

# Package ‘survidm’

January 8, 2019

**Type** Package

**Title** Inference and Prediction in an Illness-Death Model

**Version** 1.2.0

**Date** 2019-01-02

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**Description** Newly developed methods for the estimation of several probabilities in an illness-death model. The package can be used to obtain nonparametric and semiparametric estimates for: transition probabilities, occupation probabilities, cumulative incidence function and the sojourn time distributions. Additionally, it is possible to fit proportional hazards regression models in each transition of the Illness-Death Model. Several auxiliary functions are also provided which can be used for marginal estimation of the survival functions.

**Depends** R (>= 3.0.0)

**Encoding** UTF-8

**License** GPL-3

**LazyData** true

**Imports** KernSmooth, np, survival, doParallel, parallel, doRNG, foreach, TPmsm

**RoxygenNote** 6.0.1

**NeedsCompilation** yes

**Repository** CRAN

**Date/Publication** 2019-01-07 23:00:02 UTC

## R topics documented:

survidm-package . . . . .	2
Beran . . . . .	3
bladderIDM . . . . .	4
CIF . . . . .	5

colonIDM . . . . .	8
coxidm . . . . .	9
gbcsIDM . . . . .	10
KM . . . . .	11
KMW . . . . .	12
LLW . . . . .	13
markov.test . . . . .	14
nevents . . . . .	15
NWW . . . . .	16
PKM . . . . .	17
PKMW . . . . .	18
plot.survIDM . . . . .	19
sojourn . . . . .	20
summary.cmm . . . . .	23
summary.survIDM . . . . .	24
survIDM . . . . .	25
tprob . . . . .	26

<b>Index</b>	<b>31</b>
--------------	-----------

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survidm-package

*survidm: Inference and Prediction in an Illness-Death Model*

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## Description

Newly developed methods for the estimation of several probabilities in an illness-death model. The package can be used to obtain nonparametric and semiparametric estimates for: transition probabilities, occupation probabilities, cumulative incidence function and the sojourn time distributions. Additionally, it is possible to fit proportional hazards regression models in each transition of the Illness-Death Model. Several auxiliary functions are also provided which can be used for marginal estimation of the survival functions.

## Author(s)

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

Maintainer: Marta Sestelo, sestelo@uvigo.es

## References

- Aalen O. O., Johansen S. (1978) An Empirical Transition Matrix for Nonhomogeneous Markov Chains Based on Censored Observations. *Scandinavian Journal of Statistics*, 5(3), 141–150.
- Cao R., Lopez-de Ullibarri I., Janssen P., Veraverbeke N. (2005) Presmoothed kaplan-meier and nelsonaalen estimators. *Journal of Nonparametric Statistics*, 17, 31–56.
- de Una-Alvarez J. and Meira-Machado L. (2015). Nonparametric estimation of transition probabilities in a non-Markov illness-death model: a comparative study. *Biometrics*, 71, 364–375.
- Geskus R.B. (2011). Cause-specific cumulative incidence estimation and the fine and gray model under both left truncation and right censoring. *Biometrics*, 67, 39–49.

Meira-Machado L. F., de Una-Alvarez J. and Cadarso-Suarez C. (2006). Nonparametric estimation of transition probabilities in a non-Markov illness-death model. *Lifetime Data Anal* 12(3), 325–344.

Satten G.A. and Datta S. (2002) Marginal estimation for multi-stage models: waiting time distributions and competing risks analyses. *Statistics in Medicine*, 21, 3–19.

---

Beran *Estimation of the conditional distribution function of the response, given the covariate under random censoring.*

---

## Description

Computes the conditional survival probability  $P(T > y|Z = z)$

## Usage

```
Beran(time, status, covariate, delta, x, y, kernel = "gaussian", bw, lower.tail = FALSE)
```

## Arguments

time	The survival time of the process.
status	Censoring indicator of the total time of the process; 0 if the total time is censored and 1 otherwise.
covariate	Covariate values for obtaining estimates for the conditional probabilities.
delta	Censoring indicator of the covariate.
x	The first time (or covariate value) for obtaining estimates for the conditional probabilities. If missing, 0 will be used.
y	The total time for obtaining estimates for the conditional probabilities.
kernel	A character string specifying the desired kernel. See details below for possible options. Defaults to "gaussian" where the gaussian density kernel will be used.
bw	A single numeric value to compute a kernel density bandwidth.
lower.tail	logical; if FALSE (default), probabilities are $P(T > y Z = z)$ otherwise, $P(T \leq y Z = z)$ .

## Details

Possible options for argument window are "gaussian", "epanechnikov", "tricube", "boxcar", "triangular", "quartic" or "cosine".

## Author(s)

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho

## References

R. Beran. Nonparametric regression with randomly censored survival data. Technical report, University of California, Berkeley, 1981.

## Examples

```
obj <- with(colonIDM, survIDM(time1, event1, Stime, event))
obj0 <- obj

#P(T>y|age=45)
library(KernSmooth)
h <- dpik(colonIDM$age)
Beran(time = obj0$Stime, status = obj0$event, covariate = colonIDM$age,
x = 45, y = 730, bw = h)

#P(T<=y|age=45)
Beran(time = obj0$Stime, status = obj0$event, covariate = colonIDM$age,
x = 45, y = 730, bw = h, lower.tail = TRUE)
```

---

bladderIDM

*Bladder Cancer Recurrences.*

---

## Description

bladderIDM is a data frame with 8 variables and 85 observations. Data on recurrences of bladder cancer, used by many people to demonstrate methodology for recurrent event modelling.

## Usage

```
data("bladderIDM")
```

## Format

A data frame with 85 observations on the following 8 variables. Below a brief description is given for some of these variables.

- t1** Time to first recurrence/censoring, whichever occurs first.
- e1** Recurrence/censoring indicator (first recurrence=1) for the first time (t1).
- t2** Time to second recurrence/censoring, whichever occurs first.
- e2** Recurrence/censoring indicator (second recurrence=1) for the second time (t2)
- t3** Time to recurrence/censoring, whichever occurs first.
- e3** Recurrence/censoring indicator (third recurrence=1) for the third time (t3)
- t4** Time to fourth recurrence/censoring, whichever occurs first.
- e4** Recurrence/censoring indicator (fourth recurrence=1) for the fourth time (t4)

## References

Byar, D. (1980) Veterans administration study of chemoprophylaxis for recurrent stage i bladder tumors: Comparisons of placebo, pyridoxine and topical thiotepa. *Bladder Tumors and Other Topics in Urological Oncology*, 18:363–370.

**Examples**

```
data(bladderIDM)
head(bladderIDM)
```

---

CIF	<i>Nonparametric estimation of the Cumulative Incident Functions in the illness-death model</i>
-----	---

---

**Description**

This function is used to obtain nonparametric estimates of the cumulative incidence probabilities in the illness-death model. They represent the probability of one individual's being or having been in state  $j$  at time  $t$ .

**Usage**

```
CIF(formula, s, data, conf = FALSE, n.boot = 199, conf.level = 0.95,
    z.value, bw = "dpik", window = "gaussian", method.weights = "NW",
    cluster = FALSE, ncores = NULL, presmooth = FALSE)
```

**Arguments**

formula	A formula object, which must have a survIDM object as the response on the left of the $\sim$ operator and, if desired, a term on the right. The term may be a qualitative or quantitative variable. Without covariates, the right hand side should be $\sim 1$ .
s	The first time for obtaining estimates for the cumulative incidence functions. If missing, 0 will be used.
data	A data.frame including at least four columns named time1, event1, Stime and event, which correspond to disease free survival time, disease free survival indicator, time to death or censoring, and death indicator, respectively.
conf	Provides pointwise confidence bands. Defaults to FALSE.
n.boot	The number of bootstrap replicates to compute the variance of the estimator. Default is 199.
conf.level	Level of confidence. Defaults to 0.95 (corresponding to 95%).
z.value	The value of the covariate on the right hand side of formula at which the cumulative incidence probabilities are computed. For quantitative covariates, i.e. of class integer and numeric.
bw	A single numeric value to compute a kernel density bandwidth. Use "dpik" for the <b>KernSmooth</b> package based selector or "np" for the 'npudensbw' function of the <b>np</b> package.
window	A character string specifying the desired kernel. See details below for possible options. Defaults to "gaussian" where the gaussian density kernel will be used.

<code>method.weights</code>	A character string specifying the desired weights method. Possible options are "NW" for the Nadaraya-Watson weights and "LL" for local linear weights. Defaults to "NW".
<code>cluster</code>	A logical value. If TRUE (default), the bootstrap procedure for the confidence intervals is parallelized. Note that there are cases (e.g., a low number of bootstrap repetitions) that R will gain in performance through serial computation. R takes time to distribute tasks across the processors also it will need time for binding them all together later on. Therefore, if the time for distributing and gathering pieces together is greater than the time need for single-thread computing, it does not worth parallelize.
<code>ncores</code>	An integer value specifying the number of cores to be used in the parallelized procedure. If NULL (default), the number of cores to be used is equal to the number of cores of the machine - 1.
<code>presmooth</code>	A logical value. If TRUE, the presmoothed landmark estimator of the cumulative incidence function is computed.

### Details

Possible options for argument window are "gaussian", "epanechnikov", "tricube", "boxcar", "triangular", "quartic" or "cosine".

### Value

An object of class "survIDM" and one of the following two classes: "CIF" (Cumulative Incidence Function), and "cifIPCW" (Inverse Probability of Censoring Weighting for the Cumulative Incidence Function). Objects are implemented as a list with elements:

<code>est</code>	data.frame with estimates of the cumulative incidence probabilities.
<code>CI</code>	data.frame with the confidence intervals of the cumulative incidence probabilities.
<code>conf.level</code>	Level of confidence.
<code>s</code>	The first time for obtaining estimates for the cumulative incidence probabilities.
<code>t</code>	The time for obtaining the estimates of cumulative incidence probabilities.
<code>conf</code>	logical; if FALSE (default) the pointwise confidence bands are not given.
<code>callp</code>	The expression of the estimated probability.
<code>Nlevels</code>	The number of levels of the covariate. Provides important information when the covariate at the right hand side of formula is of class factor.
<code>levels</code>	The levels of the qualitative covariate (if it is of class factor) on the right hand side of formula.
<code>formula</code>	A formula object.
<code>call</code>	A call object.

### Author(s)

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

## References

Geskus, R.B. (2011). Cause-specific cumulative incidence estimation and the fine and gray model under both left truncation and right censoring. *Biometrics*, 67, 39–49.

Kalbeisch, J. D. and Prentice R. L. (1980) *The statistical analysis of failure time data*. John Wiley & Sons, New York.

## Examples

```
# Cumulative Incidence Function (CIF)
res <- CIF(survIDM(time1, event1, Stime, event) ~ 1, data = colonIDM,
conf = FALSE)
res
summary(res, time=365*1:7)
plot(res, ylim=c(0, 0.6))

res01 <- CIF(survIDM(time1, event1, Stime, event) ~ 1, data = colonIDM,
conf = FALSE, presmooth = TRUE)
res01
summary(res01, time=365*1:7)
plot(res01, ylim=c(0, 0.6))

# CIF for those in State 1 at time s=365, Y(s)=0
res1 <- CIF(survIDM(time1, event1, Stime, event) ~ 1, data = colonIDM,
s = 365, conf = FALSE)
summary(res1, time=365*1:7)
plot(res1, ylim=c(0, 0.6))

# Conditional CIF (with a factor)
res2 <- CIF(survIDM(time1, event1, Stime, event) ~ factor(sex),
data = colonIDM, s = 365, conf = FALSE)
summary(res2, time=365*1:5)
plot(res2)

res2.1 <- CIF(survIDM(time1, event1, Stime, event) ~ factor(sex), #new
data = colonIDM, s = 365, conf = FALSE, presmooth = TRUE)
summary(res2.1, time=365*1:5)
plot(res2.1)

# Conditional CIF (with continuous covariate)
res3 <- CIF(survIDM(time1, event1, Stime, event) ~ age, data = colonIDM,
z.value = 56, conf = FALSE)
summary(res3, time=365*1:6)
plot(res3)
```

---

 colonIDM

*Chemotherapy for Stage B/C colon cancer.*


---

### Description

These are data from one of the first successful trials of adjuvant chemotherapy for colon cancer. Levamisole is a low-toxicity compound previously used to treat worm infestations in animals; 5-FU is a moderately toxic (as these things go) chemotherapy agent.

### Usage

```
data("colonIDM")
```

### Format

A data frame with 929 observations on the following 15 variables. Below a brief description is given for some of these variables.

**time1** Time to recurrence/censoring/death, whichever occurs first.

**event1** Recurrence/censoring indicator (recurrence=1, alive=0).

**Stime** Time to censoring/death, whichever occurs first.

**event** Death/censoring indicator (death=1, alive=0).

**rx** Treatment - Obs(ervation), Lev(amisole), Lev(amisole)+5-FU.

**sex** Sex indicator (male=1, female=0).

**age** Age in years.

**obstruct** Obstruction of colon by tumour.

**perfor** Perforation of colon.

**adhere** Adherence to nearby organs.

**nodes** Number of lymph nodes with detectable cancer.

**differ** Differentiation of tumour (1=well, 2=moderate, 3=poor).

**extent** Extent of local spread (1=submucosa, 2=muscle, 3=serosa, 4=contiguous structures).

**surg** Time from surgery to registration (0=short, 1=long).

**node4** More than 4 positive lymph nodes.

### Source

The study is originally described in Laurie (1989). The main report is found in Moertel (1990). This data set is closest to that of the final report in Moertel (1991). A version of the data with less follow-up time was used in the paper by Lin (1994).



## References

JA Laurie, CG Moertel, TR Fleming, HS Wieand, JE Leigh, J Rubin, GW McCormack, JB Gerstner, JE Krook and J Malliard. Surgical adjuvant therapy of large-bowel carcinoma: An evaluation of levamisole and the combination of levamisole and fluorouracil: The North Central Cancer Treatment Group and the Mayo Clinic. *Journal of Clinical Oncology*, 7:1447-1456, 1989.

DY Lin. Cox regression analysis of multivariate failure time data: the marginal approach. *Statistics in Medicine*, 13:2233-2247, 1994.

CG Moertel, TR Fleming, JS MacDonald, DG Haller, JA Laurie, PJ Goodman, JS Ungerleider, WA Emerson, DC Tormey, JH Glick, MH Veeder and JA Maillard. Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. *New England Journal of Medicine*, 332:352-358, 1990.

CG Moertel, TR Fleming, JS MacDonald, DG Haller, JA Laurie, CM Tangen, JS Ungerleider, WA Emerson, DC Tormey, JH Glick, MH Veeder and JA Maillard. Fluorouracil plus Levamisole as an effective adjuvant therapy after resection of stage II colon carcinoma: a final report. *Annals of Internal Medicine*, 122:321-326, 1991.

## Examples

```
data(colonIDM)
head(colonIDM)
```

---

coxidm	<i>Fit proportional hazards regression model in each transition of the Illness-Death Model.</i>
--------	---

---

## Description

Fits a Cox proportional hazards regression model for each transition.

## Usage

```
coxidm(formula, data, semiMarkov = FALSE)
```

## Arguments

formula	A formula object, which must have a survIDM object as the response on the left of the ~ operator and, if desired, a term on the right. The term may be a qualitative or quantitative variable. Without covariates, the right hand side should be ~ 1.
data	A data.frame including at least four columns named time1, event1, Stime and event, which correspond to disease free survival time, disease free survival indicator, time to death or censoring, and death indicator, respectively.
semiMarkov	By default, FALSE.

**Value**

A data frame or a list containing the following components:

coef	Estimated coefficients.
exp(coef)	Exponent of the estimated coefficients.
lower 0.95	Lower limit of the confidence interval.
upper 0.95	Upper limit of the confidence interval.
pvalue	obtained pvalue testing that the coefficient is equals to zero.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**Examples**

```
cmm1 <- coxidm(survIDM(time1, event1, Stime, event) ~ age, data = colonIDM)
summary(cmm1, conf.level = 0.95)

cmm2 <- coxidm(survIDM(time1, event1, Stime, event) ~ rx + sex + age + nodes,
              data = colonIDM)
summary(cmm2)

cmm3 <- coxidm(survIDM(time1, event1, Stime, event) ~ rx + sex + age + nodes,
              data = colonIDM, semiMarkov = TRUE)
summary(cmm3)
```

---

gbcsIDM

*German Breast Cancer Study Data.*

---

**Description**

gbcsCS is a data frame with 16 variables and 686 observations. Cancer clinical trials are a rich source for examples of applications of methods for the analysis of time to event. Willi Sauerbrei and Patrick Royston have graciously provided us with data obtained from the German Breast Cancer Study Group, which they used to illustrate methods for building prognostic models (Sauerbrei and Royston, 1999). In the main study, a total of 720 patients with primary node positive breast cancer were recruited between July 1984, and December 1989, (see Schmoor, Olschweski and Schumacher M. 1996 and Schumacher et al. (1994)).

**Usage**

```
data("gbcsIDM")
```

**Format**

A data frame with 686 observations on the following 16 variables.

## References

Schmoor, C., Sauerbrei, W. Bastert, G., Schumacher, M. (2000). Role of Isolated Locoregional Recurrence of Breast Cancer: Results of Four Prospective Studies. *Journal of Clinical Oncology*, 18(8), 1696-1708.

Schumacher, M., Bastert, G., Bojar, H., Hiihner, K., Olschewski, M., Sauerbrei, W., Schmoor, C., Beyerle, C., Neumann, R.L.A. and Rauschecker, H.F. for the German Breast Cancer Study Group (GBSG) (1994). A randomized 2 x 2 trial evaluating hormonal treatment and the duration of chemotherapy in node-positive breast cancer patients. *Journal of Clinical Oncology*, 12, 2086-2093.

Hosmer, D.W. and Lemeshow, S. and May, S. (2008). *Applied Survival Analysis: Regression Modeling of Time to Event Data: Second Edition*, John Wiley and Sons Inc., New York, NY

## Examples

```
data(gbcsIDM)
head(gbcsIDM)
```

---

KM *Kaplan-Meier product-limit estimate of survival*

---

## Description

This function provides survival estimates using the product-limit Kaplan-Meier estimator.

## Usage

```
KM(time, status, t)
```

## Arguments

time	Survival time of the process.
status	Censoring indicator of the survival time of the process; 0 if the survival time is censored and 1 otherwise.
t	The time for obtaining survival estimates.

## Author(s)

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

## References

E. Kaplan and P. Meier. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association*, 53:457-481, 1958.

## See Also

[PKM](#)

**Examples**

```
require(survival)
obj <- with(colonIDM, survIDM(time1, event1, Stime, event))
KM(time = obj$Stime, status = obj$event, t = 1095)

fit <- survfit(Surv(obj$Stime, obj$event) ~ 1, data = obj)
summary(fit, time = 1095)$surv
```

---

KMW

*Kaplan-Meier weights*

---

**Description**

This function returns a vector with the Kaplan-Meier weights.

**Usage**

```
KMW(time, status)
```

**Arguments**

time	Survival time of the process.
status	Censoring indicator of the survival time of the process; 0 if the survival time is censored and 1 otherwise.

**Value**

Vector with Kaplan-Meier weights.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**References**

E. Kaplan and P. Meier. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association*, 53:457-481, 1958.

**See Also**

[PKMW](#)

**Examples**

```

obj <- with(colonIDM, survIDM(time1, event1, Stime, event))
kmw <- KMW(time = obj$Stime, status = obj$event)

require(survival)
colon.surv <- survfit(Surv(Stime, event) ~ 1, obj)
times <- summary(colon.surv)$time
surv <- summary(colon.surv)$surv
nevent <- summary(colon.surv)$n.event
p <- match(obj$Stime, times)
kmw2 <- -diff(c(1, surv))/nevent
kmw2 <- kmw2[p]*obj$event
kmw2[is.na(kmw2)] <- 0
all.equal(kmw, kmw2)

```

---

LLW

*Local linear weights*


---

**Description**

Computes local linear weights based on Kernel smoothing.

**Usage**

```
LLW(x, kernel = "gaussian", bw, t1)
```

**Arguments**

x	Covariate values for obtaining estimates for the conditional probabilities. If missing, unconditioned probabilities will be computed.
kernel	A character string specifying the desired kernel. See details below for possible options. Defaults to "gaussian" where the gaussian density kernel will be used.
bw	A single numeric value to compute a kernel density bandwidth.
t1	Covariate value to compute the weight at.

**Details**

Possible options for argument window are "gaussian", "epanechnikov", "tricube", "boxcar", "triangular", "quartic" or "cosine".

**Value**

A vector with local linear weights.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**See Also**[NWW](#)**Examples**

```
LLW(x = colonIDM$age, bw = 3, t1 = 60)
```

---

markov.test	<i>This function is used to test the markov assumption in the illness-death model.</i>
-------------	--

---

**Description**

The markov assumption may be tested including the sojourn time in the initial state, "times1", and other covariates in the Cox model.

**Usage**

```
markov.test(formula, s, nm.method = "LM", data)
```

**Arguments**

formula	A formula object, which must have a survIDM.
s	The first time for obtaining a graphical test of markovianity by comparison of the estimates for transition probabilities.
nm.method	The non-markov method used to compute the transition probabilities. Defaults to "LM".
data	A data.frame including at least four columns named time1, event1, Stime and event, which correspond to disease free survival time, disease free survival indicator, time to death or censoring, and death indicator, respectively.

**Details**

The markov assumption may be tested including the sojourn time in the initial state, "times1", and other covariates in the Cox model. A graphical test for Markovianity is also available.

**Value**

cox.markov.test	An object of class coxph representing the fit. See coxph.object for details.
TPestimates	Dataframe with estimates of the transition probabilities for Aalen-Johansen estimator (markovian) and for non-markov estimator. Confidence intervals for the transition probability from State 1 to State 2 are also available.
nm.method	The non-markov method used to compute the transition probabilities.
s	The first time for obtaining a graphical test of markovianity by comparison of the estimates for transition probabilities.
call	A call object.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**References**

L. Meira-Machado, J. de Una-Alvarez, C. Cadarso-Suarez, and P. Andersen. Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, 18:195-222, 2009.

J. de Una-Alvarez and L. Meira-Machado. Nonparametric estimation of transition probabilities in the non-markov illness-death model: A comparative study. *Biometrics*, 71(2):364-375, 2015.

L. Meira-Machado and M. Sestelo. Estimation in the progressive illness-death model: A nonexhaustive review. *Biometrical Journal*, 2018.

**Examples**

```
mk <- markov.test(survIDM(time1, event1, Stime, event) ~ 1, s = 365*4,
nm.method = "LM", data = colonIDM)
mk$cox.markov.test
mk$TPestimates
mk$nm.method
plot(mk)
```

---

nevents

---

*Count number of observed transitions.*


---

**Description**

Given a dataset of class "survIDM", this function counts the number of observed transitions in the multi-state model.

**Usage**

```
nevents(dataidm, state.names=NULL)
```

**Arguments**

dataidm	A dataframe including at least four columns named time1, event1, Stime and event, which correspond to disease free survival time, disease free survival indicator, time to death or censoring, and death indicator, respectively.
state.names	Names for the transition states. If NULL (default), transition states are named by "healthy", "illness" and "death".

**Details**

The columns of the dataset needs to have the format of class "survIDM", which holds the transition matrix of the multi-state model.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**References**

L. Meira-Machado, J. de Una-Alvarez, C. Cadarso-Suarez, and P. Andersen. Multi-state models for the analysis of time to event data. *Statistical Methods in Medical Research*, 18:195-222, 2009.

J. de Una-Alvarez and L. Meira-Machado. Nonparametric estimation of transition probabilities in the non-markov illness-death model: A comparative study. *Biometrics*, 71(2):364-375, 2015.

L. Meira-Machado and M. Sestelo. Estimation in the progressive illness-death model: A nonexhaustive review. *Biometrical Journal*, 2018.

**Examples**

```
nevents(colonIDM)

nevents(colonIDM, c('State1', 'State2', 'State3'))
```

---

 NWW

*Nadaraya-Watson weights.*


---

**Description**

Computes the Nadaraya-Watson weights.

**Usage**

```
NWW(covariate, x, kernel = "gaussian", bw)
```

**Arguments**

covariate	Covariate values for obtaining weights.
x	Covariate value to compute the weight at.
kernel	A character string specifying the desired kernel. See details below for possible options. Defaults to "gaussian" where the gaussian density kernel will be used.
bw	A single numeric value to compute a kernel density bandwidth.

**Details**

Possible options for argument window are "gaussian", "epanechnikov", "tricube", "boxcar", "triangular", "quartic" or "cosine".

**Value**

A vector with Nadaraya-Watson weights.



**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**See Also**

[LLW](#)

**Examples**

```
NWW(covariate = colonIDM$age, x=40, kernel = "gaussian", bw = 3)
```

---

PKM

*Presmoothed Kaplan-Meier product-limit estimate of survival*

---

**Description**

This function provides survival estimates using the presmoothed product-limit Kaplan-Meier estimator.

**Usage**

```
PKM(time, status, t)
```

**Arguments**

time	Survival time of the process.
status	Censoring indicator of the survival time of the process; 0 if the survival time is censored and 1 otherwise.
t	The time for obtaining survival estimates.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**References**

- R. Cao, I. Lopez-de Ullibarri, P. Janssen, and N. Veraverbeke. Presmoothed kaplan-meier and nelsonaalen estimators. *Journal of Nonparametric Statistics*, 17:31-56, 2005.
- G. Dikta. On semiparametric random censorship models. *Journal of Statistical Planning and Inference*, 66:253-279, 1998.
- E. Kaplan and P. Meier. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association*, 53:457-481, 1958.

**See Also**

[KM](#)

**Examples**

```
obj <- with(colonIDM, survIDM(time1, event1, Stime, event))
PKM(time = obj$Stime, status = obj$event, t = 1095)
```

---

PKMW

*Presmoothed Kaplan-Meier weights*

---

**Description**

This function returns a vector with the presmoothed Kaplan-Meier weights.

**Usage**

```
PKMW(time, status)
```

**Arguments**

<code>time</code>	Survival time of the process.
<code>status</code>	Censoring indicator of the survival time of the process; 0 if the survival time is censored and 1 otherwise.

**Value**

Vector with presmoothed Kaplan-Meier weights.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**References**

- R. Cao, I. Lopez-de Ullibarri, P. Janssen, and N. Veraverbeke. Presmoothed kaplan-meier and nelsonaalen estimators. *Journal of Nonparametric Statistics*, 17:31-56, 2005.
- G. Dikta. On semiparametric random censorship models. *Journal of Statistical Planning and Inference*, 66:253-279, 1998.
- E. Kaplan and P. Meier. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association*, 53:457-481, 1958.

**See Also**

[KMW](#)

**Examples**

```
obj <- with(colonIDM, survIDM(time1, event1, Stime, event))
PKMW(time = obj$Stime, status = obj$event)
```

---

plot.survIDM                      *Plot for an object of class "survIDM".*

---

### Description

It draws the estimated probabilities.

### Usage

```
## S3 method for class 'survIDM'
plot(x = object, y = NULL, trans = "all",
     func = "distribution", conf = NULL,
     type = NULL, conftype = NULL, col = 1:6, confcol = 1:6, lty = 1, conflty = 2,
     xlab = "Time (years)", ylab = NULL, ylim = NULL, xlim = NULL, ...)
```

### Arguments

x	An object of class "survIDM".
y	NULL
trans	The transition probabilities plotted. It is used only when the object is of class "AJ", "LIDA" "LM", "PLM", "LMAJ", "PLMAJ", "PAJ" and "tpIPCW". Possible options are "all" (default), "00", "01", "02", "11" or "12".
func	It is used only when the object is of class "soj" or "sojIPCW". The type of curve to be drawn ("distribution" or "survival"). Default to "distribution".
conf	Draw the confidence intervals into the plot. By default it is NULL, they are drawn if the "surv" object contains them.
type	The type of plot that should be drawn. See details <a href="#">par</a> for possible options. Defaults to "s" for the draw be stair steps.
conftype	The type of plot that should be drawn for confidence intervals. See details <a href="#">par</a> for possible options. Defaults to "s" for the draw be stair steps.
col	Vector of colors. Colors are used cyclically.
confcol	Vector of colors for the confidence intervals. Colors are used cyclically.
lty	The line type. Line types can either be specified as an integer (0 = blank, 1 = solid (default), 2 = dashed, 3 = dotted, 4 = dotdash, 5 = longdash, 6 = twodash). See details in <a href="#">par</a> .
conflty	The line type for confidence intervals. Line types can either be specified as an integer (0 = blank, 1 = solid (default), 2 = dashed, 3 = dotted, 4 = dotdash, 5 = longdash, 6 = twodash).
xlab	A title for the x axis: see <a href="#">title</a> .
ylab	A title for the y axis: see <a href="#">title</a> .
ylim	The y limits of the plot.
xlim	The x limits of the plot.
...	Other options.

**Value**

No value is returned.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**Examples**

```
res <- tprob(survIDM(time1, event1, Stime, event) ~ 1, s = 0,  
method = "AJ", conf = FALSE, data = colonIDM)
```

```
plot(res)  
plot(res, trans = "02")
```

```
res1 <- tprob(survIDM(time1, event1, Stime, event) ~ factor(sex), s = 365,  
method = "AJ", conf = FALSE, data = colonIDM)
```

```
plot(res1, trans="02", ylim=c(0,0.5))
```

```
res2 <- CIF(survIDM(time1, event1, Stime, event) ~ age, data = colonIDM,  
z.value = 56, conf = FALSE)
```

```
plot(res2)
```

```
res3 <- sojourn(survIDM(time1, event1, Stime, event) ~ factor(sex),  
data = colonIDM, conf = FALSE, conf.level = 0.95)
```

```
plot(res3)
```

---

sojourn

*Nonparametric estimation of the Sojourn time distributions in the  
illness-death model*

---

**Description**

This function is used to obtain nonparametric estimates of the sojourn probabilities in the illness-death model.

**Usage**

```
sojourn(formula, data, conf = FALSE, n.boot = 199, conf.level = 0.95,  
z.value, bw = "dpik", window = "gaussian", method.weights = "NW",  
method = "LM", presmooth = FALSE, cluster = FALSE, ncores = NULL)
```

**Arguments**

formula	A formula object, which must have a survIDM object as the response on the left of the ~ operator and, if desired, a term on the right. The term may be a qualitative or quantitative variable. Without covariates, the right hand side should be ~ 1.
data	A data.frame including at least four columns named time1, event1, Stime and event, which correspond to disease free survival time, disease free survival indicator, time to death or censoring, and death indicator, respectively.
conf	Provides pointwise confidence bands. Defaults to FALSE.
n.boot	The number of bootstrap replicates to compute the variance of the non-Markovian estimator. Default is 199.
conf.level	Level of confidence. Defaults to 0.95 (corresponding to 95%).
z.value	The value of the covariate on the right hand side of formula at which the sojourn probabilities are computed. For quantitative covariates, i.e. of class integer and numeric.
bw	A single numeric value to compute a kernel density bandwidth. Use "dpik" for the <b>KernSmooth</b> package based selector or "np" for the 'npudensbw' function of the <b>np</b> package.
window	A character string specifying the desired kernel. See details below for possible options. Defaults to "gaussian" where the gaussian density kernel will be used.
method.weights	A character string specifying the desired weights method. Possible options are "NW" for the Nadaraya-Watson weights and "LL" for local linear weights. Defaults to "NW".
method	The method used to compute the sojourn estimates. Possible options are "LM" and "Satten-Datta". Defaults to "LM".
presmooth	- A logical value. If TRUE, the presmoothed landmark estimator of the sojourn function is computed. Only valid for method = "LM".
cluster	A logical value. If TRUE (default), the bootstrap procedure for the confidence intervals is parallelized. Note that there are cases (e.g., a low number of bootstrap repetitions) that R will gain in performance through serial computation. R takes time to distribute tasks across the processors also it will need time for binding them all together later on. Therefore, if the time for distributing and gathering pieces together is greater than the time need for single-thread computing, it does not worth parallelize.
ncores	An integer value specifying the number of cores to be used in the parallelized procedure. If NULL (default), the number of cores to be used is equal to the number of cores of the machine - 1. #'

**Details**

Possible options for argument window are "gaussian", "epanechnikov", "tricube", "boxcar", "triangular", "quartic" or "cosine".

**Value**

An object of class "survIDM" and one of the following two classes: "soj" (Sojourn Time Distribution), and "sojIPCW" (Inverse Probability of Censoring Weighting for the Sojourn Time Distribution). Objects are implemented as a list with elements:

est	data.frame with estimates of the sojourn probabilities.
CI	data.frame with the confidence intervals of the sojourn probabilities.
conf.level	Level of confidence.
t	The time for obtaining the estimates of sojourn probabilities.
conf	logical; if FALSE (default) the pointwise confidence bands are not given.
callp	The expression of the estimated probability.
Nlevels	The number of levels of the covariate. Provides important information when the covariate at the right hand side of formula is of class factor.
levels	The levels of the qualitative covariate (if it is of class factor) on the right hand side of formula.
formula	A formula object.
call	A call object.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**References**

Satten, G.A. and Datta, S. (2002) Marginal estimation for multi-stage models: waiting time distributions and competing risks analyses. *Statistics in Medicine*, 21, 3–19.

**Examples**

```
res <- sojourn(survIDM(time1, event1, Stime, event) ~ 1,
data = colonIDM, conf = FALSE, conf.level = 0.95)
res
summary(res, time=365*1:6)
plot(res)

res1 <- sojourn(survIDM(time1, event1, Stime, event) ~ 1,
data = colonIDM, conf = FALSE, conf.level = 0.95, method = "LM",
presmooth = TRUE)
res1
summary(res1, time=365*1:6)
plot(res1)

# not run:
#res2 <- sojourn(survIDM(time1, event1, Stime, event) ~ 1,
#data = colonIDM, conf = FALSE, conf.level = 0.95, method = "Satten-Datta")
#res2
```

```

# with a factor
res3 <- sojourn(survIDM(time1, event1, Stime, event) ~ factor(sex),
data = colonIDM, conf = FALSE, conf.level = 0.95)
res3
summary(res3, time=365*1:6)
plot(res3)

# with a qualitative covariate
res4 <- sojourn(survIDM(time1, event1, Stime, event) ~ age, data = colonIDM,
z.value = 56, conf = FALSE, conf.level = 0.95)
res4
summary(res4, time=365*1:6)
plot(res4)

```

---

summary.cmm

*Summarizing fits of cmm class*


---

### Description

Produces a summary of a fitted coxidm model (proportional hazards regression model in each transition of the Illness-Death Model).

### Usage

```

## S3 method for class 'cmm'
summary(object, conf.level = 0.95, ...)

```

### Arguments

object	A fitted cmm object as produced by coxidm().
conf.level	level for computation of the confidence intervals. If set to FALSE no confidence intervals are printed.
...	Other options.

### Value

A data frame or a list containing the following components:

coef	Estimated coefficients.
exp(coef)	Exponent of the estimated coefficients.
lower 0.95	Lower limit of the confidence interval.
upper 0.95	Upper limit of the confidence interval.
pvalue	obtained pvalue testing that the coefficient is equals to zero.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**Examples**

```
cmm1 <- coxidm(survIDM(time1, event1, Stime, event) ~ age, data = colonIDM)
summary(cmm1, conf.level = 0.95)

cmm2 <- coxidm(survIDM(time1, event1, Stime, event) ~ rx + sex + age + nodes,
              data = colonIDM)
summary(cmm2)

cmm3 <- coxidm(survIDM(time1, event1, Stime, event) ~ rx + sex + age + nodes,
              data = colonIDM, semiMarkov = TRUE)
summary(cmm3)
```

---

summary.survIDM

*Summarizing fits of survIDM class*


---

**Description**

Returns a a data.frame or list containing the estimates of the probabilities, its confidence limits and other information.

**Usage**

```
## S3 method for class 'survIDM'
summary(object, times = NULL, ...)
```

**Arguments**

object	A fitted survIDM object as produced by tprob(), CIF() or sojourn().
times	Vector of times; the returned data frame will contain 1 row for each time. Missing values are not allowed.
...	For future methods.

**Value**

A data frame or a list containing the following components:

y	The total time for obtaining the estimates of the probabilities.
est	Estimates of the probability.
lower 95% CI	The lower probabilities of the interval.
upper 95% CI	The upper probabilities of the interval.



**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**Examples**

```
fit <- tprob(survIDM(time1,event1,Stime, event) ~ 1, s = 365,
method = "AJ", conf = TRUE, conf.level = 0.95,
conf.type = "linear", n.boot = 50, data = colonIDM)

summary(fit)
summary(fit, times = c(400, 1000, 2900))
```

---

survIDM

---

*Create a survIDM object*


---

**Description**

Creates a "survIDM" object, usually used as a response variable in a model formula.

**Usage**

```
survIDM(time1, event1, Stime, event, ...)
```

**Arguments**

time1	First time or censoring time.
event1	Indicator of the first time; 0 if the first time is censored and 1 otherwise.
Stime	The total time of the process.
event	Censoring indicator of the survival time of the process; 0 if the total time is censored and 1 otherwise.
...	Other options.

**Details**

Arguments in this function must be introduced in the following order: time1, event1, Stime and event, where time1 and Stime are ordered event times and event1 and event their corresponding indicator statuses.

**Value**

An object of class "survIDM". "survIDM" objects are implemented as a single dataframe.

**Author(s)**

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

**Examples**

```
with(colonIDM, survIDM(time1, event1, Stime, event))
```

---

tprob	<i>Nonparametric estimation of transition probabilities in the illness-death model</i>
-------	--

---

**Description**

This function is used to obtain nonparametric estimates of the transition probabilities in the illness-death model.

**Usage**

```
tprob(formula, s, method = "AJ", conf = FALSE, conf.level = 0.95,
      conf.type = "linear", n.boot = 199, data, z.value, bw = "dpik",
      window = "gaussian", method.weights = "NW", cluster = FALSE,
      ncores = NULL, na.rm = TRUE)
```

**Arguments**

formula	A formula object, which must have a survIDM object as the response on the left of the ~ operator and, if desired, a term on the right. The term may be a qualitative or quantitative variable. Without covariates, the right hand side should be ~ 1.
s	The first time for obtaining estimates for the transition probabilities. If missing, 0 will be used.
method	The method used to compute the transition probabilities. Possible options are "AJ", "LIDA", "LM", "PLM", "LMAJ", "PLMAJ", "PAJ", "IPCW" and "breslow". Defaults to "AJ". The "IPCW" method is recommended to obtain conditional transition probabilities (i.e., with a quantitative term on the right hand side of formula).
conf	Provides pointwise confidence bands. Defaults to FALSE.
conf.level	Level of confidence. Defaults to 0.95 (corresponding to 95%).
conf.type	Method to compute the confidence intervals. Transformation applied to compute confidence intervals. Possible choices are "linear", "log", "log-log" and "bootstrap". Default is "linear".
n.boot	The number of bootstrap replicates to compute the variance of the non-Markovian estimator. Default is 199.
data	A data.frame including at least four columns named time1, event1, Stime and event, which correspond to disease free survival time, disease free survival indicator, time to death or censoring, and death indicator, respectively.
z.value	The value of the covariate on the right hand side of formula at which the transition probabilities are computed. For quantitative covariates, i.e. of class integer and numeric.

bw	A single numeric value to compute a kernel density bandwidth. Use "dpik" for the <b>KernSmooth</b> package based selector or "np" for the 'npudensbw' function of the <b>np</b> package.
window	A character string specifying the desired kernel. See details below for possible options. Defaults to "gaussian" where the gaussian density kernel will be used.
method.weights	A character string specifying the desired weights method. Possible options are "NW" for the Nadaraya-Watson weights and "LL" for local linear weights. Defaults to "NW".
cluster	A logical value. If TRUE (default), the bootstrap procedure for the confidence intervals is parallelized. Note that there are cases (e.g., a low number of bootstrap repetitions) that R will gain in performance through serial computation. R takes time to distribute tasks across the processors also it will need time for binding them all together later on. Therefore, if the time for distributing and gathering pieces together is greater than the time need for single-thread computing, it does not worth parallelize.
ncores	An integer value specifying the number of cores to be used in the parallelized procedure. If NULL (default), the number of cores to be used is equal to the number of cores of the machine - 1.
na.rm	A logical value indicating whether NA values should be stripped in the computation.

### Details

Possible options for argument window are "gaussian", "epanechnikov", "tricube", "boxcar", "triangular", "quartic" or "cosine".

Possible methods are:

- AJ Aalen-Johansen estimator
- PAJ Presmoothed Aalen-Johansen estimator
- LIDA LIDA estimator
- LM Landmark approach estimator
- PLM Presmoothed Landmark approach estimator
- LMAJ Landmark approach Aalen-Johansen estimator
- PLDAJ Presmoothed Landmark approach Aalen-Johansen estimator
- tpIPCW Inverse Probability of Censoring Weighting for Transition Probabilities
- tpBreslow Breslow method

### Value

An object of class "survIDM" and one of the following five classes: "AJ", "LIDA", "LM", "PLM", "LMAJ", "PLMAJ", "PAJ", "tpIPCW" and "tpBreslow". Objects are implemented as a list with elements:

est	data.frame with estimates of the transition probabilities.
CI	data.frame with the confidence intervals of the transition probabilities.

conf.level	Level of confidence.
s	The first time for obtaining estimates for the transition probabilities.
t	The time for obtaining the estimates of transition probabilities.
conf	logical; if FALSE (default) the pointwise confidence bands are not given.
conf.type	Type of the confidence interval.
callp	The expression of the estimated probability.
Nlevels	The number of levels of the covariate. Provides important information when the covariate at the right hand side of formula is of class factor.
levels	The levels of the qualitative covariate (if it is of class factor) on the right hand side of formula.
formula	A formula object.
call	A call object.

### Author(s)

Luis Meira-Machado, Marta Sestelo and Gustavo Soutinho.

### References

Aalen O. O., Johansen S. (1978) An Empirical Transition Matrix for Nonhomogeneous Markov Chains Based on Censored Observations. *Scandinavian Journal of Statistics* 5(3), 141–150.

Meira-Machado L. F., de Una-Alvarez J. and Cadarso-Suarez C. (2006). Nonparametric estimation of transition probabilities in a non-Markov illness-death model. *Lifetime Data Anal* 12(3), 325–344.

de Una-Alvarez J. and Meira-Machado L. (2015). Nonparametric estimation of transition probabilities in a non-Markov illness-death model: a comparative study. *Biometrics* 71, 364–375.

### Examples

```
# Aalen-Johansen
res <- tprob(survIDM(time1, event1, Stime, event) ~ 1, s = 0, method = "AJ",
conf = FALSE, data = colonIDM)
summary(res, time=365*1:6)
plot(res)
# Transition Probabilities Pij(t)=Pij(365,t)
# LIDA
res1 <- tprob(survIDM(time1, event1, Stime, event) ~ 1, s = 365,
method = "LIDA", conf = FALSE, data = colonIDM)

summary(res1, time = 365*1:6)
plot(res1)
plot(res1, trans = "01", ylim = c(0,0.15))
# Landmark (LM)
res2 <- tprob(survIDM(time1, event1, Stime, event) ~ 1, s = 365,
method = "LM", conf = FALSE, data = colonIDM)
summary(res2, time = 365*1:6)
plot(res2)
# Presmoothed LM
```

```

res3 <- tprob(survIDM(time1, event1, Stime, event) ~ 1, s = 365,
             method = "PLM", conf = FALSE, data = colonIDM)
summary(res3, time = 365*1:6)
plot(res3)
# Conditional transition probabilities
# With factor
res4 <- tprob(survIDM(time1, event1, Stime, event) ~ factor(sex), s = 365,
             method = "AJ", conf = FALSE, data = colonIDM)
summary(res4, time = 365*1:6)
plot(res4, trans = "02", ylim = c(0,0.5))
res5 <- tprob(survIDM(time1, event1, Stime, event) ~ rx, s = 365,
             method = "breslow", z.value = 'Lev', conf = FALSE, data = colonIDM)
summary(res5, time = 365*1:6)
plot(res5,trans = "02", ylim = c(0,0.5))
## Not run: # with continuous covariate (IPCW and Breslow Method)
res6 <- tprob(survIDM(time1, event1, Stime, event) ~ age, s = 365,
             method = "IPCW", z.value = 48, conf = FALSE, data = colonIDM,
             bw = "dpik", window = "gaussian", method.weights = "NW")
summary(res6, time = 365*1:6)
plot(res6)
#res7 <- tprob(survIDM(time1, event1, Stime, event) ~ age, s =365,
#             method = "breslow", z.value = 60, conf = FALSE,
#             data = colonIDM)
summary(res7, time = 365*1:6)
plot(res7)
res8 <- tprob(survIDM(time1, event1, Stime, event) ~ age, s =365,
             method = "breslow", conf.type = 'bootstrap', n.boot = 2,
             z.value = 60, conf = TRUE, data = colonIDM)
summary(res8, time = 365*1:6)
plot(res8)
res9 <- tprob(survIDM(time1, event1, Stime, event) ~ rx, s =365,
             method = "breslow", conf.type='bootstrap',
             conf = TRUE, data =colonIDM)
summary(res9, time = 365*1:6)
plot(res9, trans = "02", ylim = c(0,0.5))
# more than a covariate (Breslow Method)
res10 <- tprob(survIDM(time1, event1, Stime, event) ~ nodes + factor(rx),
s = 365, method = "breslow", conf = TRUE, data =colonIDM)
summary(res10,t = 365*1:5)
plot(res10)
res11 <- tprob(survIDM(time1, event1, Stime, event) ~ nodes + factor(rx),
s = 365, method = "breslow", z.value = c(10,'Obs'), conf = TRUE,
data = colonIDM)
summary(res11,t = 365*1:5)
plot(res11)
# more than a covariate for Non Linear Models (Breslow Method)
res12 <- tprob(survIDM(time1, event1, Stime, event) ~ pspline(age) + nodes +
factor(rx), s =365, method = "breslow", conf = TRUE, data = colonIDM)
summary(res12,t = 365*1:5)
plot(res12)
# Confidence intervals
res13 <- tprob(survIDM(time1, event1, Stime, event) ~ 1, s = 365,
             method = "AJ", conf = TRUE, n.boot = 5, conf.level = 0.95,

```

```
          conf.type = "log", data = colonIDM)
summary(res13, time=365*1:7)
plot(res13)
res14 <- tprob(survIDM(time1, event1, Stime, event) ~ pspline(age) + nodes +
factor(rx), s =365, method = "breslow", conf.type = 'bootstrap', conf = TRUE,
conf.level = 0.95, data = colonIDM)
summary(res14,t = 365*1:5)
plot(res14)

## End(Not run)
```

# Index

## \*Topic **datasets**

- bladderIDM, [4](#)
- colonIDM, [8](#)
- gbcsIDM, [10](#)

Beran, [3](#)  
bladderIDM, [4](#)

CIF, [5](#)  
colonIDM, [8](#)  
coxidm, [9](#)

gbcsIDM, [10](#)

KM, [11](#), [17](#)  
KMW, [12](#), [18](#)

LLW, [13](#), [17](#)

markov.test, [14](#)

nevents, [15](#)  
NWW, [14](#), [16](#)

par, [19](#)  
PKM, [11](#), [17](#)  
PKMW, [12](#), [18](#)  
plot.survIDM, [19](#)  
print.cmm (summary.cmm), [23](#)  
print.survIDM (summary.survIDM), [24](#)

sojourn, [20](#)  
summary.cmm, [23](#)  
summary.survIDM, [24](#)  
survIDM, [25](#)  
survidm (survidm-package), [2](#)  
survidm-package, [2](#)

title, [19](#)  
tprob, [26](#)