Package ‘RMSTdesign’

December 30, 2019

Title Sample Size and Power Calculation for the Difference in Restricted Mean Survival Time

Version 0.0.0.9000

Description Calculates the asymptotic power of the test of the difference in
restricted mean survival time under user-specified trial design parameters,
or the sample size required for a specified power. It also provides
the probability restricted mean survival time will be estimable using the area
under the Kaplan-Meier curve, and, if desired, plots of power versus design
parameters and empirical power based on simulations.

License MIT + file LICENSE

Encoding UTF-8

LazyData true

URL https://anneae.github.io/RMSTdesign/

BugReports https://github.com/anneae/RMSTdesign/issues

Imports stats,
survival,
graphics

Roxygen list(markdown = TRUE)

RoxygenNote 6.1.1

Suggests knitr,
rmarkdown,
SSRMST,
PWEALL

VignetteBuilder knitr

R topics documented:

`plotsurvdef` *Plots two survival distributions.*

Description

Plots two survival distributions.

Usage

```
plotsurvdef(survdefC, survdefT, xupper)
```

Arguments

`survdefC`	the survival distribution of the control group (will be plotted as a solid line), as a list in the form output by `survdef`.
`survdefT`	the survival distribution of the control group (will be plotted as a dashed line), as a list in the form output by `survdef`.
`xupper`	the upper x axis limit for the plot.

Examples

```
RIC<-survdef(times = 18, surv = .6)
MAC<-survdef(times = 3, haz=c(4.375*RIC$h(1),RIC$h(1)))
plotsurvdef(RIC, MAC, 24)
```

`RMSTpow` *Sample Size and Power for the Test of the Difference in Restricted Mean Survival Time*

Description

Determine the asymptotic power of the test of RMST under a given trial design, or calculate the samples size needed to achieve a desired power.

Usage

```
RMSTpow(survdefC, survdefT, k1, k2, tau, n = NA, power = NA,
  plot = F, sim = F, M = 1000, method = "tau_star", alpha = NA,
  two.sided = F)
```

Arguments

`survdefC`	the survival distribution of the control group, as a list in the form output by `survdef`.
`survdefT`	the survival distribution of the treatment group, as a list in the form output by `survdef`.
`k1`	length of the accrual period. We assume subjects will accrue uniformly over the interval `(0, k1)` and then be followed until trial time `k1+k2`.
`k2`	length of the follow-up period.

`tau`	restriction time for the RMST.
`n`	total sample size for both groups. 1:1 randomization is assumed. Either `n` or `power` can be specified, and the other value will be calculated.
`power`	the desired power.
`plot`	if T, plots of the assumed survival distributions and power as a function of sample size, accrual time ka1and follow-up time k2 will be produced. Default is F. The power of the RMST test, the log-rank test using all available followup and the log-rank test using only followup to time tau after randomization will be displayed. If two-sided=T, the power of the test for superiorty (treatment over control) and inferiority (control over treatment), are represented with solid and dashed lines, respectively.
`sim`	if T, simulations will be conducted and empirical power and other summary statistics will be provided. Default is F. The hypothesis tests are carried out based on the normal approximation with the variance estimated according to the Greenwood plug-in/infinitesimal jackknife method. Specifying situations where survival doesn't go to zero in a reasonable amount of time (trial length times 1000) will lead to problems if the `sim=T` option is used.
`M`	number of simualations. Default is 1000.
`method`	modification to be used in simulations if the Kaplan-Meier estimate is not defined at time `tau` in either group. Default is 'tau_star', which changes the restriction time to the last censoring time, if the last observation is censored at a time earlier than `tau`. Other possible values are 'gill', 'efron', 'tau_star', 'risk1', 'risk2', and 'risk5'. The riskX' options indicate estimating RMST difference at the latest time at which at least X people are at risk in each group, irrespective of the value of `tau`.
`alpha`	type I error level. Default is 0.025 if 'two.sided'=F and 0.05 if 'two.sided'=T.
`two.sided`	whether a two-sided test is desired. Default is F, meaning that all reported power values correspond to a test of the superiority of treatment over control. If set to T, the power for a test of superiority (treatment over control) and inferiority (control over treatment) will be reported separately in the results; the power of a two-sided test is the sum of two.

Value

a list with components

`n`	the user-specified n, or if n was left blank, the n needed to achieve the user-specified power.
`powerRMST`	the user-specified power, or if power was left blank, the asymptotic power of the RMST test. If `one-sided=T`, `powerRMST` is equivalent to `powerRMSToverC`. If `one-sided=F`, `powerRMST` is equivalent to the sum of the power of a one-sided test in each direction, i.e. `powerRMSToverC + powerRMSCoverT`.
`powerRMSToverC`	the asymptotic power for a test of superiority of treatment over control.
`powerRMSCoverT`	the asymptotic power for a test of superiority of control over treatment. If a one-sided test is specified, this is set to NA.
`powerLRToverC`	the asymptotic power of the log-rank test of superiority of treatment over control.
`powerLRCoverT`	the asymptotic power of the log-rank test of superiority of control over treatment. If a one-sided test is specified, this is set to NA.

`powerLRtauToverC`
: the asymptotic power of the log-rank test of superiority of treatment over control, using only data up to time tau after randomization.

`powerLRtauCoverT`
: the asymptotic power of the log-rank test of superiority of control over treatment, using only data up to time tau after randomization. If a one-sided test is specified, this is set to NA.

`pKME`
: the probability that you will be able to estimate RMST difference at time tau using the standard Kaplan-Meier estimator. If the last observation in either group is censored, and the censoring time is less than tau, the Kaplan-Meier estimate is not defined through time tau, and the RMST difference cannot be estimated using the standard area under the Kaplan-Meier curve. A modified estimator must be used.

`simout`
: a list returned if `sim = T`, with components:

- `emppowRMSTToverC` empirical power of the RMST test for the superiority of treatment over control.
- `emppowRMSTCoverT` empirical power of the RMST test for the superiority of control over treatment. If a one-sided test is specified, this is set to NA.
- `emppowLRToverC` empirical power of the log-rank test for the superiority of treatment over control.
- `emppowLRCoverT` empirical power of the log-rank testthe superiority of control over treatment. If a one-sided test is specified, this is set to NA.
- `emppowLRtauToverC` empirical power of the log-rank test for the superiority of treatment over control, using only data up to time tau after randomization.
- `emppowLRtauCoverT` empirical power of the log-rank testthe superiority of control over treatment, using only data up to time tau after randomization. If a one-sided test is specified, this is set to NA.
- `emppKME` proportion of simulations where the standard KM estimator was used.
- `meandiff` mean estimated difference in RMST across the simulated datasets.
- `SDdiff` standard deviation of the estimated difference in RMST across the simulated datasets.
- `meantrunc` mean truncation time used in the simulated datasets (may be smaller than tau if method = 'tau_star' or 'riskX' options are used).
- `SDtrunc` standard deviation of the truncation time used in the simulated datasets.

Examples

```
con<-survdef(times = 3, surv = 0.5)
trt<-survdef(haz = 0.67*con$h(1))
RMSTpow(con, trt, k1 = 0, k2 = 3, tau = 3, power = 0.8)
RMSTpow(con, trt, k1 = 0, k2 = 3, tau = 3, n = 552)
```

shortest_duration *Find Shortest Duration Trial*

Description

Find the trial with the shortest duration in calendar time with a specified power and probability that RMST difference will be estimable with the Kaplan-Meier estimator. Within all trials of that minimum duration, the function finds the one with the smallest sample size. This function is based on a one-sided test of the superiority of the treatment arm.

Usage

```
shortest_duration(survdefC, survdefT, tau, power, accrual_rate,
  pKME = 0.95, alpha = 0.025, altdesign = F, multiplier = 1.1)
```

Arguments

survdefC	the survival distribution of the control group, as a list in the form output by survdef.
survdefT	the survival distribution of the treatment group, as a list in the form output by survdef.
tau	restriction time for the RMST.
power	the desired power.
accrual_rate	the planned accrual rate, per unit of time.
pKME	The desired probability that the RMST difference will be estimable using the Kaplan-Meier estimator. Default is 0.95.
alpha	one-sided type I error level. Default is 0.025.
altdesign	if T, the function will look for an alternative design that is not the shortest in duration, but has duration equal to some multiple of the shortest possible duration. Default is F. The sample size of the shortest duration trial can be much larger than a slightly longer trial, so we recommend considering an alternative design slightly longer than the shortest trial in addition to the shortest trial.
multiplier	the factor by which the duration of the shortest possible trial is multiplied to acquire the duration of the alternative trial design. Default is 1.1, meaning a trial that is 10 shortest possible trial. This argument is ignored if altdesign=F.

Value

a list with components:

n	total number of patients.
k1	length of the accrual period. We assume subjects will accrue uniformly over the interval (0, k1) and then be followed until trial time k1+k2.
k2	length of the follow-up period.
duration	trial duration in calendar time, k1+k2.
powerRMSTToverC	the asymptotic power of the RMST test for the superiority of treatment over control.

powerLRToverC
: the asymptotic power of the log-rank test using all available follow-up for the superiority of treatment over control.

powerLRtauToverC
: the asymptotic power of the log-rank test using follow-up to time tau for the superiority of treatment over control.

pKME
: the probability that you will be able to estimate RMST difference at time tau using the standard Kaplan-Meier estimator.

Examples

```
con<-survdef(times = 3, surv = 0.5)
trt<-survdef(haz = 0.67*con$h(1))
shortest_duration(con, trt, 3, .8, 552/4)
```

---

survdef — *Create a Survdef Object for a Piecewise Exponential Distribution*

Description

Create a new object which stores user-specified survival distribution information in the format needed for the main function, `RMSTpow`. `survdef` is used when the user wishes to specify a piecewise expoenential survival distribution. Either the hazard on fixed intervals or survival probabilities at fixed times can be specified.

Usage

```
survdef(haz = NA, surv = NA, times = NA)
```

Arguments

haz
: a vector of hazards of length<=10. If a single hazard is specified, the survival distribution is exponential with the specified hazard. If `haz` has length>2, the survival distribution has constant hazard equal to `haz` over the intervals `[0, t_1), [t_1, t_2), ..., [t_m, Inf)` where `t_i` are the entries of `times` and `times` has length `m`. One of `haz`, `surv` must be specified.

surv
: a vector of survival probabilities of length<=10 corresponding to `times`. If `surv` is specified, the survival distribution has constant hazard over the intervals `[0, t_1), [t_1, t_2), ..., [t_m, Inf)` where `t_i` are the entries of `times` and `times` has length `m+1`. The hazards are calculated so that the curve passes through each entry in `surv` at the corresponding time from `times`. One of `haz`, `surv` must be specified.

times
: a vector of the same length as surv (if surv is specified) or one element shorter than haz (if haz is specified). No times term is required if a single hazard is specified in haz.

Value

a list with components:

S
: a vectorized function that takes time as input and returns the survival probability at that time

h
: a vectorized function that takes time as input and returns the hazard at that time

Examples

```
survdef(times = 1:8, surv=c(.771, .523,.342,.236,.172,.130,.1,.078))
```

---

survdefHR — *Create a Survdef Object Based on a Hazard Ratio*

Description

Creates a new object which stores user-specified survival distribution information in the format needed for the main function, `RMSTpow`. `survdefHR` is used when the user wishes to specify a survival distribution that is defined by its relationship to another distribution via a constant hazard ratio.

Usage

```
survdefHR(survdefC, HR)
```

Arguments

`survdefC`	the survival distribution for the reference/control group, as a list in the form output by `survdef`.
`HR`	the hazard ratio defining the relationship between the two distributions.

Value

a list with components:

`S`	a vectorized function that takes time as input and returns the survival probability at that time
`h`	a vectorized function that takes time as input and returns the hazard at that time

Examples

```
con<-survdef(times = 3, surv = 0.5); survdefHR(con, 0.5)
```

---

survdefWeibull — *Create a Survdef Object for a Weibull Distribution*

Description

Create a Survdef Object for a Weibull Distribution

Usage

```
survdefWeibull(shape, scale)
```

Arguments

- `shape` — the shape parameter for the Weibull distribution. Parametrization is according to built-in R functions for the Weibull distribution, see `?Weibull` for more information.
- `scale` — the scale parameter for the Weibull distribution.

Value

a list with components:

- `S` — a vectorized function that takes time as input and returns the survival probability at that time
- `h` — a vectorized function that takes time as input and returns the hazard at that time

Examples

```
survdefWeibull(shape = 1.05, scale = 8573)
```

Index