Multistate models with multiple time scales

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- Timescale matters — like any other covariate.

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- Time scales are **covariates**

Useful representation of 2 timescales

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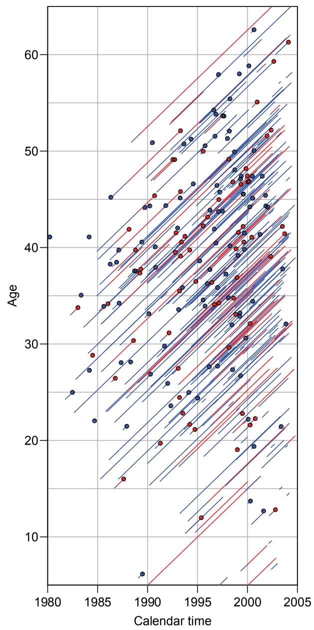

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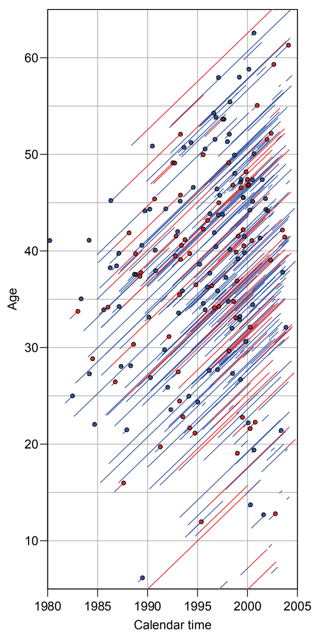

A **Lexis** diagram.

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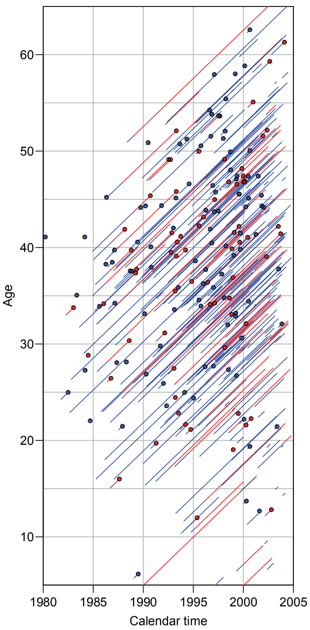

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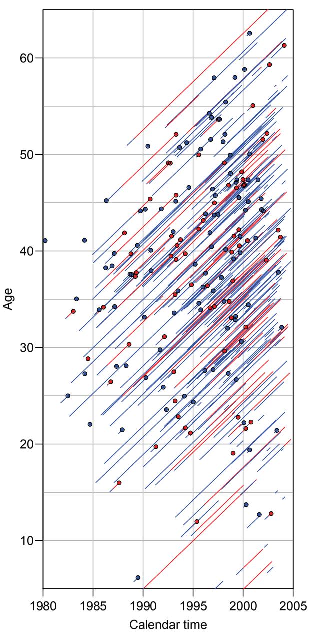
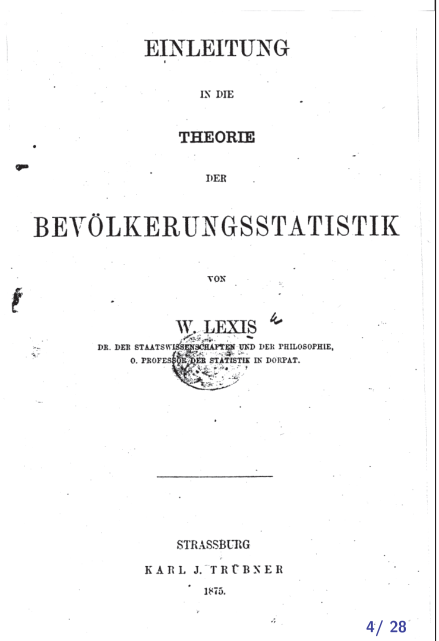




EINLEITUNG

IN DIE

THEORIE

DER

BEVÖLKERUNGSSTATISTIK

VON

W. LEXIS

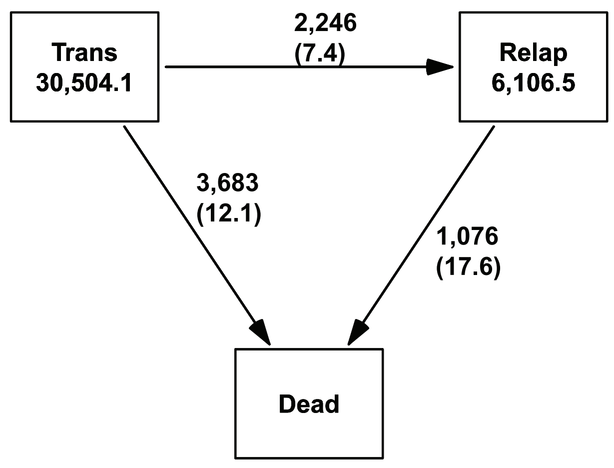
DR. DER STAATSWISSENSCHAFTEN UND DER PHILOSOPHIE,
O. PROFESSOR DER STATISTIK IN DORPAT.

STRASSBURG

KARL J. TRÜBNER

1875.

Transplant data



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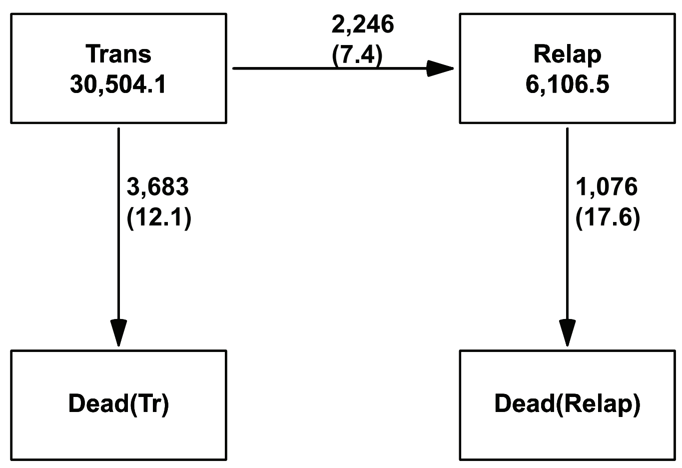

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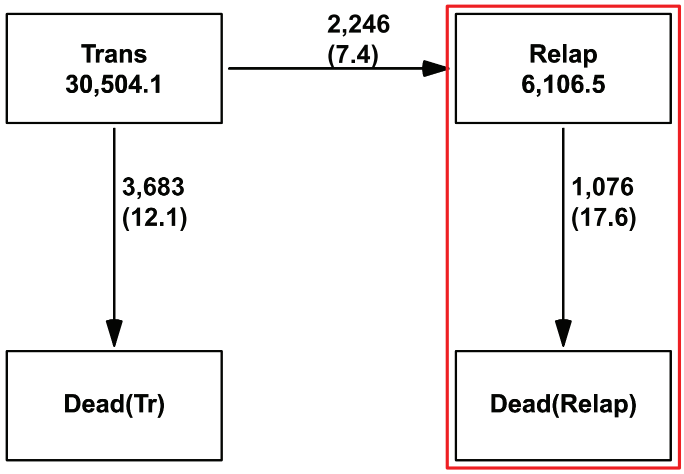

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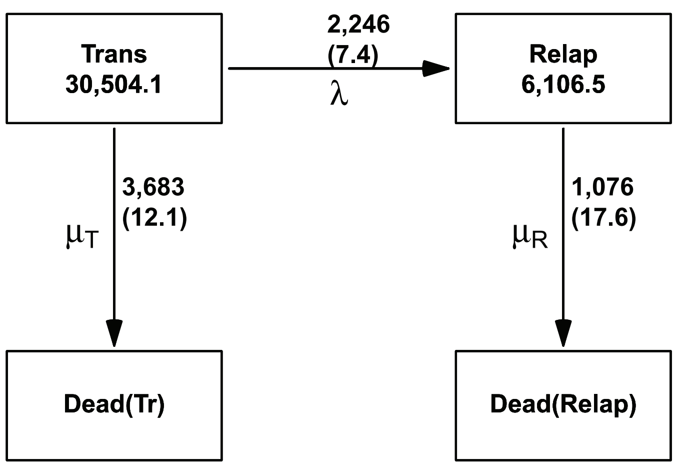

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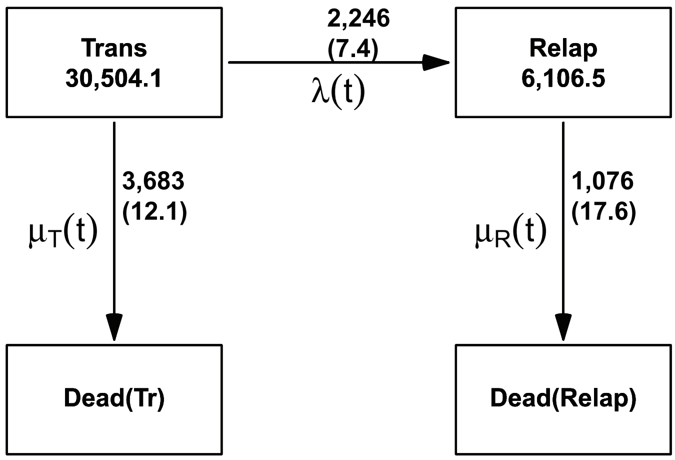

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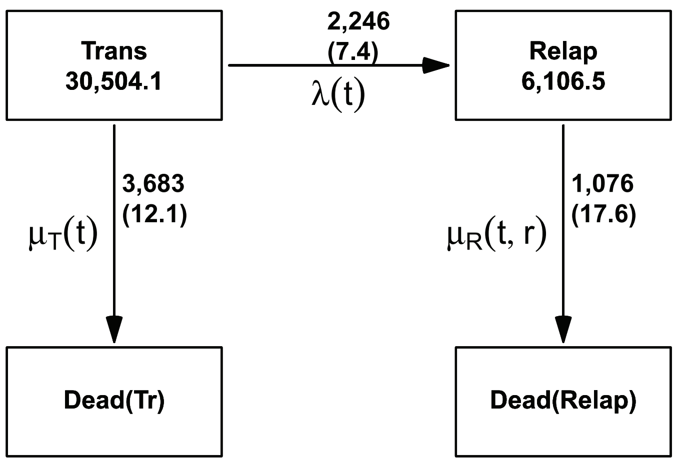

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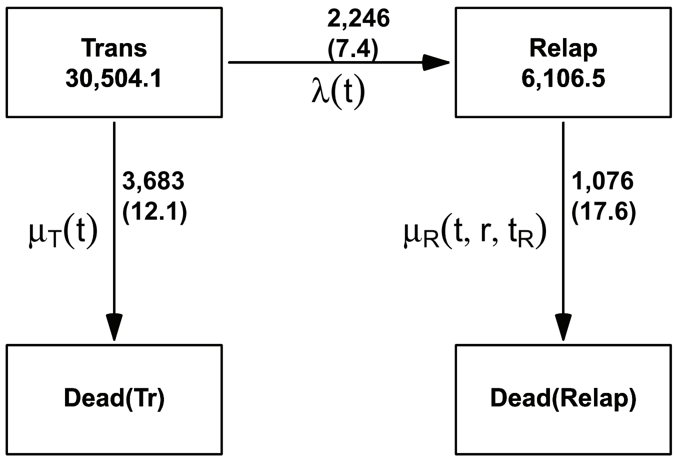

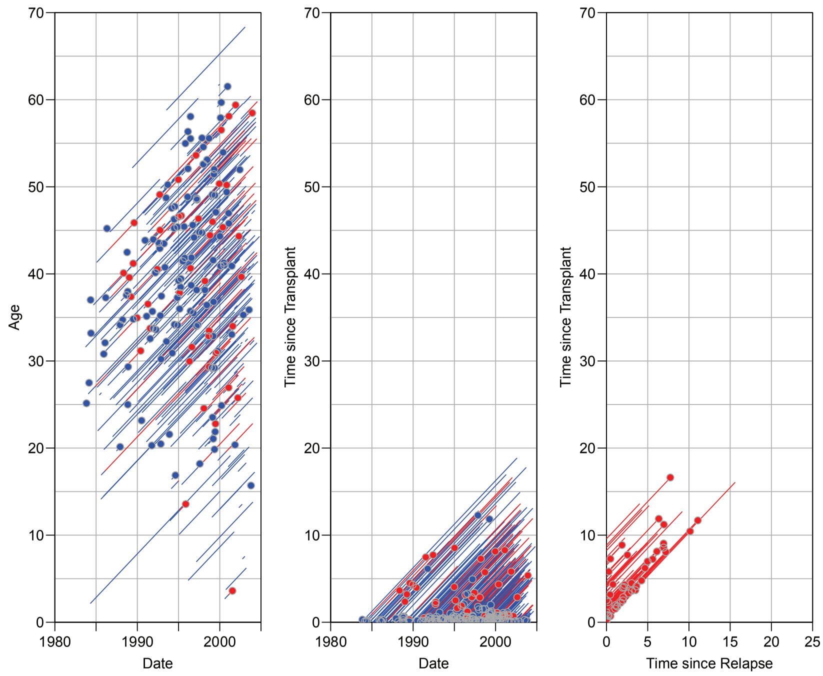

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- Ultimate purpose: $\mathrm{P}\{\text{in state X at time } t\}$
- If only one time scale is used, this reduces to simple multiplication of (infinitesimal) transition probability matrices.

Approximate transition probabilities

If h is sufficiently small:

$$
\begin{aligned}
p_{\mathsf{T,T}}(t, t+h) &= 1 - \lambda(t)h - \mu_T(t)h \\
p_{\mathsf{T,R}}(t, t+h) &= \lambda(t)h \\
p_{\mathsf{T,D(T)}}(t, t+h) &= \mu_T(t)h \\
p_{\mathsf{R,R}}(t, t+h) &= 1 - \mu_R(t)h \\
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\end{aligned}
$$

Transition matrix
— a matrix of transition probabilities:

	To:	T	R	D(T)	D(R)
From:	T	$p_{\mathsf{T,T}}$	$p_{\mathsf{T,R}}$	$p_{\mathsf{T,D(T)}}$	0
	R	0	$p_{\mathsf{R,R}}$	0	$p_{\mathsf{R,D(R)}}$
	D(T)	0	0	1	0
	D(R)	0	0	0	1

Using the transition probabilities

Put these in $\mathbf{P}(t, t+h)$ (for all t) and then compute $\mathbf{P}(t, s)$ by computing the transitions in small bits of time:

$$\mathbf{P}(t, s) = \prod_{i=1}^{i=(t-s)/h} \mathbf{P}(t + (i-1)h, t + ih)$$

All you need is $\mu_T(t)$, $\mu_T(t)$ and $\lambda(t)$ for any t:

- Poisson-model with smooth parametric expressions of rates

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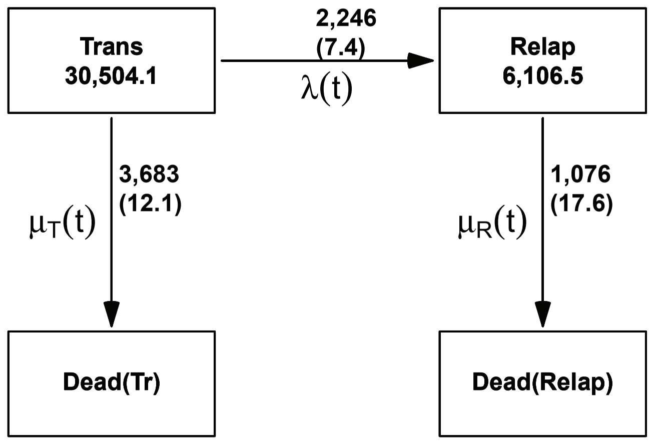
All you need is $\mu_T(t)$, $\mu_T(t)$ and $\lambda(t)$ for any t:

- Poisson-model with smooth parametric expressions of rates
- Recovery of the integrated intensity from a Cox-model, followed by smoothing / differentiation.

Transplant data

Markov property?



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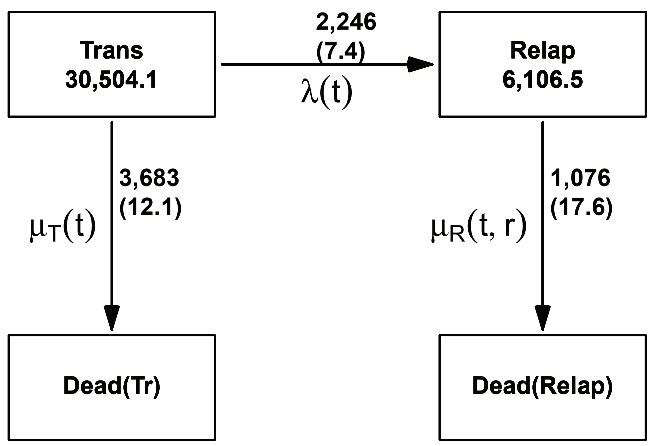

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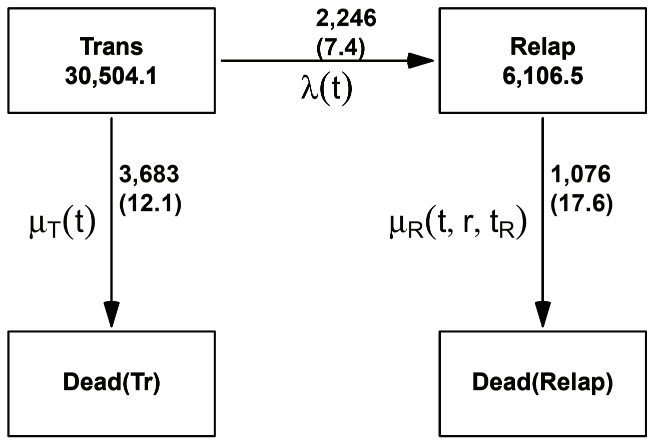

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- — highly unrealistic in practice

Markov property: Empirical question

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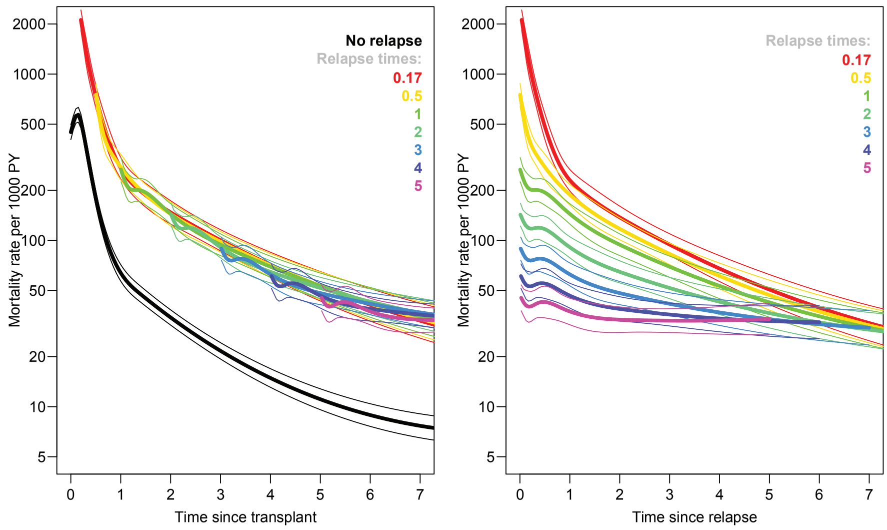
- Lexis machinery from the **Epi** package for **R**.

$$\log(\mu) = h(t)+k(r) \qquad + X\beta$$



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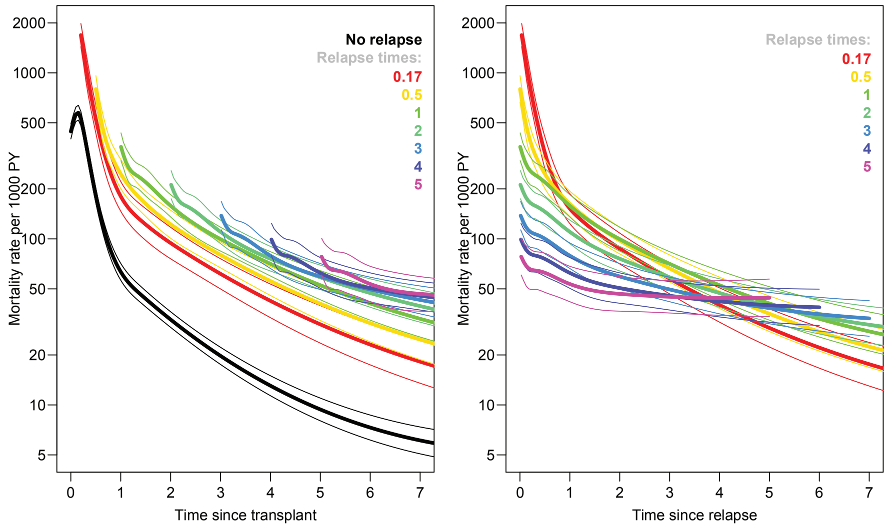

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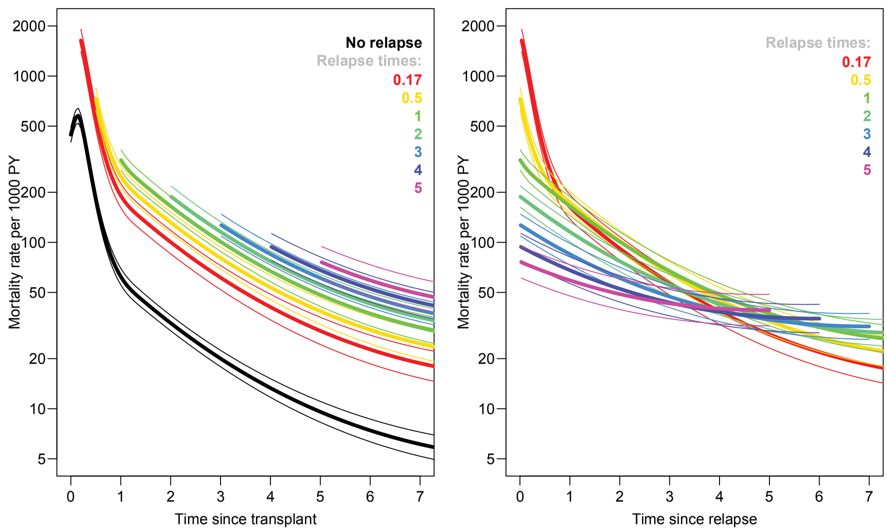

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- Note: It is an **empirical** question what timescales to use.
- Note: We also need a model for the incidence rates to compute probabilities.

Not Markov: the hard way

$$\mathrm{P}\{\text{T at } t\} = \exp\Big(-\int_0^t \lambda(s) + \mu_T(s)\,\mathrm{d}s\Big)$$

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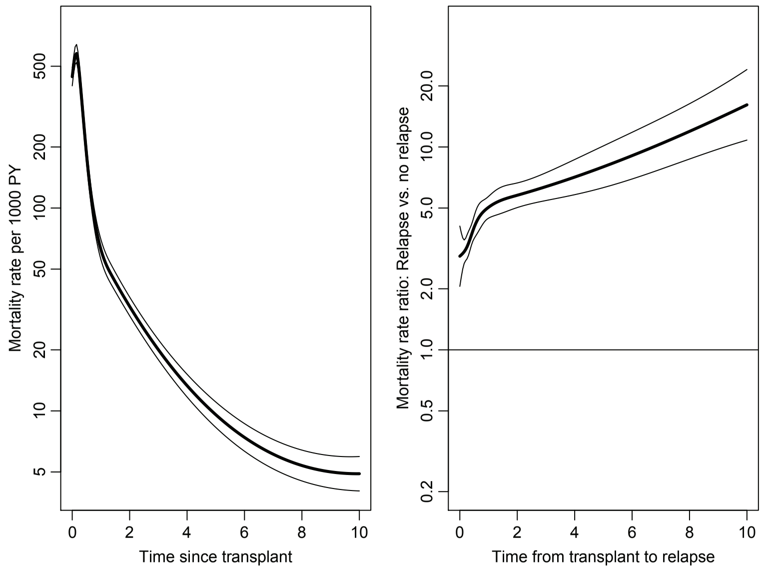

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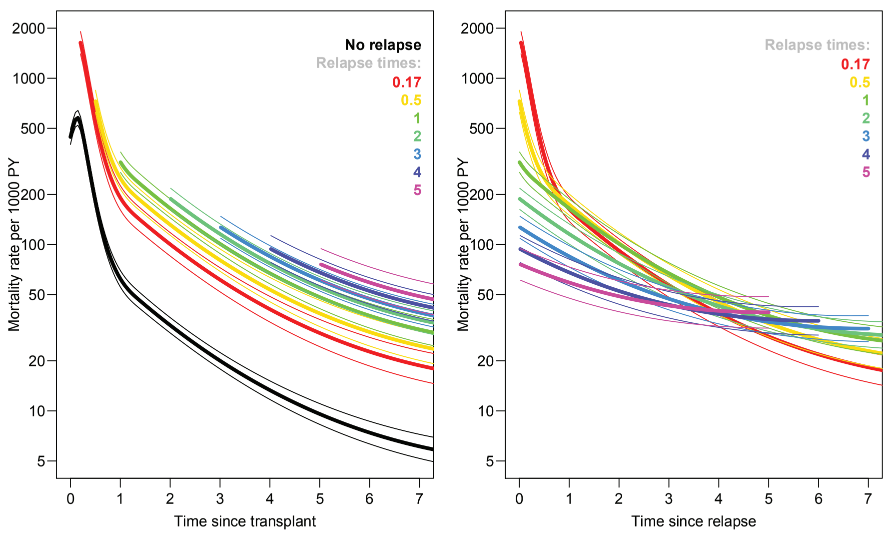
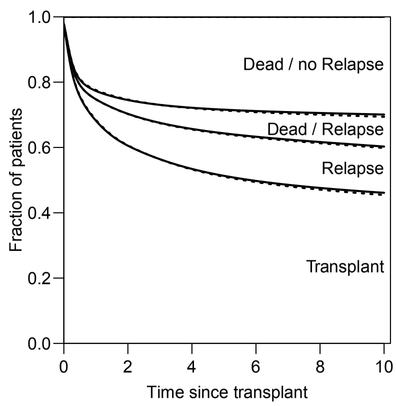
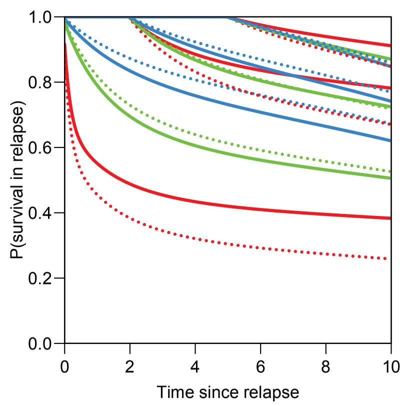


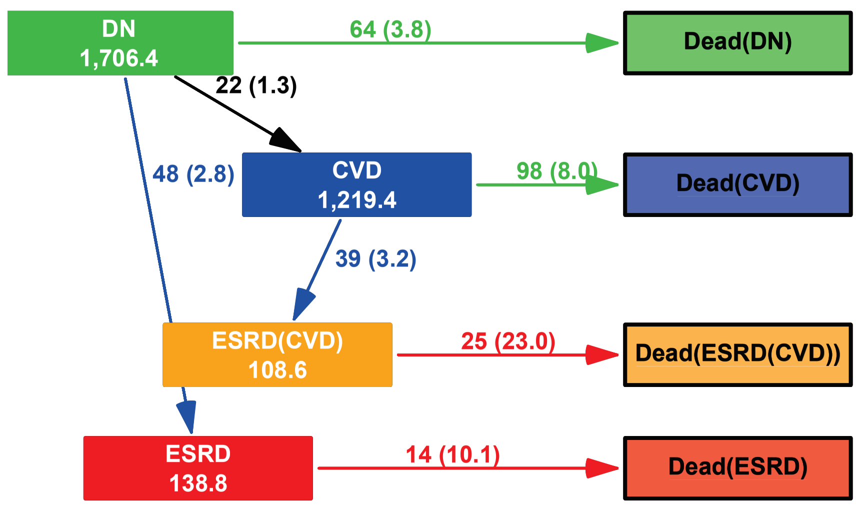




Survival in state "Relapse" conditional on different survival times in the state (curves starting at 0,2,5 years after relapse)
Different times *to* relapse: red: 2 months; green: 1 year; blue: 3 years.

Full lines based on the model with effects of time since transplant and time to relapse, broken lines based on the Markov model with only time since transplant.

A more complicated multistate model



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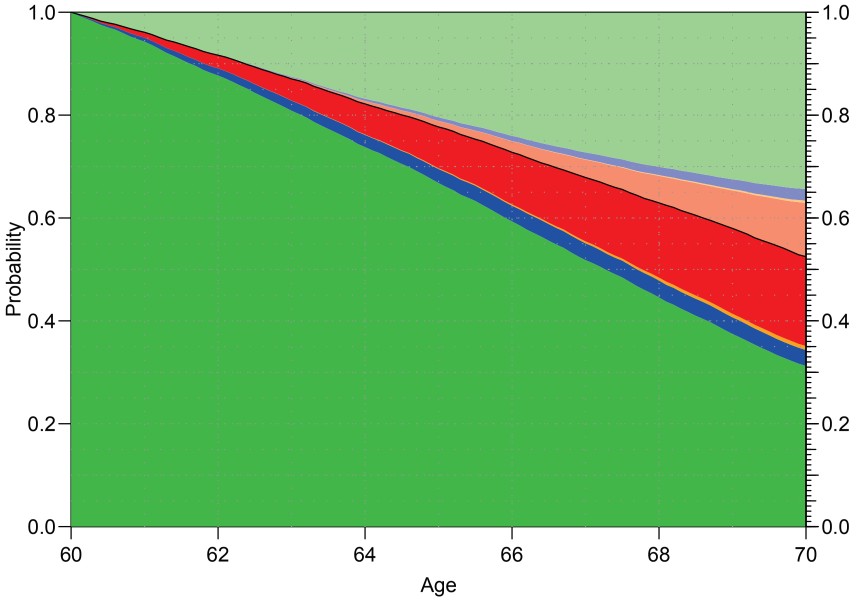

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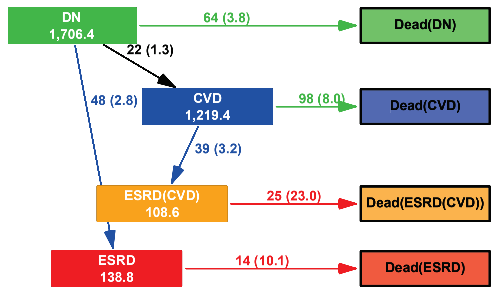

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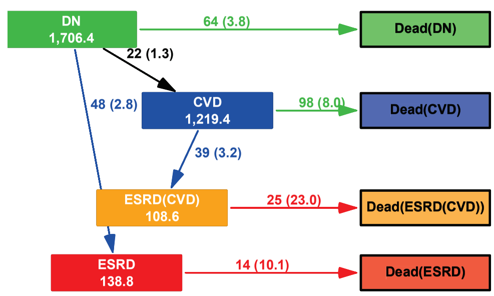

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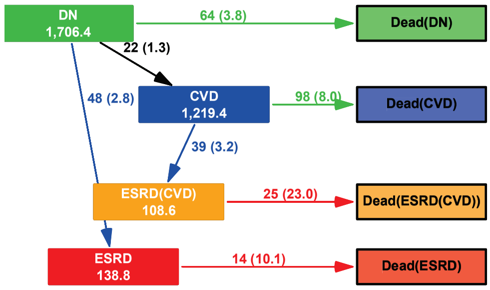

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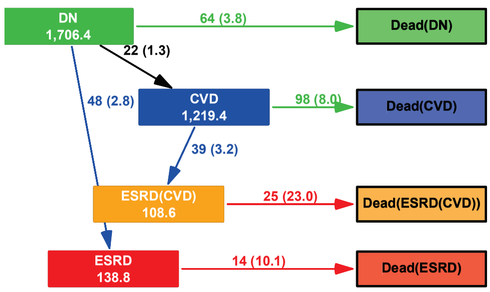

- Simulate a "survival time" for each possible transition **out** of a state.
- The smallest of these is the transition time.
- Choose the corresponding transition type as transition.

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Implemented in the `simLexis` function in the `Epi` package for **R**.

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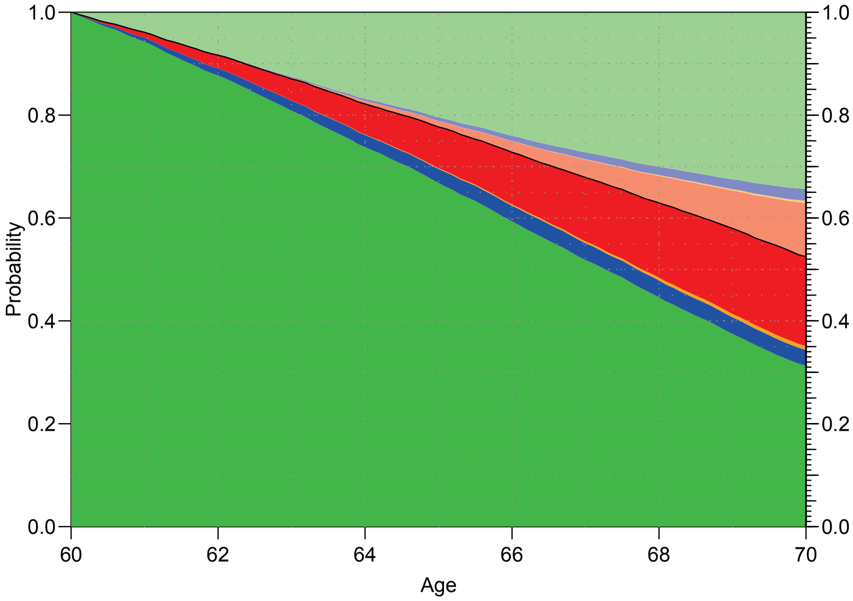
- Repeat for another type of person.

Simulated probabilities



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