

# Package ‘mvna’

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**Title** Nelson-Aalen estimator of the cumulative hazard in multistate models

**Version** 1.1-9

**Author** Arthur Allignol

**Description** This package computes the Nelson-Aalen estimator of the cumulative transition hazard for multistate models.

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**License** GPL (>= 2)

**Depends** lattice

**Suggests** Rgraphviz, gridBase

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`abortion`*Pregnancies exposed to coumarin derivatives*

---

**Description**

Outcomes of pregnancies exposed to coumarin derivatives. The aim is to investigate whether exposure to coumarin derivatives increases the probability of spontaneous abortions. Apart from spontaneous abortion pregnancy, may end in induced abortion or live birth. Moreover, data are left-truncated as women usually enter the study several weeks after conception

**Usage**

```
data(abortion)
```

**Format**

A data frame with 1186 observations on the following 5 variables.

**id** Identification number

**entry** Entry times into the cohort

**exit** Event times

**group** Group. 0: control, 1: exposed to coumarin derivatives

**cause** Cause of failure. 1: induced abortion, 2: life birth, 3: spontaneous abortion

**Source**

Meiester, R. and Schaefer, C (2008). Statistical methods for estimating the probability of spontaneous abortion in observational studies – Analyzing pregnancies exposed to coumarin derivatives. *Reproductive Toxicology*, 26, 31–35

**Examples**

```
data(abortion)
```

---

`msmplot`*Combined plot of the multistate model and the cumulative hazards.*

---

**Description**

This function uses the package **Rgraphviz** to display the multistate model. Next **GrisBase** is used to put the cumulative hazard plots near the arrows representing transitions.

**Usage**

```
## S3 method for class 'mvna':
msmplot(object, tr.choice, graph, layout = "dot",
        recip.edges = "combined", order = "LR", unit = "npc",
        width, height, just = "center",
        mgp = c(1.3, 0.4, 0), cex = 0.6,
        mtext = TRUE, label.plots, side = 3, lcex = 0.9,
        conf.int = TRUE, level = 0.05, xlab = "Time", ylab = "",
        ...)
```

**Arguments**

<code>object</code>	An object of class 'mvna'.
<code>tr.choice</code>	A character vector of the form ("from to", "from to") describing the transitions to plot. By default, the estimated cumulative hazards are displayed for all transitions.
<code>graph</code>	Optional. An object of class <code>Ragraph</code> . People familiar with the <b>Rgraphviz</b> and/or willing to have a better control on how the multistate model is displayed can provide here their own <code>Ragraph</code> object. If not provided, the multistate plot is done internally.
<code>layout</code>	If <code>graph</code> is not provided, permits to specify the layout of the multistate plot.
<code>recip.edges</code>	If <code>graph</code> is not provided, permits to specify how to handle reciprocated edges, defaults is 'combined'.
<code>order</code>	Order for the display of the nodes. Default is 'LR', that is from left to right.
<code>unit</code>	A string specifying the units used for creating the viewports in which the cumulative hazards will be plotted. Default is "npc". See the <b>grid</b> vignette for the possible values.
<code>width</code>	A vector giving the width of the viewport for plotting the cumulative hazards.
<code>height</code>	A vector giving the height of the viewport.
<code>just</code>	A string or numeric vector indicating the justification of the viewport.
<code>mgp</code>	Margin line for the axis title, axis labels and axis line in the cumulative hazards plots. Default is <code>c(1.3, 0.4, 0)</code> , smaller than the default value in <code>par</code> due to the fact the plots will usually be small.
<code>cex</code>	A numerical value giving the amount by which plotting text and symbols should be magnified relative to the default.
<code>mtext</code>	A logical indicating whether to display a label above the plot.
<code>label.plots</code>	If <code>mtext = TRUE</code> , specifies the labels. Default is the transition numbers.
<code>side</code>	Gives the side where to put the label (1=bottom, 2=left, 3=top, 4=right). Default is 3.
<code>lcex</code>	Character expansion factor. This is an absolute value. Therefore, this value will be evaluate with respect with <code>cex</code> above.
<code>conf.int</code>	A logical indicating whether plot confidence intervals. Default is TRUE
<code>level</code>	Level for the confidence interval. Default is 0.05

xlab	Label for the x-axis.
ylab	Label for the y-axis.
...	Further arguments for the plot method.

### Details

This functions permits to display the cumulative hazards estimates in multistate models in an original manner. A drawing of the multistate model is provided along with the display of the estimated cumulative hazards that are put along the arrows that describes the possible transitions.

The multistate model is displayed using the **Rgraphviz** package. By default, the `Ragraph` object needed for the display is computed internally, letting few options for the user to be modified. For a finer control, the user can provide his own `Ragraph` object using the `agopen` function.

The cumulative hazards plots are positioned by the user using the `grid.locator` function. One has just to click where he wants the plot to be. The order of the transitions is displayed on the prompt. The `width`, `height`, `angle` and `just` arguments permit to adjust the way the plots are displayed.

### Value

object with the invisible flag set

### Note

The **Rgraphviz** package requires the graphviz software to be installed.

**Rgraphviz** binaries for windows are not available on CRAN, but are on bioconductor.

### Author(s)

Arthur Allignol, (arthur.allignol@fdm.uni-freiburg.de)

### See Also

[mvna](#)

### Examples

```
data(sir.cont)

sir.cont <- sir.cont[order(sir.cont$id, sir.cont$time), ]
for (i in 2:nrow(sir.cont)) {
  if (sir.cont$id[i]==sir.cont$id[i-1]) {
    if (sir.cont$time[i]==sir.cont$time[i-1]) {
      sir.cont$time[i-1] <- sir.cont$time[i-1] - 0.5
    }
  }
}

### Computation of the transition probabilities
# Possible transitions
```

```

tra <- matrix(ncol=3,nrow=3,FALSE)
tra[1, 2:3] <- TRUE
tra[2, c(1, 3)] <- TRUE

# mvna
temp <- mvna(sir.cont, c("0", "1", "2"), tra, "cens")

## Not run:
msmplot(temp, width = c(0.25, 0.25, 0.2, 0.25),
         height = c(0.2, 0.2, 0.18, 0.2), lcx=0.8)
## End(Not run)

```

mvna

*Nelson-Aalen estimator in multistate models*

## Description

This function computes the multivariate Nelson-Aalen estimator of the cumulative transition hazards in multistate models, that is, for each possible transition, it computes an estimate of the cumulative hazard.

## Usage

```
mvna(data, state.names, tra, cens.name)
```

## Arguments

<code>data</code>	A data.frame of the form <code>data.frame(id,from,to,time)</code> or <code>(id,from,to,entry,exit)</code> <b>id:</b> patient id <b>from:</b> the state from where the transition occurs <b>to:</b> the state to which a transition occurs <b>time:</b> time when a transition occurs <b>entry:</b> entry time in a state <b>exit:</b> exit time from a state This data.frame is transition-oriented, <i>i.e.</i> it contains one row per transition, and possibly several rows per patient. Specifying an entry and exit time permits to take into account left-truncation.
<code>state.names</code>	A vector of character giving the states names.
<code>tra</code>	A quadratic matrix of logical values describing the possible transitions within the multistate model.
<code>cens.name</code>	A character giving the code for censored observations in the column 'to' of <code>data</code> . If there is no censored observations in your data, put 'NULL'.

## Details

This functions computes the Nelson-Aalen estimator as described in Anderson et al. (1993), along with the two variance estimators described in eq. (4.1.6) and (4.1.7) of Andersen et al. (1993) at each transition time.

**Value**

Returns a list named after the possible transitions, *e.g.* if we define a multistate model with two possible transitions: from state 0 to state 1, and from state 0 to state 2, the returned list will have two parts named "0 1" and "0 2". Each part contains a data.frame with columns:

`na`: Nelson-Aalen estimates at each transition times.

`var1`: Variance estimator given in eq. (4.1.6) of Andersen et al. (1993).

`var2`: Variance estimator given in eq. (4.1.7) of Andersen et al. (1993).

`time`: The transition times.

The list also contains:

`time`            All the event times.

`nrisk`           A matrix giving the number at individual at risk in the transient states just before an event.

`nev`             An array which gives the number of transitions at each event times.

`ncens`           A matrix giving the number a censored observations at each event times.

`state.names`    The same as in the function call.

`cens.name`      The same as in the function call.

**Note**

The variance estimator (4.1.6) may overestimate the true variance, and the one defined eq. (4.1.7) may underestimate the true variance (see Klein (1991) and Andersen et al. (example IV.1.1, 1993)), especially with small sample set. Therefore, a warning will be produced for risk-sets smaller than 5. Klein (1991) recommends the use of the variance estimator of eq. (4.1.6) because he found it less biased.

**Author(s)**

Arthur Allignol, (arthur.allignol@fdm.uni-freiburg.de)

**References**

Andersen, P.K., Borgan, O., Gill, R.D. and Keiding, N. (1993). *Statistical models based on counting processes*. Springer Series in Statistics. New York, NY: Springer.

Klein, J.P. Small sample moments of some estimators of the variance of the Kaplan-Meier and Nelson-Aalen estimators. *Scandinavian Journal of Statistics*, 18:333–340, 1991.

**See Also**

[sir.adm](#), [sir.cont](#)

**Examples**

```

data(sir.cont)

# Modification for patients entering and leaving a state
# at the same date
sir.cont <- sir.cont[order(sir.cont$id, sir.cont$time), ]
for (i in 2:nrow(sir.cont)) {
  if (sir.cont$id[i]==sir.cont$id[i-1]) {
    if (sir.cont$time[i]==sir.cont$time[i-1]) {
      sir.cont$time[i-1] <- sir.cont$time[i-1] - 0.5
    }
  }
}

# Matrix of logical giving the possible transitions
tra <- matrix(ncol=3,nrow=3,FALSE)
tra[1, 2:3] <- TRUE
tra[2, c(1, 3)] <- TRUE

# Computation of the Nelson-Aalen estimates
na <- mvna(sir.cont,c("0","1","2"),tra,"cens")

# plot
xyplot(na)

### example with left-truncation
data(abortion)

# Data set modification in order to be used by mvna
names(abortion) <- c("id", "entry", "exit", "from", "to")
abortion$to <- abortion$to + 1

## computation of the matrix giving the possible transitions
tra <- matrix(FALSE, nrow = 5, ncol = 5)
tra[1:2, 3:5] <- TRUE

na.abortion <- mvna(abortion, as.character(0:4), tra, NULL)

plot(na.abortion, tr.choice = c("0 4", "1 4"),
     curvlab = c("Control", "Exposed"),
     bty = "n", legend.pos = "topleft")

```

---

plot.mvna

*Plot method for a mvna object*


---

**Description**

plot method for an object of class 'mvna'. This function plots estimates of the cumulative transition hazards in one panel.

**Usage**

```
## S3 method for class 'mvna':
plot(x, tr.choice, xlab = "Time",
     ylab = "Nelson-Aalen estimates",
     col, lty, xlim, ylim, legend = TRUE,
     legend.pos, curvlab, legend.bty = "n", ...)
```

**Arguments**

<code>x</code>	An object of class 'mvna'
<code>tr.choice</code>	A character vector of the form 'c("from to", "from to")' specifying which transitions should be plotted. Default, all the cumulative transition hazards are plotted
<code>xlab</code>	x-axis label. Default is "Time"
<code>ylab</code>	y-axis label. Default is "Nelson-Aalen estimates"
<code>col</code>	Vector of colour. Default is black
<code>lty</code>	Vector of line type. Default is 1:number of transitions
<code>xlim</code>	Limits of x-axis for the plot
<code>ylim</code>	Limits of y-axis for the plot
<code>legend</code>	A logical specifying if a legend should be added
<code>legend.pos</code>	A vector giving the legend's position. See <a href="#">legend</a> for further details
<code>curvlab</code>	A character or expression vector to appear in the legend. Default is the name of the transitions
<code>legend.bty</code>	Box type for the legend
<code>...</code>	Further arguments for plot

**Details**

This plot method permits to draw several cumulative transition hazards on the same panel.

**Value**

`x` with the invisible flag set

**Author(s)**

Arthur Allignol <arthur.allignol@fdm.uni-freiburg.de>

**See Also**

[mvna](#)

**Examples**

```

data(sir.cont)

# Modification for patients entering and leaving a state
# at the same date
sir.cont <- sir.cont[order(sir.cont$id, sir.cont$time), ]
for (i in 2:nrow(sir.cont)) {
  if (sir.cont$id[i]==sir.cont$id[i-1]) {
    if (sir.cont$time[i]==sir.cont$time[i-1]) {
      sir.cont$time[i-1] <- sir.cont$time[i-1] - 0.5
    }
  }
}

tra <- matrix(ncol=3,nrow=3,FALSE)
tra[1, 2:3] <- TRUE
tra[2, c(1, 3)] <- TRUE

na.cont <- mvna(sir.cont,c("0", "1", "2"),tra,"cens")

plot(na.cont, tr.choice=c("0 2", "1 2"))

```

---

predict.mvna	<i>Calculates Nelson-Aalen estimates at specified time-points</i>
--------------	---

---

**Description**

This function gives the Nelson-Aalen estimates at time-points specified by the user, along with the two variance estimators.

**Usage**

```

## S3 method for class 'mvna':
predict(object, times, tr.choice, ...)

```

**Arguments**

object	An object of class 'mvna'
times	Time-points at which you want the estimates
tr.choice	A vector of character giving for which transitions you want estimates. By default, the function will give the Nelson-Aalen estimates for all the transitions.
...	Other arguments to predict

**Value**

Returns a list named after the possible transitions, *e.g.* if we define a multistate model with two possible transitions: from state 0 to state 1, and from state 0 to state 2, the returned list will have two parts named "0 1" and "0 2". Each part contains a data.frame with columns:

na	Nelson-Aalen estimates at each transition times.
var1	Variance estimator given in eq. (4.1.6) of Andersen et al. (1993).
var2	Variance estimator given in eq. (4.1.7) of Andersen et al. (1993).
time	The given timepoints.

**Author(s)**

Arthur Allignol, (arthur.allignol@fdm.uni-freiburg.de)

**References**

Andersen, P.K., Borgan, O., Gill, R.D. and Keiding, N. (1993). *Statistical models based on counting processes*. Springer Series in Statistics. New York, NY: Springer.

**See Also**

[mvna](#), [sir.adm](#), [sir.cont](#)

**Examples**

```
data(sir.cont)

# Modification for patients entering and leaving a state
# at the same date
sir.cont <- sir.cont[order(sir.cont$id, sir.cont$time), ]
for (i in 2:nrow(sir.cont)) {
  if (sir.cont$id[i]==sir.cont$id[i-1]) {
    if (sir.cont$time[i]==sir.cont$time[i-1]) {
      sir.cont$time[i-1] <- sir.cont$time[i-1] - 0.5
    }
  }
}

# Matrix of logical giving the possible transitions
tra <- matrix(ncol=3,nrow=3,FALSE)
tra[1, 2:3] <- TRUE
tra[2, c(1, 3)] <- TRUE

# Computation of the Nelson-Aalen estimates
na <- mvna(sir.cont,c("0","1","2"),tra,"cens")

# Using predict
predict(na,times=c(1,5,10,15))
```

---

print.mvna                      *Print method for 'mvna' object*

---

**Description**

Print method for an object of class 'mvna'. It prints estimates of the cumulative hazard along with estimates of the variance described in eq. (4.1.6) and (4.1.7) of Andersen et al. (1993) at several timepoints obtained with the 'quantile' function.

**Usage**

```
## S3 method for class 'mvna':  
print(x, ...)
```

**Arguments**

x	An object of class 'mvna'
...	Other arguments for print method

**Value**

x with the invisible flag set

**Author(s)**

Arthur Allignol, <arthur.allignol@fdm-freiburg.de>

**See Also**

[mvna](#)

---

sir.adm                      *Pneumonia on admission in intensive care unit patients*

---

**Description**

Pneumonia status on admission for intensive care unit (ICU) patients, a random sample from the SIR-3 study.

**Usage**

```
data(sir.adm)
```

**Format**

The data contains 765 rows and 4 variables:

**id:** Randomly generated patient id

**pneu:** Pneumonia indicator. 0: No pneumonia, 1: Pneumonia

**status** Status indicator. 0: censored observation, 1: discharged, 2: dead

**time:** Follow-up time in day

**Source**

Beyersmann, J., Gastmeier, P., Grundmann, H., Baerwolff, S., Geffers, C., Behnke, M., Rueden, H., and Schumacher, M. Use of multistate models to assess prolongation of intensive care unit stay due to nosocomial infection. *Infection Control and Hospital Epidemiology*, 27:493-499, 2006.

**Examples**

```
# data set transformation
data(sir.adm)
id <- sir.adm$id
from <- sir.adm$pneu
to <- ifelse(sir.adm$status==0, "cens", sir.adm$status+1)
times <- sir.adm$time
dat.sir <- data.frame(id, from, to, time=times)

# Possible transitions
tra <- matrix(ncol=4, nrow=4, FALSE)
tra[1:2, 3:4] <- TRUE

na.pneu <- mvna(dat.sir, c("0", "1", "2", "3"),
               tra, "cens")
xyplot(na.pneu, tr.choice=c("0 2", "1 2", "0 3", "1 3"),
       aspect=1, strip=strip.custom(bg="white",
       factor.levels=c("No pneumonia on admission -- Discharge",
                       "Pneumonia on admission -- Discharge",
                       "No pneumonia on admission -- Death",
                       "Pneumonia on admission -- Death"),
       par.strip.text=list(cex=0.9)),
       scales=list(alternating=1), xlab="Days",
       ylab="Nelson-Aalen estimates")
```

---

 sir.cont

*Ventilation status in intensive care unit patients*


---

**Description**

Time-dependent ventilation status for intensive care unit (ICU) patients, a random sample from the SIR-3 study.

**Usage**

```
data(sir.cont)
```

**Format**

A data frame with 1161 rows and 4 columns:

**id:** Randomly generated patient id

**from:** State from which a transition occurs

**to:** State to which a transition occurs

**time:** Time when a transition occurs

The possible states are:

0: No ventilation

1: Ventilation

2: End of stay.

And `cens` stands for censored observations.

**Details**

This data frame consists in a random sample of the SIR-3 cohort data. It focuses on the effect of ventilation on the length of stay (combined endpoint discharge/death). Ventilation status is considered as a transient state in an illness-death model.

The data frame is directly formatted to be used with the `mvna` function, i.e. it is transition-oriented with one row per transition.

**Source**

Beyersmann, J., Gastmeier, P., Grundmann, H., Baerwolff, S., Geffers, C., Behnke, M., Rueden, H., and Schumacher, M. Use of multistate models to assess prolongation of intensive care unit stay due to nosocomial infection. *Infection Control and Hospital Epidemiology*, 27:493-499, 2006.

**Examples**

```
data(sir.cont)

# Matrix of possible transitions
tra <- matrix(ncol=3,nrow=3,FALSE)
tra[1, 2:3] <- TRUE
tra[2, c(1, 3)] <- TRUE

# Modification for patients entering and leaving a state
# at the same date
sir.cont <- sir.cont[order(sir.cont$id, sir.cont$time), ]
for (i in 2:nrow(sir.cont)) {
  if (sir.cont$id[i]==sir.cont$id[i-1]) {
    if (sir.cont$time[i]==sir.cont$time[i-1]) {
      sir.cont$time[i-1] <- sir.cont$time[i-1] - 0.5
    }
  }
}
```

```

    }
  }
}

# Computation of the Nelson-Aalen estimates
na.cont <- mvna(sir.cont,c("0", "1", "2"),tra,"cens")

xyplot(na.cont,tr.choice=c("0 2", "1 2"),aspect=1,
       strip=strip.custom(bg="white",
                           factor.levels=c("No ventilation -- Discharge/Death",
                                             "Ventilation -- Discharge/Death"),
                           par.strip.text=list(cex=0.9)),
       scales=list(alternating=1,xlab="Days",
                   ylab="Nelson-Aalen estimates")

```

---

xyplot.mvna

*Panel plots for object of class 'mvna'*


---

### Description

xyplot function for objects of class 'mvna'. Estimates of the cumulative hazards are plotted as a function of time for all the transitions specified by the user. This function could also plot several types of pointwise confidence interval (see Andersen et al. (1993) p.208).

### Usage

```

## S3 method for class 'mvna':
xyplot(x, data = NULL, xlab = "Time",
       ylab = "Cumulative Hazard", tr.choice = "all",
       conf.int = TRUE, ci.type = c(1, 2), level = 0.05,
       col = c(1, 1, 1), lty = c(1, 3, 3), ...)

```

### Arguments

x	An object of class 'mvna'.
data	<i>Useless</i> . Just to avoid warnings while compiling the package.
xlab	x-axis label. Default is "Time".
ylab	y-axis label. Default is "Cumulative Hazard"
tr.choice	A character vector of the form 'c("from to","from to")' specifying which transitions should be plotted. Default is "all".
conf.int	A logical whether plot pointwise confidence interval. Default is TRUE
ci.type	A vector of 2 integer coding for the confidence interval type. The first part of the vector can be 1 or 2, 1 for the variance estimator described in eq. (4.1.6) of Andersen et al. (1993), 2 for the one described in eq. (4.1.7). The second part of the vector can be 1,2 or 3. 1 for a linear confidence interval, 2 for log-transformation, 3 for arcsin-transformation. Default is c(1,2).

level	Level of the confidence interval. Default is 0.05.
col	Vector of colour for the plot. Default is black.
lty	Vector of line type. Default is c(1,3,3)
...	Other arguments for xyplot

**Value**

An object of class 'trellis'.

**Note**

These plots are highly customizable, see [Lattice](#) and [xyplot](#). For example, if one want to change strip background color and the title of each strip, it can be added 'strip=strip.custom(bg="a color",factor.levels="a title","another title")'. One can use 'aspect="1"' to get the size of the panels isometric.

**Author(s)**

Arthur Allignol, <arthur.allignol@fdm-freiburg.de>

**References**

Andersen, P.K., Borgan, O., Gill, R.D. and Keiding, N. (1993). *Statistical models based on counting processes*. Springer Series in Statistics. New York, NY: Springer.

Deepayan Sarkar (2006). lattice: Lattice Graphics. R package version 0.13-8.

**See Also**

[xyplot](#), [mvna](#), [sir.adm](#), [sir.cont](#)

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