

# Generalized multistate simulation model “gems” to test the effectiveness of health interventions: development and first applications

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## Package ‘gems’

August 16, 2012

**Type** Package

**Title** General multistate simulation model

**Version** 0.8

**Date** 2012-08-14

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**Maintainer** Luisa Salazar <l.salazar@ispm.ch>

**Depends** MASS, methods, msm, mstate

**Description**

This package allows to simulate and analyze multistate models with general hazard functions.

**License** GPL-2

### R topics documented:

gems-package	1
generateHazardMatrix	2
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gems-package	<i>General multistate simulation model</i>
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### Description

Provides functionality to preparation of hazard functions and parameters, simulate from a general multistate model and making predictions. The multistate model is not required to be a Markov model and may take the history of previous events into account. In the basic version, it allows to simulate from transition-specific hazard function, whose parameters are multivariable normally distributed.

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- **Mathematical models**
  - Progression of diseases
  - Evaluation of strategies
- Traditional models
  - Efficient computational implementations
  - Have succeeded in explaining the dynamics of different epidemics
  - Not flexible enough to capture details of transition times

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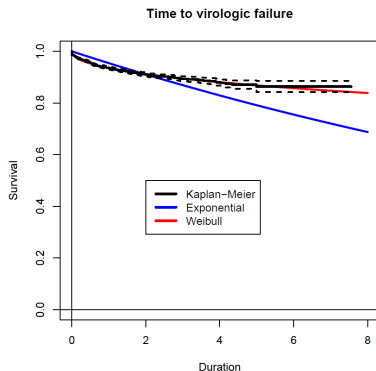
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- Time-to-event distribution
  - Exponential distribution
  - Multiple Weibull distributions
  - Others
- Transition-specific hazard functions



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We developed a multistate model that:

- Monitors disease progression in a cohort of individual patients
- Takes baseline characteristics and history of previous events into account
- Samples the parameters of transition functions
- Can be combined with a transmission model

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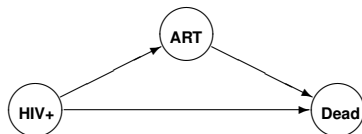
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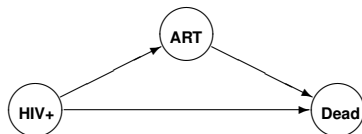
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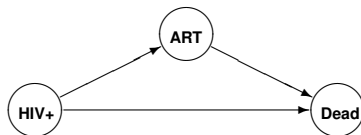
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- Choose minimum time and corresponding state
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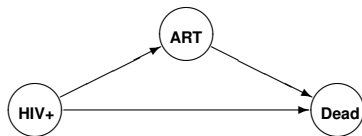
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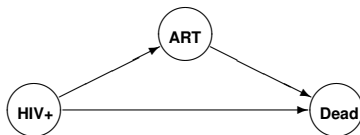
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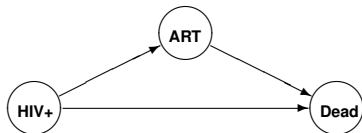
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$$h_{12}^{intervention}(t) = \lambda \cdot h_{12}(t)$$

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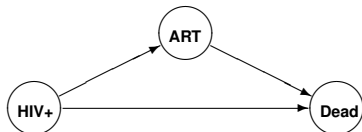
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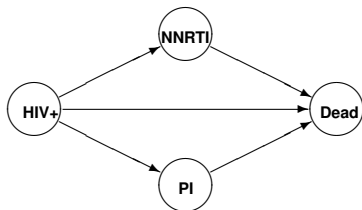
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The model has been validated by reproducing previously obtained results from:

- An individual based model on HIV monitoring strategies (Estill J. et al, 2012)
- A deterministic model on tuberculosis control in South Africa (Bacaer N. et al, 2008)

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- Model states and parameters by Bacaer et al.
- The progression of patients was simulated to obtain an artificial cohort

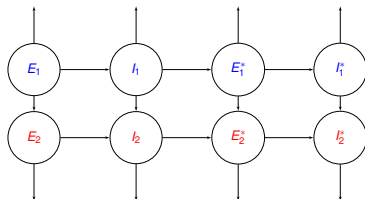


- HIV -:

- $E_1$ : latently infected
- $I_1$ : primary disease
- $E_1^*$ : recovered
- $I_1^*$ : secondary disease

- HIV+:

- $E_2$ : latently infected
- $I_2$ : primary disease
- $E_2^*$ : recovered
- $I_2^*$ : secondary disease



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```
R > head(cohort)
```

	Latent TB	Primary disease	Recovered
Patient 1	0	6.687370	6.723881
Patient 2	0	1.774813	1.829103
Patient 3	0	7.389355	NA
Patient 4	0	1.479336	1.801086
Patient 5	0	NA	NA

	Secondary disease	Dead
Patient 1	NA	14.613206
Patient 2	7.14286	11.031754
Patient 3	NA	7.951290
Patient 4	NA	3.292260
Patient 5	NA	7.159878

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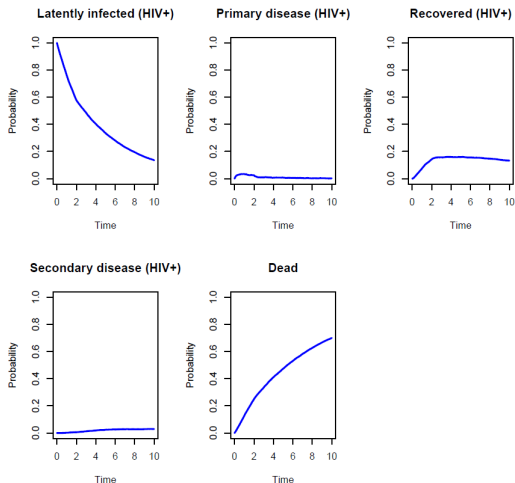
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# Probabilities over time

## Probabilities for HIV+



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- The R package `gems` for simulating multistate models with general transition-specific hazard functions will be available at CRAN soon
- It is a flexible tool for modelling individual patients to evaluate and plan interventions
- We are working on several applications and extensions

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Ongoing projects include:

- HIV monitoring strategies for children in South Africa
- Early diagnosis and treatment of Hepatitis C to reduce the incidence of advanced liver diseases
- Extension of the model by Bacaer et al. to include age structure
- Tracing strategies to reduce HIV transmission

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- Co-authors: Cindy Zahnd, Janne Estill, Matthias Egger, Thomas Gsponer, Olivia Keiser
- Funding sources: Swiss National Science Foundation, UNITAID, NIH

- Discrete time steps
- Calculate transmission potential
- Simulate number of new infections
- Use multistate model to simulate newly infected patients

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