Package ‘SurvGSD’

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Type Package

Title Group Sequential Design for a Clinical Trial with Censored Survival Data

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Description Sample size calculation utilizing the information fraction and the alpha spending function in a group sequential clinical trial with censored survival data from underlying generalized gamma survival distributions or log-logistic survival distributions.
Hsu, C.-H., Chen, C.-H, Hsu, K.-N. and Lu, Y.-H. (2018) A useful design utilizing the information fraction in a group sequential clinical trial with censored survival data.
To appear in Biometrics.

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R topics documented:

Find.h	*To find parameter of a uniform dropout censoring distribution under a generalized gamma survival distribution or a log-logistic survival distribution.*

Description

A function finds parameter h of a uniform dropout censoring distribution U(0,h) with a generalized gamma survival distribution or a log-logistic survival distribution for a given dropout censoring probability.

Usage

```
Find.h(lfu, R, T, q, mu, sigma, eta, theta)
```

Arguments

`lfu`	the dropout censoring probability.
`R`	the recuritment duration.
`T`	the study duration.
`q, mu, sigma`	shape, location and scale parameters of an assumed generalized gamma distribution for the control arm. A character string q="LLG" indiactes an assumed log-logistic survival distribution $F_0(y;\xi,\zeta) = 1/(1+(y/\xi)^{-\zeta})$ for the control arm, where ξ = mu and ζ = sigma.
`eta, theta`	parameters of the entry distribution with $\eta \geq -\theta/R$ and $\eta > 0$ ($\theta = 0$ for the uniform dropout censoring).

Value

the parameter h of the uniform dropout censoring distribution U(0,h).

Examples

```
Find.h(lfu=0.15, R=2, T=3, q=1, mu=0.367, sigma=1, eta=1, theta=0)
Find.h(lfu=0.15, R=2, T=3, q="LLG", mu=1, sigma=1.75, eta=1, theta=0)
```

General.tau	*Information fractions under a generalized gamma survival distribution or a log-logistic survival distribution.*

Description

A function calculates information fractions with a generalized gamma survival distribution or a log-logistic survival distribution for a given dropout censoring probability.

Usage

```
General.tau(t, R, T, FUN.C, q, mu, sigma, rho, eta, theta)
```

Arguments

`t`	the interim analysis time (vector).
`R`	the recuritment duration.
`T`	the study duration.
`FUN.C`	the cumulative distribution function of dropout censoring. FUN.C = function(y) punif(y,0,h) for a uniform dropout censoring U(0,h); FUN.C = function(y) rep(0,length(y)) for assuming no dropout censoring.
`q, mu, sigma`	shape, location and scale parameters of an assumed generalized gamma distribution for the control arm. A character string q="LLG" indiactes an assumed log-logistic survival distribution $F_0(y; \xi, \zeta) = 1/(1 + (y/\xi)^{-\zeta})$ for the control arm, where ξ = mu and ζ = sigma.
`rho`	the power in the weight of the Harrington-Fleming statistic. $\rho = 0$ for the logrank test; $\rho = 1$ for the Wilcoxon test.
`eta, theta`	parameters of the entry distribution with $\eta \geq -\theta/R$ and $\eta > 0$ ($\theta = 0$ for the uniform dropout censoring).

Value

`Info.fractions`	information fractions at times of all the interim analyses.
`Event.prob`	the probability of events accumulated up to T.
`Total.censor.prob`	the probability of censoring including the dropout and administrative censoring.

Examples

```
General.tau(t=c(1,1.5,2,2.5), R=2, T=3, FUN.C=function(y) punif(y,0,7.018),
         q=1, mu=0.367, sigma=1, rho=0, eta=1, theta=0)
General.tau(t=c(1,1.5,2,2.5), R=2, T=3, FUN.C=function(y) punif(y,0,7.211),
         q="LLG", mu=1, sigma=1.75, rho=0, eta=1, theta=0)
```

`SSize.FixAlter` *Maximum sample size for a group sequential test under a generalized gamma survival distribution or a log-logistic survival distribution.*

Description

A function obtains maximum sample sizes and associated expected values for a group sequential design under a generalized gamma survival distribution or a log-logistic survival distribution for a given dropout censoring distribution.

Usage

```
SSize.FixAlter(t, R, T, FUN.C, para0, para1 = NULL, haz.r, rho = 0,
  eta = 1, theta = 0, px = 0.5, spf = 1, alpha = 0.05, power = 0.8)
```

Arguments

`t`	the interim analysis time (vector).
`R`	the recuritment duration.
`T`	the study duration.
`FUN.C`	the cumulative distribution function of dropout censoring. FUN.C = function(y) punif(y,0,h) for a uniform dropout censoring U(0,h); FUN.C = function(y) rep(0,length(y)) for assuming no dropout censoring.
`para0`	c(q0,mu0,sigma0), parameters of an assumed generalized gamma distribution for the control arm. A character string q0="LLG" indiactes an assumed log-logistic survival distribution $F_0(y;\xi,\zeta) = 1/(1+(y/\xi)^{-\zeta})$ for the control arm, where ξ = mu0 and ζ = sigma0.
`para1`	c(q1,mu1,sigma1), parameters of an assumed generalized gamma distribution for the treatment arm. A character string q1="LLG" indiactes an assumed log-logistic survival distribution $F_1(y;\xi,\zeta) = 1/(1+(y/\xi)^{-\zeta})$ for the treatment arm, where ξ = mu1 and ζ = sigma1.
`haz.r`	the hazard ratio of the treatment arm to the control arm (numeric or function).
`rho`	the power in the weight of the Harrington-Fleming statistic. $\rho = 0$ for the logrank test; $\rho = 1$ for the Wilcoxon test.
`eta, theta`	parameters of the entry distribution with $\eta \geq -\theta/R$ and $\eta > 0$ ($\theta = 0$ for the Uniform dropout censoring).
`px`	the proportion of patients assigned to the treatment arm. The default is px = 0.5 indicating 1:1 allocation.
`spf`	1 = O'Brien-Fleming-type; 2 = Pocock-type alpha-spending function. The default is spf = 1.
`alpha`	the type I error. The default is alpha = 0.05.
`power`	A desired value of the power. The default is power = 0.8.

Value

`MaxSize`	the maximum sample size.
`ExpSize`	the expected sample size.
`ExpEvent`	the expected number of events.
`A.power`	actual achieved power.
`Info.fractions`	information fractions at times of all the interim analyses.
`boundary`	the monitoring boundary values of the standardized Harrington-Fleming statistic at all the interim analyses.

References

Hsu, C.-H., Chen, C.-H, Hsu, K.-N. and Lu, Y.-H. (2018). A useful design utilizing the information fraction in a group sequential clinical trial with censored survival data. To appear in Biometrics.

Azzalini, A. and Genz, A. (2015). The R package 'mnormt': The multivariate normal and 't' distributions (version 1.5-3). URL *http://azzalini.stat.unipd.it/SW/Pkg-mnormt*.

Casper, C. and Perez, O. A. (2014). The R package 'ldbounds': Lan-DeMets method for group sequential boundaries (version 1.1-1). URL *https://cran.r-project.org/web/packages/ldbounds/index.html*.

Jackson, C., Metcalfe, P. and Amdahl, J. (2017). The R package 'flexsurv': Flexible Parametric Survival and Multi-State Models (version 1.1). URL *https://github.com/chjackson/flexsurv-dev*.

Examples

```
# Assume an exponential (log-logistic) survival distribution
# with q0=sigma0=1, mu0=0.367 (xi0=1, zeta0=1.75) for the control arm,
# a uniform patient entry (eta=1,theta=0) and a uniform dropout censoring distribution Unif(0,h)
# having a 15% censoring probability (lfu=0.15) for a study with R=2, T=3 and the interim
# analysis time at t=1,1.5,2,2.5.

# To obtain the required h for the uniform dropout censoring distribution.
Find.h(lfu=0.15, R=2, T=3, q=1, mu=0.367, sigma=1, eta=1, theta=0) ## exponential
Find.h(lfu=0.15, R=2, T=3, q="LLG", mu=1, sigma=1.75, eta=1, theta=0) ## log-logistic

# To obtain the maximum sample size for testing a treatment difference of a hazard ratio of 2/3
# with a type-I error of 0.05 and a power of 0.8.
SSize.FixAlter(t=c(1,1.5,2,2.5), R=2, T=3, FUN.C=function(y) punif(y,0,7.018),
para0=c(1,0.367,1), para1=NULL, haz.r=2/3, rho=0, eta=1, theta=0) # exponential
SSize.FixAlter(t=c(1,1.5,2,2.5), R=2, T=3, FUN.C=function(y) punif(y,0,7.211),
para0=c("LLG",1,1.75), para1=NULL, haz.r=2/3, rho=0, eta=1, theta=0) # log-logistic

# To obtain the maximum sample size for testing H_0:F_0=F_1 with a type-I error of 0.05
# and a power of 0.8, where F_1 is an exponential (log-logistic) distribution
# with the parameter para1=c(1,0.772,1) (para1=c("LLG",1.5,1.75)).
SSize.FixAlter(t=c(1,1.5,2,2.5), R=2, T=3, FUN.C=function(y) punif(y,0,7.018),
para0=c(1,0.367,1), para1=c(1,0.772,1), haz.r=NULL, rho=0, eta=1, theta=0) # exponential
SSize.FixAlter(t=c(1,1.5,2,2.5), R=2, T=3, FUN.C=function(y) punif(y,0,7.211),
para0=c("LLG",1,1.75), para1=c("LLG",1.5,1.75), haz.r=NULL, rho=0, eta=1, theta=0) # log-logistic
```

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