Package: condSURV (via r-universe)

October 11, 2026

Type Package

Title Estimation of the Conditional Survival Function for Ordered Multivariate Failure Time Data

Version 2.0.4

Date 2023-02-28

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Description Method to implement some newly developed methods for the estimation of the conditional survival function. See Meira-Machado, Sestelo and Goncalves (2016) <doi:10.1002/bimj.201500038>.

Depends R (>= 3.0.0)

License GPL (>= 2)

LazyData TRUE

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

RoxygenNote 7.1.2

Encoding UTF-8

Config/pak/sysreqs make

Repository https://sestelo.r-universe.dev

Date/Publication 2023-03-01 15:07:21 UTC

RemoteUrl https://github.com/sestelo/condsurv

RemoteRef HEAD

RemoteSha ddf5a39d5cda872b5cf15719da0aed5f05d1b2d4

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`condSURV-package` *condSURV:A package for nonparametric estimation of the survival functions for ordered multivariate failure time data.*

Description

Newly developed methods for the estimation of the conditional survival function are implemented in this package. The condSURV package implements nonparametric and semiparametric estimators for these quantities. The package also implements feasible estimation methods for these quantities conditionally on current or past covariate measures. Other related estimators are also implemented in the package. One of these estimators is the Kaplan-Meier estimator typically assumed to estimate the survival function. A modification of the Kaplan-Meier estimator, based on a preliminary estimation (presmoothing) of the censoring probability for the survival time, given the available information is also implemented.

Author(s)

Luis Meira-Machado and Marta Sestelo.

Maintainer: Marta Sestelo, sestelo@uvigo.es

References

L. Meira-Machado, M. Sestelo, and A. Goncalves (2016). Nonparametric estimation of the survival function for ordered multivariate failure time data: a comparative study. Biometrical Journal, 58(3), 623–634.

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, $P(T <= y\|Z = z)$.

Details

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

Author(s)

Luis Meira-Machado and Marta Sestelo

References

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

Examples

```
obj <- with(colonCS, survCS(time1, event1, Stime, event))

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

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

---

bladderCS *Bladder Cancer Recurrences.*

Description

bladderCS 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.

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(bladderCS)
head(bladderCS)
```

---

colonCS *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.

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 and effective adjuvant therapy after resection of stage II colon carcinoma: a final report. Annals of Internal Medicine, 122:321-326, 1991.

Examples

```
data(colonCS)
head(colonCS)
```

---

gbcsCS *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)).

Format

A data frame with 686 observations on the following 16 variables. Below a brief description is given for some of these variables.

rectime Time to recurrence/censoring, whichever occurs first.

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

survtime Time to censoring/death, whichever occurs first.

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

age Age in years.

size Tumour size. #'

deathdate

diagdateb

estrg_recp

grade

hormone

id

nodes

prog_recp

recdate

menopause

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., Hiibner, 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(gbcsCS)
head(gbcsCS)
```

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 and Marta Sestelo

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(colonCS, survCS(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 and Marta Sestelo

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(colonCS, survCS(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 and Marta Sestelo

See Also

NWW

Examples

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

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 and Marta Sestelo

See Also

LLW

Examples

```
NWW(covariate = colonCS$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 and Marta Sestelo

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(colonCS, survCS(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

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 presmoothed Kaplan-Meier weights.

Author(s)

Luis Meira-Machado and Marta Sestelo

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(colonCS, survCS(time1, event1, Stime, event))
PKMW(time = obj$Stime, status = obj$event)
```

`plot.survCS` *Plot for an object of class "survCS".*

Description

It draws the estimated conditional survival probabilities.

Usage

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

Arguments

x	An object of class "survCS".
y	NULL
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 par 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 par 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 par.
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 title.
ylab	A title for the y axis: see title.
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 and Marta Sestelo

Examples

```
fit1 <- survCOND(survCS(time1, event1, Stime, event) ~ 1, x = 365,
   data = colonCS, method = "LDM", conf = TRUE)

plot(fit1, xlab = "Time (days)", ylab = "S(y|365)", ylim = c(0.5, 1))

fit4 <- survCOND(survCS(time1, event1, Stime, event) ~ rx,
   x = 365, data = colonCS, method = "LDM")

plot(fit4, xlab = "Time (days)", ylab = "S(y|365)", ylim = c(0.5, 1))
```

summary.survCS *Summarizing fits of* survCS *class*

Description

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

Usage

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

Arguments

object	A fitted survCS object as produced by survCOND().
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 conditional survival probabilities.
est	Estimates of the conditional survival probability.
lower 95% CI	The lower conditional survival probabilities of the interval.
upper 95% CI	The upper conditional survival probabilities of the interval.

Author(s)

Luis Meira-Machado and Marta Sestelo

References

L. Meira-Machado, M. Sestelo, and A. Goncalves (2016). Nonparametric estimation of the survival function for ordered multivariate failure time data: a comparative study. Biometrical Journal, 58(3), 623–634.

Examples

```
fit <- survCOND(survCS(time1, event1, Stime, event) ~ 1, x = 365,
data = colonCS, method = "LDM", conf = TRUE, n.boot = 50, cluster = FALSE)
summary(fit)
summary(fit, times = c(400, 1000, 2900))
```

survCOND *Conditional survival probabilities based on the Kaplan-Meier weights, Landmark approaches and Inverse probability of censoring weighted.*

Description

Provides estimates for the conditional survival probabilities based on Kaplan-Meier weighted estimators, the Landmark approaches and Inverse probability of censoring weighted.

Usage

```
survCOND(
  formula,
  x,
  y,
  lower.tail = FALSE,
  method = "LDM",
  presmooth = FALSE,
  conf = TRUE,
  n.boot = 200,
  data,
  conf.level = 0.95,
  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 survCS 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. For a single survival curve the right hand side should be ~ 1.
x	Time or vector of times for the condional event(s).
y	The total time for obtaining estimates for the conditional survival probabilities.
lower.tail	vector of logical values with the same size as 'x'. If 'x' has dimension one and if lower.tail = FALSE (default), probabilities are $P(T > y \mid T1 > x)$ otherwise, $P(T > y \mid T1 <= x)$. If the conditional event is 2-dimensional, then, for example, given $x = c(x1, x2)$ and lower.tail = c(TRUE, FALSE) must be used to obtain probabilities $P(T > y \mid T1 <= x1, T2 > x2)$. Multi-dimensional conditional events are introduced similarly.

method	The method used to compute the conditional survival function. Possible options are "LDM" and "KMW". Defaults to "LDM".
presmooth	A logical value. If TRUE, the presmoothed landmark estimator of the conditional survival function is computed. Only valid for method = "LDM".
conf	Provides pointwise confidence bands. Defaults to TRUE.
n.boot	The number of bootstrap samples. Defaults to 200 samples.
data	A data frame in which to interpret the variables named in the formula argument.
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 conditional survival 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 KernSmooth package based selector or "np" for the 'npudensbw' function of the np 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".

Value

An object of class "survCS" and one of the following four classes: "KMW", "LMD", "PLDM" and "IPCW". Objects are implemented as a list with elements:

est	data.frame with estimates of the conditional probabilities.
estimate	Estimates of the conditional survival probability.
LCI	The lower conditional survival probabilities of the interval.

UCI	The upper conditional survival probabilities of the interval.
conf.level	Level of confidence.
y	The total time for obtaining the estimates of the conditional survival probabilities.
x	The first time for obtaining the estimates of the conditional survival probabilities.
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.
conf	logical; if FALSE (default) the pointwise confidence bands are not given.
callp	The expression of the estimated probability.
levels	The levels of the qualitative covariate (if it is of class factor) on the right hand side of formula.

Author(s)

Luis Meira-Machado and Marta Sestelo

References

L. Meira-Machado, M. Sestelo, and A. Goncalves (2016). Nonparametric estimation of the survival function for ordered multivariate failure time data: a comparative study. Biometrical Journal, 58(3), 623–634.

Examples

```
fit <- survCOND(survCS(time1, event1, Stime, event) ~ 1, x = 365, y = 730,
data = colonCS, method = "KMW", conf = FALSE)

fit1 <- survCOND(survCS(time1, event1, Stime, event) ~ 1, x = 365,
data = colonCS, method = "LDM", conf = FALSE)

fit2 <- survCOND(survCS(time1, event1, Stime, event) ~ 1, x = 365,
data = colonCS, method = "LDM", lower.tail = TRUE, conf = FALSE)

fit3 <- survCOND(survCS(time1, event1, Stime, event) ~ 1, x = 365,
y = c(730, 1095, 1460), data = colonCS, method = "LDM", presmooth = TRUE,
lower.tail = TRUE, conf = TRUE, n.boot = 100, conf.level = 0.95,
cluster = FALSE)

fit4 <- survCOND(survCS(time1, event1, Stime, event) ~ rx, x = 365,
data = colonCS, method = "LDM", conf = FALSE)

fit5 <- survCOND(survCS(time1, event1, Stime, event) ~ factor(sex),
x = 365, data = colonCS, method = "LDM", conf = FALSE)

## Not run:
fit6 <- survCOND(survCS(time1, event1, Stime, event) ~ age,
x = 365, y = 730, z.value = 48, data = colonCS, conf = TRUE)
```

```
## End(Not run)
```

`survCS` *Create a survCS object.*

Description

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

Usage

```
survCS(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, time2, ..., Stime and event, where time1, time2, ..., Stime are ordered event times and event1, event2,..., event their corresponding indicator statuses.

Value

An object of class "survCS" and of class "surv". "survCS" objects are implemented as a single dataframe.

Author(s)

Luis Meira-Machado and Marta Sestelo

Examples

```
with(colonCS, survCS(time1, event1, Stime, event))
```

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