

# 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	<code>n_cycles</code>	scalar		numeric
	Cycle length	<code>cycle_length</code>	scalar		numeric
$v_s$	Names of the health states	<code>v_names_states</code>	vector	<code>n_states</code> x 1	character

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Element	Description	R name	Data structure	Dimensions	Data type
$n_s$	Number of health states	<b>n_states</b>	scalar		numeric
$n_{S_{tunnels}}$	Number of health states with tunnels	<b>n_states_tunnels</b>	scalar	numeric	
$v_{str}$	Names of the strategies	<b>v_names_str</b>	scalar		character
$n_{str}$	Number of strategies	<b>n_str</b>	scalar		character
<b>d<sub>c</sub></b>	Discount rate for costs	<b>d_c</b>	scalar		numeric
<b>d<sub>e</sub></b>	Discount rate for effects	<b>d_e</b>	scalar		numeric
	Discount weights for costs	<b>v_dwc</b>	vector	$(n_t \times 1) + 1$	numeric
	Discount weights for effects	<b>v_dwe</b>	vector	$(n_t \times 1) + 1$	numeric
	Sequence of cycle numbers	<b>v_cycles</b>	vector	$(n_t \times 1) + 1$	numeric
<b>wcc</b>	Within-cycle correction weights using Simpson's 1/3 rule	<b>v_wcc</b>	vector	$(n_t \times 1) + 1$	numeric
$age_0$	Age at baseline	<b>n_age_init</b>	scalar		numeric
$age$	Maximum age of follow up	<b>n_age_max</b>	scalar		numeric
$M$	Cohort trace matrix	<b>m_M</b>	matrix	$(n_t + 1) \times n_{states}$	numeric
$M_{tunnels}$	Aggregated Cohort trace for state-dependency	<b>m_M_tunnels</b>	matrix	$(n_t + 1) \times n_{states}$	numeric
	List of the cohort trace matrix for all strategies	<b>l_m_M</b>	list		numeric
$m_0$	Initial state vector	<b>v_m_init</b>	vector	$1 \times n_{states}$	numeric
$m_t$	State vector in cycle t	<b>v_mt</b>	vector	$1 \times n_{states}$	numeric
<b>Life table input</b>					
	State vector in cycle t	<b>lt_usa_2005</b>	list		numeric
	Vector of age-specific mortality rates	<b>v_r_mort_by_age</b>	vector		numeric
<b>Transition probabilities</b>					
$p_{[H,S1]}$	From Healthy to Sick conditional on surviving	<b>p_HS1</b>	scalar		numeric
$p_{[S1,H]}$	From Sick to Healthy conditional on surviving	<b>p_S1H</b>	scalar		numeric
$p_{[S1,S2]}$	From Sick to Sicker conditional on surviving	<b>p_S1S2</b>	scalar		numeric
$r_{[H,D]}$	Constant rate of dying when Healthy (all-cause mortality rate)	<b>r_HD</b>	scalar		numeric
$r_{[S1,S2]}$	Constant rate of becoming Sicker when Sick	<b>r_S1S2</b>	scalar		numeric
$r_{[S1,S2]_{trtB}}$	Constant rate of becoming Sicker when Sick for treatment B	<b>r_S1S2_trtB</b>	scalar		numeric
$hr_{[S1,H]}$	Hazard ratio of death in Sick vs Healthy	<b>hr_S1</b>	scalar		numeric
$hr_{[S2,H]}$	Hazard ratio of death in Sicker vs Healthy	<b>hr_S2</b>	scalar		numeric
$hr_{[S1,S2]_{trtB}}$	Hazard ratio of becoming Sicker when Sick under treatment B	<b>hr_S1S2_trtB</b>	scalar		numeric

Element	Description	R name	Data structure	Dimensions	Data type
$p_{[S1,S2]_{trtB}}$	probability to become Sicker when Sick under treatment B conditional on surviving	p_S1S2_trtB	scalar		numeric
<b>Weibull parameters for transition probability of becoming Sicker when Sick conditional on surviving</b>					
$\lambda$	scale of the Weibull hazard function	p_S1S2_scale	scalar		numeric
$\gamma$	shape of the Weibull hazard function	p_S1S2_shape	scalar		numeric
<b>Simulation-time dependent mortality</b>					
$r_{[H,D,t]}$	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
$r_{[S1,S2,t]}$	State-residence-dependent transition rate of becoming Sicker when Sick	v_r_S1S2_tunnels	vector	n_t x 1	numeric
<b>Annual costs</b>					
	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
	Vector of state costs for a strategy	v_c_str	vector	1 x n_states	numeric
	List that stores the vectors of state costs for each strategy	l_c	List		numeric
<b>Utility weights</b>					
	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

Element	Description	R name	Data structure	Dimensions	Data type
	Treated with treatment A	<b>u_trtA</b>	scalar		numeric
	Vector of state utilities for a strategy	<b>v_u_str</b>	vector	$1 \times \mathbf{n\_states}$	numeric
	Vector of S1 utilities when including state-residency for a strategy SoC for	<b>v_u_S1_SoC</b>	vector	$1 \times \mathbf{n\_tunnel\_size}$	numeric
	List that stores the vectors of state utilities for each strategy	<b>l_u</b>	List		numeric
	<b>Transition weights</b>				
	Utility decrement of healthy individuals when transitioning to S1	<b>du_HS1</b>	scalar		numeric
	Cost of healthy individuals when transitioning to S1	<b>ic_HS1</b>	scalar		numeric
	Cost of dying	<b>ic_D</b>	scalar		numeric
	<b>Tunnel state structures</b>				
	number of tunnel states	<b>n_tunnel_size</b>	scalar		numeric
	vector with cycles for tunnels states	<b>v_cycles_tunnel</b>	vector	$1 \times \mathbf{n\_tunnel\_size}$	numeric
	tunnel names of the Sick state	<b>v_Sick_tunnel</b>	vector	$1 \times \mathbf{n\_states}$	numeric
	state names including tunnel states	<b>v_names_states_tunnels</b>	vector	$1 \times \mathbf{n\_states\_tunnels}$	character
	number of states including tunnel states	<b>n_states_tunnels</b>	scalar		numeric
	Initial state vector for the model with tunnels	<b>v_m_init_tunnels</b>	vector	$1 \times \mathbf{n\_states\_tunnels}$	numeric
<b>P</b>	Time-dependent transition probability array	<b>a_P</b>	array	$\mathbf{n\_states} \times \mathbf{n\_states} \times \mathbf{n\_t}$	numeric
<b>P<sub>tunnels</sub></b>	Transition probability array for the model with tunnels	<b>a_P_tunnels</b>	array	$\mathbf{n\_states\_tunnels} \times \mathbf{n\_states\_tunnels} \times \mathbf{n\_t}$	numeric
<b>A</b>	Transition dynamics array	<b>a_A</b>	array	$\mathbf{n\_states} \times \mathbf{n\_states} \times (\mathbf{n\_t} + 1)$	numeric
	List of the transition dynamics arrays for all strategies	<b>l_m_A</b>	list		numeric
<b>R<sub>u</sub></b>	Transition rewards for effects	<b>a_R_u</b>	array	$\mathbf{n\_states} \times \mathbf{n\_states} \times (\mathbf{n\_t} + 1)$	numeric
<b>R<sub>c</sub></b>	Transition rewards for costs	<b>a_R_c</b>	array	$\mathbf{n\_states} \times \mathbf{n\_states} \times (\mathbf{n\_t} + 1)$	numeric
<b>Y<sub>u</sub></b>	Expected effects per states per cycle	<b>a_Y_u</b>	array	$\mathbf{n\_states} \times \mathbf{n\_states} \times (\mathbf{n\_t} + 1)$	numeric

Element	Description	R name	Data structure	Dimensions	Data type
<b>Y<sub>c</sub></b>	Expected costs per state per cycle	<b>a_Y_c</b>	array	<b>n_states</b> x <b>n_states</b> x ( <b>n_t</b> + 1)	numeric
	*NOTE: these structures can have <b>_strX</b> to indicate the strategy of interest				
	Expected QALYs per cycle under a strategy	<b>v_qaly_str</b>	vector	1 x ( <b>n_t</b> + 1)	numeric
	Expected costs per cycle under a strategy	<b>v_cost_str</b>	vector	1 x ( <b>n_t</b> + 1)	numeric
	Vector of expected discounted QALYs for each strategy	<b>v_tot_qaly</b>	vector	1 x <b>n_states</b>	numeric
	Vector of expected discounted costs for each strategy	<b>v_tot_cost</b>	vector	1 x <b>n_states</b>	numeric
	Summary matrix with costs and QALYS per strategy	<b>m_outcomes</b>	table	<b>n_states</b> x 2	
	Summary of the model outcomes	<b>df_cea</b>	data frame		
	Summary of the model outcomes	<b>table_cea</b>	table		
	Input parameters values of the model for the cost-effectiveness analysis	<b>df_psa</b>	data frame		
	<b>Probabilistic analysis structures</b>				
	Number of PSA iterations	<b>n_sim</b>	scalar		numeric
	List that stores all the values of the input parameters	<b>l_params_all</b>	list		numeric
	Data frame with the parameter values for each PSA iteration	<b>df_psa_input</b>	data frame		numeric
	Vector with the names of all the input parameters	<b>v_names_params</b>	vector		character
	List with the model outcomes of the PSA for all strategies	<b>l_psa</b>	list		numeric
	Vector with a sequence of relevant willingness-to-pay values	<b>v_wtp</b>	vector		numeric
	Data frame to store expected costs and effects for each strategy from the PSA	<b>df_out_ce_psa</b>	data frame		numeric
	Data frame to store incremental cost-effectiveness ratios (ICERs) from the PSA	<b>df_cea_psa</b>	data frame		numeric
	For more details about the PSA structures read the vignettes of <b>dampack</b>				