Package 'bpcp'

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Type Package

Title Beta Product Confidence Procedure for Right Censored Data

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Depends stats

Suggests survival

Description Calculates nonparametric pointwise confidence intervals for the survival distribution for right censored data. Has two-sample tests for dissimilarity (e.g., difference, ratio or odds ratio) in survival at a fixed time. Especially important for small sample sizes or heavily censored data. Includes mid-p options.

License GPL (>= 2)

LazyLoad yes

NeedsCompilation no

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R topics documented:

`bpcp-package` *Pointwise Confidence Intervals Associated with the Survival Distribution for Right Censored Data*

Description

The package has functions to give several different methods for calculating pointwise confidence intervals for a single survival distribution for right censored data. There is also a two-sample test for dissimilarity (measured by difference, ratio, or odds ratio) between two survival distributions at a fixed point in time.

The recommended confidence interval for a single sample is the beta product confidence procedure (using `bpcp`), and the recommended test for the two-sample test is the melded BPCP test (using `bpcp2samp`).

Other confidence intervals and two sample tests are included in the package primarily to compare them to the recommended ones. (And justify the recommendations).

Also included is a difference in medians test that applies only to non-censored data and is designed to guarantee coverage for all sample sizes (see `mdiffmedian.test`). The test makes no assumptions about the distributions, so that, unlike the Hodges-Lehmann method, tied data are allowed and a shift assumption is not needed.

Details

Package:	bpcp
Type:	Package
Version:	1.3.4
Date:	2016-06-14
License:	GPL2
LazyLoad:	yes

The most important function for the single sample case is the `bpcp` which gives confidence intervals for the survival distribution for right censored data with nice small sample properties. That function creates an `kmciLR` object which has 6 methods: `summary` (create a data frame with estimates and confidence intervals), `plot` (plot Kaplan-Meier with confidence intervals), `lines` (add confidence intervals to a plot), `StCI` (pick out survival and confidence interval at specific times), `median` (pick out median and confidence interval on median), and `quantile` (pick out any quantile and its confidence interval). A mid-p option for `bpcp` is now available. It gives closer to nominal coverage than

the standard (midp=FALSE) BPCP. For details see Fay et al (2013) on the standard BPCP and Fay and Brittain (2016) on the mid-p option.

For the two-sample test see bpcp2samp. This test for equality reduces to Fisher's exact test when there is no censoring. When there is censoring, the test is expected to maintain at least nominal coverage. For details see Fay et al (2015).

Author(s)

Michael P. Fay

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References

Fay, MP, Brittain, E, and Proschan, MA. (2013). Pointwise Confidence Intervals for a Survival Distribution with Small Samples or Heavy Censoring. Biostatistics 14(4): 723-736 doi: 10.1093/biostatistics/kxt016. (copy available at http://www.niaid.nih.gov/about/organization/dcr/brb/staff/Pages/michael.aspx).

Fay, MP, Proschan, MA, and Brittain, E (2015). Combining One Sample Confidence Procedures for Inference in the Two Sample Case. Biometrics 71:146-156.

Fay, MP, and Brittain, E (2016). Finite Sample Pointwise Confidence Intervals for a Survival Distribution with Right-Censored Data. Statistics in Medicine. doi: 10.1002/sim.6905.

See Also

bpcp

Examples

```
data(leuk)
## since there are ties at time=6
## and the data are truncated to the nearest integer, use Delta=1
bfit<-bpcp(leuk$time,leuk$status,Delta=1)
## plot Kaplan-Meier and 95 pct Beta Product Confidence Intervals
plot(bfit,xlab="time (weeks)")
## details
summary(bfit)
quantile(bfit)
StCI(bfit,2)
```

---

betaMeldTest *Melded Beta Test*

Description

This function gives a two sample melded beta test together with the associated melded confidence intervals. It can be used when the confidence distributions (or upper and lower confidence distributions) for the one sample parameters are beta, and one is interested in either the difference, odds ratio, or ratio of those two one sample parameters. The betaMeldTest is usually called by bpcp2samp, and not called directly by the user.

Usage

```
betaMeldTest(betaParms1, betaParms2,
    nullparm = NULL,
    parmtype = c("difference", "oddsratio", "ratio"),
    conf.level = 0.95, conf.int = TRUE,
    alternative = c("two.sided", "less", "greater"),
    eps = 10^-8, dname = "", estimate1 = NA, estimate2 = NA)
```

Arguments

betaParms1	a list of the beta parameters for group 1
betaParms2	a list of the beta parameters for group 2
nullparm	null value of the parameter of interest, default of NULL gives 0 if parmtype='difference' and 1 otherwise
parmtype	parameter type for comparing the survival function of the two groups, either 'difference' 'ratio' or 'oddsratio'
conf.level	confidence level, e.g., 0.95
conf.int	logical, calculate confidence interval?
alternative	character, either 'two.sided','less', or 'greater'
eps	small value to make integration tractable
dname	name describing data
estimate1	estimate of mean for beta parameter of group 1 (statistic of htest object)
estimate2	estimate of mean for beta parameter for group 2 (parameter of htest object)

Details

If the upper and lower confidence distributions for both samples are described by beta distributions, then you can create a CD test using this function. For example, if you have sample 1 is binomial with x (with 0<x<n) out of n positive responses, then the 100(1-alpha) confidence interval is qbeta(alpha/2, x, n-x+1) and qbeta(1-alpha/2, x+1, n-x). So the lower confidence distribution is beta with parameters a=x and b=n-x+1, and the upper CD is beta with parameters a=x+1 and b=n-x.

Value

an object of class 'htest'

Examples

```
fisher.test(matrix(c(4,5,2,22),2,2),alternative="greater")

betaMeldTest(
    betaParms1=list(alower=2,blower=22+1,aupper=2+1,bupper=22),
    betaParms2=list(alower=4,blower=5+1,aupper=4+1,bupper=5),
    alternative="greater",parmtype="oddsratio",
    estimate1=2/24,estimate2=4/9)
```

bpcp2samp *Melded BPCP test*

Description

Tests for dissimilarity between two groups in their survival distributions at a fixed point in time. Can operationalize that dissimilarity as 'difference', 'ratio' or 'oddsratio'.

Usage

```
bpcp2samp(time, status, group, testtime,
    parmtype = c("difference", "oddsratio", "ratio"),
    nullparm = NULL,
    alternative = c("two.sided", "less", "greater"),
    conf.level = 0.95,
    midp=FALSE,
    control = bpcp2sampControl())
```

Arguments

time	time to event for each observation
status	status of event time, 1 is observed, 0 is right censored
group	group for test, should have two levels, to change order use as factor and change order of levels
testtime	fixed time when you want to test for a difference
parmtype	parameter type for comparing the survival function of the two groups, either 'difference' 'ratio' or 'oddsratio'
nullparm	null value of the parameter of interest, default of NULL gives 0 if parmtype='difference' and 1 otherwise
alternative	character, either 'two.sided','less', or 'greater'
conf.level	confidence level, e.g., 0.95
midp	logical, do mid-p tests and confidence intervals?
control	list of control parameters, see bpcp2sampControl

Details

The melded confidence interval method is a very general procedure to create confidence intervals for the two sample tests by combining one sample confidence intervals. If S1 and S2 are the survival value at testtime from sample 1 (first value of group) and sample 2 (second value of group) respectively, then we can get confidence intervals on the S2-S1 (parmtype='difference'), S2/S1 (parmtype='ratio'), or (S2*(1-S1))/(S1*(1-S2)) (parmtype='oddsratio').

The resulting melded CIs appear to guarantee coverage as long as the one sample confidence intervals from which the melded CIs are derived have guaranteed coverage themselves. So since we use the BPCP for the one sample intervals and they appear to guarantee coverage (see Fay, Brittain,

and Proschan, 2013), we expect the melded BPCP intervals to have at least nominal coverage. Note that when there is no censoring the melded CIs derived from the one-sample BPCPs, give matching inferences to Fisher's exact test (i.e., give theoretically identical p-values) when testing the null hypothesis of equality (S1=S2). For details see Fay, Proschan and Brittain (2015).

The original melded CIs focused on combining one sample CIs that that guarantee coverage. We can apply the melding to other CIs as well, such as the mid-p style CIs. The mid-p CIs are not designed to guarantee coverage, but are designed to have close to the nominal coverage 'on average' over all the possible values of the parameters. The usual p-value is derived from Pr[see observed data or more extreme under null], while the mid p-value version comes from (1/2) Pr[see obs data] + Pr[see more extreme data]. Mid-p CIs come from inverting the test that uses the mid p-value instead of the usual p-value.

Value

A list with class "htest" containing the following components:

`statistic`	estimate of S1, survival at testtime for group 1
`parameter`	estimate of S2, survival at testtime for group 2
`p.value`	p-value for the test
`conf.int`	a confidence interval for the parameter determined by `parmtype`
`estimate`	estimate of parameter determined by `parmtype`
`null.value`	the specificed null hypothesized value of the parameter determined by `parmtype`
`alternative`	type of alternative with respect to the null.value, either 'two.sided', 'greater' or 'less'
`method`	a character string describing the test
`data.name`	a character string describing the parameter determined by `parmtype`

Author(s)

Michael P. Fay

References

Fay, MP, Brittain, E, and Proschan, MA. (2013). Pointwise Confidence Intervals for a Survival Distribution with Small Samples or Heavy Censoring. Biostatistics 14(4): 723-736 doi: 10.1093/biostatistics/kxt016. (copy available at http://www.niaid.nih.gov/about/organization/dcr/brb/staff/Pages/michael.aspx).

Fay, MP, Proschan, MA, and Brittain, E (2015) Combining One Sample Confidence Procedures for Inferences in the Two Sample Case. Biometrics 71:146-156.

Examples

```
data(leuk2)
bpcp2samp(leuk2$time,leuk2$status,leuk2$treatment,35,parmtype="ratio")

bpcp2samp(leuk2$time,leuk2$status,leuk2$treatment,35,parmtype="difference")
```

bpcp2sampControl *Control function for* bpcp2samp

Description

Call function to change any one of options, and outputs a list with all defaults except argument that you changed.

Usage

```
bpcp2sampControl(Delta = 0, stype = "km", eps = 10^-8,
    nmc=10^6, method="mm.mc", seed=391291)
```

Arguments

Delta	width of grouped confidence intervals, defaults to 0
stype	type of survival estimate, either "km" for Kaplan-Meier or "mue" for median unbiased estimator
eps	small value to make integration tractable
nmc	number of Monte Carlo replications
method	either 'mm.mc' (method of moments for one sample, meld with Monte Carlo) or 'mc.mc' (Monte Carlo for one sample and melding)
seed	random number seed, if NULL do not set random number seed

Details

We set the seed by default, so that the same data set will always give the same results. If you are doing simulations, this setting of the seed will give problems. So use seed=NULL.

Value

A list containing the 6 arguments.

See Also

bpcp2samp

Examples

```
bpcp2sampControl(Delta=1)
```

bpcpControl *Inputs for adjusting numerical calculations in* bpcp

Description

Function that returns a list of arguments.

Usage

```
bpcpControl(midpMMTol = .Machine$double.eps^0.25,
    seed=49911,
    tolerance=.Machine$double.eps^0.5)
```

Arguments

midpMMTol	value used for tol argument in uniroot call for calculating the midp method of moments method.
seed	seed for set.seed() when using Monte Carlo method. If is.null(seed) then do not set the seed.
tolerance	lowest positive value, such that abs(x-y)<tolerance treats x as equal to y. Used in bpcp for seeing if difference between times are equal to Delta or not.

Details

When doing simulations on the Monte Carlo method, set seed=NULL. Then the seed will not be set at each replication. The default is to set the seed to 49911, so two analyses of the same data on the same version of R will give identical results.

Value

A list with components named as the arguments.

fixtdiff *Two sample test for Difference in Survival at Fixed Time*

Description

Asymptotic two sample tests for difference in survival at a fixed time, using normal approximations and transformations. See Klien, et al (2007) for details.

Usage

```
fixtdiff(time,status,group, testtime,
    trans=c("identity","cloglog","log"),
    varpooled=TRUE, correct=FALSE, doall=FALSE)
```

Arguments

time	time to event for each observation
status	status of event time, 1 is observed, 0 is right censored
group	group for test, should have two levels, to change order use as factor and change order of levels
testtime	fixed time when you want to test for a difference
trans	type of transformation, one of 'identity', 'cloglog' or 'log'
varpooled	logical, pool the variance?
correct	logical, do continuity correction? Continuity correction for when trans='identity' and varpooled (see Warning)
doall	logical, do all transformations and corrections

Details

This function provides p-values for the two sample tests that the survival distributions are equal at time testtime. The tests are asymptotically normal tests and are described in Klein, et al (2007). These functions are mostly for simulations to evaluate the melded BPCP tests, see bpcp2samp and Fay et al (2015).

Value

A list with the following components:

plo	one-sided p-value, alternative: S1(testtime)>S2(testtime)
phi	one-sided p-value, alternative: S1(testtime)<S2(testtime
p2	two-sided p-value, min(1,2*plo,2*phi)

Warning

Continuity correction derived from the case with no censoriing (see Fleiss et al 3rd edition, pp. 50-55). May not make sense when there is censoring. Use at own risk.

Author(s)

Michael P. Fay

References

Fay, MP, Proschan, MA, and Brittain, E (2015) Combining One Sample Confidence Procedures for Inferences in the Two Sample Case. Biometrics 71:146-156.

Fleiss, Levin, Paik (2003) Statistical Methods for Rates and Proportions, 3rd edition.

Klein, Logan, Harhoff, and Andersen (2007). Analyzing survival curves at a fixed point in time. Statistics in Medicine 26(24): 4505-4519.

Examples

```
data(leuk2)
# Note that since the Kaplan-Meier survival at time=35 goes to
# zero for one group, the results for the log and cloglog
# transformations are undefined
fixtdiff(leuk2$time,leuk2$status,leuk2$treatment,35,doall=TRUE)
```

`kmci.object` *Kaplan-Meier (Survival Curve) Confidence Interval Object*

Description

The `kmci` class is returned by the functions `kmciTG` or `kmciSW`. The class represents a fitted survival curve with pointwise confidence intervals.

Unlike the `kmciLR` class, which allows for confidence intervals to change at any time point, the `kmci` class only has the confidence intervals change at observed failures.

Objects of this class has methods for the functions `summary`, `plot`, `lines`.

Arguments

`time`	the time points of observed failures (assumed surv and lower and upper steps that these times)
`cens`	time points where there is censoring but no observed failure
`surv`	the estimate of survival at time t+0. This is a vector.
`upper`	upper confidence limit for the survival curve.
`lower`	lower confidence limit for the survival curve.
`conf.level`	the level of the confidence limits, e.g., 0.95.

Structure

The following components must be included in a legitimate `kmci` object.

See Also

`kmciLR.object` `plot.kmci`, `summary.kmci`, `StCI.kmci`, `median.kmci`, `quantile.kmci`.

kmciLR.object *Kaplan-Meier (Survival Curve) Confidence Interval LR Object*

Description

The kmciLR class returned by the functions bpcp or kmciBorkowf, and represents a fitted survival curve with pointwise confidence intervals.

The kmciLR class allows for confidence intervals to change at any time point, while the kmci class only has the confidence intervals change at observed failures.

Objects of this class has methods for the functions summary, plot, lines.

Arguments

cens	time points where there is censoring but no observed failure
surv	the estimate of survival in the interval described by L and R. This is a vector.
upper	upper confidence limit for the survival curve in the interval described by L and R.
lower	lower confidence limit for the survival curve in the interval described by L and R.
L	vector of left ends of interval associated with lower and upper
Lin	vector of logicals, should left end of interval be included?
R	vector of right ends of interval associated with lower and upper
Rin	vector of logicals, should right end of interval be included?
Interval	character vector describing intervals
stype	character vector giving type of survival estimate, either 'km' or 'mue'
conf.level	the level of the confidence limits, e.g., 0.95.

Structure

The following components must be included in a legitimate kmciLR object.

See Also

plot.kmci, summary.kmci, StCI.kmci, median.kmci, quantile.kmci.

kmtestALL *Pointwise confidence intervals for survival for right censored data.*

Description

These functions give several different methods for calculating pointwise confidence intervals for the survival distribution for right censored data. The recommended confidence intervals are the beta product ones given by bpcp.

The other confidence intervals are included primarily to show that the beta product confidence procedure (using bpcp) has better coverage than the best alternatives. See details for a description of all the methods.

Usage

```
bpcp(time,status,nmc=0,alpha=.05,Delta=0,stype="km",midp=FALSE,
    monotonic=NULL, control=bpcpControl())


kmciBorkowf(time, status, type="log", alpha = 0.05)
kmtestBoot(time, status, tstar, pstar, M = 1000, alpha = 0.05)
kmtestConstrainBoot(time, status, tstar, pstar, M = 1000, alpha = 0.05)
kmtestConstrainBeta(time,status,tstar,pstar,alpha=.05)
kmciSW(time, status, alpha = 0.05)
kmciTG(time, status, alpha = 0.05)
kmci1TG(time, status, tstar, alpha = 0.05)

kmtestALL(time,status,t0,S0,cens=NULL,M=1000,NMC=10^5,alpha=0.05)
```

Arguments

time	time to event or censoring
status	status vector, 1 is event, 0 is censoring
alpha	1- conf.level
nmc	number of Monte Carlo replications from each beta distribution, nmc=0 means use method of moments for beta parameters instead
NMC	same as nmc
Delta	width of grouped confidence intervals, defaults to 0 (rarely need to change this, even with ties, see details)
stype	type of survival estimate, either "km" for Kaplan-Meier or "mue" for median unbiased estimator
midp	logical, calculate the mid-p type of interval?
monotonic	logical, force lower and upper confidence limits to be monotonic over time? If NULL: nmc=0 gives TRUE, nmc>0 gives FALSE

control	list with arguments for adjusting numeric calculation. Generally does not need to be changed. See bpcpControl
tstar	time to test survival distribution
pstar	null survival distribution
M	number of bootstrap replications
t0	null hypothesis time for survival test
S0	null hypothesis value of survival at t0
cens	vector of censoring times (even those with failures before it), used for Binomial test. If NULL gives NA for binom test
type	see details

Details

The standard beta product confidence procedure (i.e., with midp=FALSE) will give pointwise confidence intervals for right censored data with the following properties. When there is no censoring or Progressive Type II censoring the BPCP guarantees central coverage (e.g., the error rate on either side of the 95 percent confidence interval is guaranteed to be less than 2.5 percent). For general independent censoring the BPCP is asymptotically equivalent to standard methods such as the normal approximation with Greenwood variance, and hence the BPCP (as with the other confidence interval given here) goes to the correct confidence interval for any t.

There is also a mid-p version of the BPCP. The BPCP is derived from using the known distribution of the failure times, and acting conservatively between the failure times (see Fay, Brittain, and Proschan, 2013 for details). Instead of acting conservatively between the failure times, the midp=TRUE version combines the distributions for the previous failure and the future failure time (see Fay and Brittain, 2016).

For description of how bpcp with different values of Delta works, see "Beta Product Confidence Intervals for Discrete Failure Times" vignette (especially Section 2.2). Note especially that confidence intervals exactly at the failure times when Delta=0 are handled differently before Version 1.3.0 than from Version>=1.3.0. For users not interested in details who only want to know the recommended confidence intervals on right censored data when ties are allowed, we recommend the bpcp function version 1.3.0 or greater using the default Delta=0 argument. That recommendation will give pointwise confidence intervals that treats ties similarly to the way that the Kaplan-Meier estimator treats ties, and hence will give confidence intervals that enclose the Kaplan-Meier estimate.

Now we describe the other methods. In general the functions are of three naming types: kmtestXX, kmci1XX and kmciXX, where XX changes for different methods. Functions kmtestXX only test whether S(tstar)=pstar and return a vector of 1s for reject and 0s for fail to rejecting either of the one-sided or the two-sided hypotheses. Functions kmci1XX only give confidence intervals at S(tstar), while kmciXX give confidence intervals for all values of t. The standard methods calculate the confidence intervals at the observed failure times and carry them forward (e.g., kmciTG, kmciSW) and the results are objects of class kmci. More involved methods allow confidence intervals to change after censored objects (e.g., kmciBorkowf, bpcp) and the results are objects of class kmciLR.

The function kmtestBoot tests S(tstar)=pstar using the nonparametric bootstrap (sampling vectors of (time,status) with replacement) with the percentile method as described in Efron (1981). The function kmtestConstrainBoot and kmtestConstrainBeta tests S(tstar)=pstar using the constrained Bootstrap or constrained Beta method described in Barber and Jennison (1999).

The function kmci1TG does a confidence interval only at tstar, while kmciTG does a confidence interval at all the observed event times. The method can be derived as a likelihood ratio test and is described in Thomas and Grunkemeier (1975). It has asymptoticly correct coverage, which is rigorously proved in Murphy (1995). You can also think of the method as the empirical likelihood applied to the survival distribution for right censored data (see Owen, 2001, p. 144-145).

The function `kmciSW` calculates confidence intervals using Edgeworth expansions as described in Strawderman and Wells (1997). Note, Strawderman, Parzen and Wells (1997) is easier to understand than Strawderman and Wells (1997).

Borkowf (2005) creates confidence intervals for the Kaplan-Meier survival estimate for right censored data. He allows the confidence interval to change at censoring times as well as at failure times.

Four types of confidence intervals may be selected. The asymptotic normal approximation (type="norm"), the shifted K-M estimate with normal approximation (type="norms"), the log transformed normal approximation using the delta method (type="log"), and the log transformed normal approximation using the delta method with the shifted K-M (type="logs").

The function `kmtestALL` performs hypothesis tests on all the methods except the unconstrained bootstrap method (unless M=0 then it does not test the constrained bootstrap method either). The output is a matrix with three columns with a value of 1 representing either (1) rejection for two-sided test implying the estimate is greater than the null, (2) rejection for two-sided test implying the estimate less than the null, or (3) any rejection of the two-sided test. Each row represents a different test.

The `kmci` or `kmciLR` classes have the following methods: `"plot"`,`"lines"`, `"summary"`, `"quantile"`, and `"median"`. Additionally, you can pull out survival and confidence intervals from these objects at specific times using `"StCI"`.

Value

The functions return an object of class either `kmci` or `kmciLR` see details).

both kmci and kmciLR objects are lists, and both contain elements

`surv`	survival distribution in interval
`lower`	lower pointwise confidence limit in interval
`upper`	upper pointwise confidence limit in interval

additionally the kmci objects have an element

`time`	time of survival or confidence interval

while the kmciLR have intervals represented by the four elements

`L`	left endpoint of interval
`Lin`	logical vector, include left endpoint?
`R`	right endpoint of interval
`Rin`	logical vector, include right endpoint?

and results from bpcp additionally have an element

`betaParms`	list with 4 elements of beta parameters associated with the CIs: alower, blower, aupper, bupper

Author(s)

Michael Fay

References

Fay, MP, Brittain, E, and Proschan, MA. (2013). Pointwise Confidence Intervals for a Survival Distribution with Small Samples or Heavy Censoring. Biostatistics 14 (4): 723-736. (copy available at http://www.niaid.nih.gov/about/organization/dcr/brb/staff/Pages/michael.aspx).

Fay, MP, and Brittain, E (2016). Finite Sample Pointwise Confidence Intervals for a Survival Distribution with Right-Censored Data. Statistics in Medicine. doi: 10.1002/sim.6905.

Barber and Jennison (1999) Biometrics, 55: 430-436.

Borkowf (2005) Statistics in Medicine, 24: 827-851.

Efron (1981) JASA 76:312-319.

Murphy (1995) JASA 90: 1399-1405.

Owen (2001) Empirical Likelihood. Chapman and Hall: New York.

Strawderman and Wells (1997) JASA 92:1356-1374.

Strawderman, Parzen and Wells (1997) Biometrics 53: 1399-1415.

Thomas and Grunkemeier (1975) JASA 70: 865-871.

See Also

The kmci and kmciLR objects have methods: "plot","lines", "summary", "quantile", and "median","StCI".

Examples

```
library(bpcp)
data(leuk)

### Recommended method is bpcp
### since the data are truncated to the nearest integer
### use Delta=1 option
out<-bpcp(leuk$time,leuk$status,Delta=1)
summary(out)
median(out)
plot(out)



### Borkowf 2005 method
norm<-kmciBorkowf(leuk$time,leuk$status,type="norm")
norms<-kmciBorkowf(leuk$time,leuk$status,type="norms")
## check Table VII of Borkowf
I<-c(1,2,3,5,7,8,9,11,13,15,17,19,21,23,25,27,29,31,33)
round(data.frame(lowerNorm=norm$lower[I],
    upperNorm=norm$upper[I],lowerNormS=norms$lower[I],
    upperNorms=norms$upper[I],row.names=norm$Interval[I]),3)
```

```
### Strawderman and Wells (1997) method
swci<-kmciSW(leuk$time,leuk$status)
summary(swci)


### Thomas and Grunkemeier 1975 method
x<-kmciTG(leuk$time,leuk$status)
summary(x)
## compare to Table 1, Sample 2, of Thomas and Grunkemeier (1975)
StCI(x,c(10,20))
```

---

leuk *Acute Leukemia data (treatment only) from Freireich et al (1963).*

Description

This is only the 21 patients who received 6-mercaptopurine (6-MP). There were 21 patients who got placebo (see leuk2 for complete data).

See also Borkowf (2005)

Usage

```
data(leuk)
```

Format

A data frame with 21 observations on the following 2 variables.

`time` time in remission (in weeks)

`status` event status, 1 is relapse, 0 is censored

References

Borkowf (2005) Statistics in Medicine, 24: 827-851.

Freireich et al (1963) Blood 21(6):699-716.

See Also

leuk2 for complete data.

Examples

```
data(leuk)
```

leuk2 *Acute Leukemia data from Freireich et al (1963).*

Description

In this study there were 21 pairs of subjects, and within each pair one subject received 6-mercaptopurine (6-MP) and one got placebo. The data are right censored.

See also Gehan (1965) who used the data ignoring the pairing so that he could illustrate his famous two-sample (non-paired) rank test.

Usage

```
data(leuk2)
```

Format

A data frame with 42 observations on the following variables.

`time` time in remission (in weeks)

`status` event status, 1 is relapse, 0 is censored

`treatment` treatment group: either 'placebo' or '6-MP'

`pair` pair id number

References

Gehan (1965) Biometrika 52:203-223.

Freireich et al (1963) Blood 21(6):699-716.

See Also

`leuk` is only the treated group

Examples

```
data(leuk2)
```

`mdiffmedian.test` *Melded Difference in Medians Test*

Description

Tests for a difference in two medians. No assumptions about the two distributions are needed (may be discrete with ties allowed, no shift assumption is required). Uses the melded confidence interval derived from the one sample confidence intervals associated with the sign test (a version that allows for ties). Derivation of the test does not require large samples, and confidence intervals are intended to guarantee coverage regardless of sample size.

Usage

```
mdiffmedian.test(x1, x2, nulldiff = 0,
    alternative = c("two.sided", "less", "greater"),
    conf.level = 0.95)
```

Arguments

`x1`	vector of numeric responses from group 1
`x2`	vector of numeric responses from group 2
`nulldiff`	difference in medians under the null, median(x2)-median(x1)
`alternative`	a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less". You can specify just the initial letter.
`conf.level`	confidence level of the interval.

Details

The melded confidence interval method is a general method for combining two one-sample confidence intervals (CIs). In this function, we use the melded CI method on the two one-sample CIs from the sign test that allows for ties. This creates CIs for the difference in medians that requires very few assumptions. In particular, ties are allowed and no shift assumption is needed. For details see Fay, Proschan and Brittain (2014).

Value

a list of class 'htest' with elements:

`statistic`	median of x1
`parameter`	median of x2
`p.value`	p-value of the test
`conf.int`	confidence interval for the difference in medians
`estimate`	median(x2)-median(x1)
`null.value`	null hypothesis value for difference in medians
`alternative`	type of alternative hypothesis

method	description of test
data.name	description of input

Note

This function does not allow censoring. Also, there is a price for not needing large samples nor assumptions about the distributions: if you do not have enough data, your confidence intervals may be the entire real line. For example, if you have continuous data with equal sample sizes in both groups, then if you have 6 or fewer observations in each group, then the 95 percent confidence interval on the difference in medians will be (-Inf,Inf).

Author(s)

Michael P. Fay

References

Fay, MP, Proschan, MA, Brittain, E (2014). Combining One-sample confidence procedures for inference in the two-sample case. (unpublished manuscript).

Examples

```
set.seed(1)
trtA<-rpois(20,1.5)
trtB<-rpois(23,5.5)
mdiffmedian.test(trtA,trtB)
```

---

plot.kmciLR *Plot and lines methods for* kmci *and* kmciLR *objects.*

Description

Plots survival curves and/or confidence intervals.

Usage

```
## S3 method for class 'kmci'
plot(x, ...)

## S3 method for class 'kmciLR'
plot(x, XLAB = "time", YLAB = "Survival", YLIM = c(0, 1),
    ciLTY = 2, ciCOL = gray(0.8), mark.time = NULL, linetype = "both", ...)

## S3 method for class 'kmciLR'
lines(x, lty = c(2, 1), col = c(gray(0.8), gray(0)),
    linetype = "both", mark.time = NULL, ...)
```

```
## S3 method for class 'kmci'
lines(x, ...)
```

Arguments

x	kmci or kmciLR object (created by functions described in kmtestALL)
XLAB	label for x axis
YLAB	label for y axis
YLIM	limits for y axis
ciLTY	lty (line type) for confidence intervals
ciCOL	col (color) for confidence intervals
col	vector of colors, first element used for ci second for survival curve
lty	vector of line types, first element used for ci second for survival curve
mark.time	put hash marks for censored objects (default puts marks of stype="km" but not if stype="mue")
linetype	character, which lines to draw: either 'both', 'surv' or 'ci'
...	Extra parameters to be passed. Any argument in plot.kmciLR can be passed from plot.kmci, similarly for line. Other parameters are usually graphical parameters passed to plot and segment calls within function.

Examples

```
data(leuk)
## kmciTG creates kmci object
fitTG<-kmciTG(leuk$time,leuk$status)
plot(fitTG)
## bpcp creates kmciLR object
fitBP<-bpcp(leuk$time,leuk$status)
lines(fitBP,lwd=3,lty=1,col=gray(.5))
legend(0,.2,legend=c("Kaplan-Meier","Thomas-Grunkemeier 95 pct CI","Beta Product 95 pct CI"),
    lwd=c(1,1,3),lty=c(1,2,1),col=c(gray(0),gray(.8),gray(.5)))
```

---

quantile.kmciLR *Quantiles or Medians from* kmci *or* kmciLR *objects.*

Description

Get quantiles or median with the associated confidence intervals from a kmci or kmciLR object.

Usage

```
## S3 method for class 'kmciLR'
quantile(x, probs = c(0.25, 0.5, 0.75), ...)
## S3 method for class 'kmci'
quantile(x, probs = c(0.25, 0.5, 0.75), ...)
## S3 method for class 'kmciLR'
median(x, ...)
## S3 method for class 'kmci'
median(x, ...)
```

Arguments

x	a kmci or kmciLR object
probs	vector of probability to calculate quantiles
...	parameters passed

Value

matrix same number of rows as probs and with 4 columns

S(q)	probs, survival estimate at quantile
q	quantile
lower	lower confidence limit of q
upper	upper confidence limit of q

Examples

```
data(leuk)
## kmciTG creates kmci object
fitTG<-kmciTG(leuk$time,leuk$status)
quantile(fitTG)
## bpcp creates kmciLR object
fitBP<-bpcp(leuk$time,leuk$status)
median(fitBP)
```

---

sclerosis *Pilot study of treatment of severe systemic sclerosis (Nash, et al, 2007).*

Description

Severe systemic sclerosis is a serious autoimmune disease affecting multiple organs including the heart, lungs, kidney, and skin. Between 1997 and 2005, a cohort of 34 patients was enrolled in a single arm pilot study of high-dose immunosuppressive therapy and autologous hetapoietic cell transplantation

Usage

```
data(sclerosis)
```

Format

A data frame with 34 observations on the following 3 variables.

`day` time to death or censoring, in days

`year` time to death or censoring, in years (day/365.25)

`status` 0 is censored, 1 is event

References

Nash, R.A., McSweeney, P.A., Crofford, L.J., Abidi, M., Chen, C.S., Godwin, J.D., Gooley, T.A., Holmberg, L., Henstorf, G., LeMaistre, C.F., others (2007). "High-dose immunosuppressive therapy and autologous hematopoietic cell transplantation for severe systemic sclerosis: long-term follow-up of the US multicenter pilot study" Blood 110 (4): 1388-.

Examples

```
data(sclerosis)
plot(bpcp(sclerosis$year,sclerosis$status))
```

StCI *Get survival and confidence interval at t from* `kmci`, `kmciLR`, *or* `survfit` *object*

Description

Just picks out the survival function and confidence interval in a different way depending on the type of object.

Usage

```
## Default S3 method:
StCI(x,tstar, afterMax = "continue", ...)


## S3 method for class 'kmciLR'
StCI(x,tstar, ...)
```

Arguments

x	a kmci or kmciLR object
tstar	a vector of times that you want survival and CI values
afterMax	character, what to do after tmax (see details)
...	further arguments to be passed to or from methods.

Details

Since the Kaplan-Meier estimator is undefined after the last observation if it is censored and many confidence interval methods are not defined there either, we need to explicitly define what to do. (For objects of the kmciLR class, the confidence intervals are defined over the positive real line and the afterMax is ignored.) The afterMax has four options for this: 'continue' (keep surv and ci values the same as the last calculated one), 'zero' (surv and lower go to zero, upper stays same), 'zeroNoNA' (surv and lower go to zero, upper stays same unless it is NA, then it takes on the last non-missing upper value), 'half' (surv goes to half value, lower goes to zero, upper stays same).

Value

The function StCI returns a data frame with the following variables. (It also has an attribute: 'conf.level').

time	this is tstar
survival	survival at tstar
lower	lower confidence limit at tstar
upper	upper confidence limit at tstar

Author(s)

Michael Fay

See Also

kmci, kmciLR

Examples

```
data(leuk)
## compare to table 1 of Thomas and Grunkmeier (1975)
StCI(kmciTG(leuk$time,leuk$status),c(10,20))
```

summary.kmciLR *Summay method for* kmci *or* kmciLR *object.*

Description

Creates a data frame with time (for kmci) or time interval (for kmciLR), survival, lower and upper pointwise confidence intervals.

Usage

```
## S3 method for class 'kmciLR'
summary(object, ...)
## S3 method for class 'kmci'
summary(object, ...)
```

Arguments

object	kmci or kmciLR object
...	extra arguments

Value

creates a data frame. See description.

Examples

```
data(leuk)
## kmciTG creates kmci object
fitTG<-kmciTG(leuk$time,leuk$status)
summary(fitTG)
## bpcp creates kmciLR object
fitBP<-bpcp(leuk$time,leuk$status)
summary(fitBP)
```

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