[S1,S2]_{trtB}}$	probability to become Sicker when Sick under treatment B conditional on surviving	`p_S1S2_trtB`	scalar		numeric
	Age-specific mortality				
$r_{[H,D,t]}$	Age-specific background mortality rates	`v_r_HDage`	vector	`n_t` x 1	numeric
$r_{[S1,D,t]}$	Age-specific mortality rates in the Sick state	`v_r_S1Dage`	vector	`n_t` x 1	numeric
$r_{[S2,D,t]}$	Age-specific mortality rates in the Sicker state	`v_r_S2Dage`	vector	`n_t` x 1	numeric
$p_{[H,D,t]}$	Age-specific mortality risk in the Healthy state	`v_p_HDage`	vector	`n_t` x 1	numeric
$p_{[S1,D,t]}$	Age-specific mortality rates in the Sick state	`v_p_S1Dage`	vector	`n_t` x 1	numeric
$p_{[S2,D,t]}$	Age-specific mortality rates in the Sicker state	`v_p_S2Dage`	vector	`n_t` x 1	numeric
$p_{[S1,S2,t]}$	Time-dependent transition probabilities from sick to sicker	`v_p_S1S2_tunnels`	vector	`n_t` x 1	numeric

Element	Description	R name	Data structure	Dimensions	Data type
	Annual costs				
	Healthy individuals	c_H	scalar		numeric
	Sick individuals in Sick	c_S1	scalar		numeric
	Sick individuals in Sicker	c_S2	scalar		numeric
	Dead individuals	c_D	scalar		numeric
	Additional costs treatment A	c_trtA	scalar		numeric
	Additional costs treatment B	c_trtB	scalar		numeric
	Utility weights				
	Healthy individuals	u_H	scalar		numeric
	Sick individuals in Sick	u_S1	scalar		numeric
	Sick individuals in Sicker	u_S2	scalar		numeric
	Dead individuals	u_D	scalar		numeric
	Treated with treatment A	u_trtA	scalar		numeric
	Transition weights				
	Utility decrement of healthy individuals when transitioning to S1	du_HS1	scalar		numeric
	Cost of healthy individuals when transitioning to S1	ic_S1	scalar		numeric
	Cost of dying	ic_D	scalar		numeric
	Lists				
	Cohort traces for each strategy	l_m_M	list		numeric
	Transition arrays for each strategy	l_A_A	list		numeric
	number of tunnel states	n_tunnel_size	scalar		numeric
	tunnel names of the Sick state	v_Sick_tunnel	vector	1 x n_states	numeric
	state names including tunnel states	v_n_tunnel	vector	1 x n_states	character
	number of states including tunnel states	n_states_tunnels	scalar		numeric
	initial state vector for the model with tunnels	v_s_init_tunnels			numeric
$\mathbf{P}$	Time-dependent transition probability array	a_P	array	n_states x n_states x n_t	numeric
$\mathbf{P}_{tunnels}$	Transition probability array for the model with tunnels	a_P_tunnels	array	n_states_tunnels x n_states_tunnels x n_t	numeric

Element	Description	R name	Data structure	Dimensions	Data type
$\mathbf{A}$	Transition dynamics array	`a_A`	array	`n_states` x `n_states` x (`n_t` + 1)	numeric
$\mathbf{R_u}$	Transition rewards for effects	`a_R_u`	array	`n_states` x `n_states` x (`n_t` + 1)	numeric
$\mathbf{R_c}$	Transition rewards for costs	`a_R_c`	array	`n_states` x `n_states` x (`n_t` + 1)	numeric
$\mathbf{Y_u}$	Expected effects per states per cycle	`a_Y_u`	array	`n_states` x `n_states` x (`n_t` + 1)	numeric
$\mathbf{Y_c}$	Expected costs per state per cycle	`a_Y_c`	array	`n_states` x `n_states` x (`n_t` + 1)	numeric
	Data structures				
	Expected QALYs per cycle under a strategy	`v_qaly_str`	vector	1 x (`n_t` + 1)	numeric
	Expected costs per cycle under a strategy	`v_cost_str`	vector	1 x (`n_t` + 1)	numeric
	Total expected discounted QALYs for a strategy	`n_tot_qaly_str`	scalar		numeric
	Total expected discounted costs for a strategy	`n_tot_cost_str`	scalar		numeric
	Summary of the model outcomes	`df_cea`	data frame		
	Summary of the model outcomes	`table_cea`	table		
	Input parameters values of the model for the cost-effectiveness analysis	`df_psa`	data frame		

Table II: Input parameters for probabilistic analysis of the time-dependent 3-state model

Parameter	Distribution	Distribution values	Parameter mean	Parameter standard error
Number of simulation	`n_sim`	1000		
Annual transition probabilities				
- Disease onset (Healthy to Sick)	*Beta*	$\alpha = 30$, $\beta = 170$	0.15	0.026
- Recovery (Sick to Healthy)	*Beta*	$\alpha = 60$, $\beta = 60$	0.5	0.045
- Disease progression (Sick to Sicker) in the age-dependent model	*Beta*	$\alpha = 84$, $\beta = 716$	0.106	0.011
Risks of disease and treatment				

Parameter	Distribution	Distribution values	Parameter mean	Parameter standard error
- Hazard ratio of death in Sick vs Healthy	*Lognormal*	$log(\mu) = log(3)$, $log(\sigma) = 0.01$	3	0.03
- Hazard ratio of death in Sicker vs Healthy	*Lognormal*	$log(\mu) = log(10)$, $log(\sigma) = 0.2$	10	0.2
- Hazard ratio of Sick to Sicker under treatment B	*Lognormal*	$log(\mu) = log(0.6)$, $log(\sigma) = 0.2$	0.60	0.013
Annual costs				
- Healthy individuals	*Gamma*	$Shape = 100$, $Scale = 20$	2000	200
- Sick individuals in Sick	*Gamma*	$Shape = 177.8$, $Scale = 22.5$	4000	300
- Sick individuals in Sicker	*Gamma*	$Shape = 225$, $Scale = 66.7$	15000	1000
- Cost of treatment A for individuals in Sick or Sicker	*Gamma*	$Shape = 73.5$, $Scale = 163.3$	12000	1400
- Cost of treatment B for individuals in Sick or Sicker	*Gamma*	$Shape = 86.2$, $Scale = 150.8$	13050	1430
Utility weights				
- Healthy individuals	*Beta*	$\alpha = 200$, $\beta = 3$	0.985	0.008
- Sick individuals in Sick	*Beta*	$\alpha = 130$, $\beta = 45$	0.74	0.033
- Sick individuals in Sicker	*Beta*	$\alpha = 230$, $\beta = 230$	0.5	0.023
- Individuals treated with treatment A	*Beta*	$\alpha = 300$, $\beta = 15$	0.95	0.012
Transition rewards				
- Disutility when transitioning from Healthy to Sick	*Beta*	$\alpha = 11$, $\beta = 1088$	0.01	0.003
- Increase in cost when transitioning from Healthy to Sick	*Gamma*	$\alpha = 25$, $\beta = 40$	1000	195
- Increase in cost when dying	*Gamma*	$\alpha = 100$, $\beta = 20$	2000	200