Package 'NPHMC'

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Title Sample Size Calculation for the Proportional Hazards Mixture Cure Model

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NPHMC-package *An R-package for Estimating Sample Size of Proportional Hazards Mixture Cure Model*

Description

Estimating sample size for survival trial with or without cure fractions

Details

Package:	NPHMC
Type:	Package
Version:	2.2
Date:	2013-09-23
License:	GPL-2
LazyLoad:	yes

Author(s)

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References

S. Wang, J. Zhang, and W. Lu. Sample size calculation for the proportional hazards cure model. Statistics in medicine, 31:3959-3971, 2012

C. Cai, et al., smcure: An R-Package for estimating semiparametric mixture cure models. Computer Methods and Programs in Biomedicine, 108(3):1255-60, 2012

See Also

smcure

e1684szdata *Eastern Cooperative Oncology Group (ECOG) Data*

Description

Example data of nonparametric estimation approach with treatment as only covariate

Usage

```
data(e1684szdata)
```

Format

A data frame with 285 observations on the following 3 variables:

`Time` observed relapse-free time

`Status` censoring indicator (1 = event of interest happens, and 0 = censoring)

`X` arm indicator (1 = treatment and 0 = control)

Examples

```
data(e1684szdata)
```

---

f1 *Function One*

Description

The first integrate function

Usage

```
f1(t, survdist, k, lambda0)
```

Arguments

`t`	time variable
`survdist`	survival distribution of uncured patients. It can be "`exp`" or "`weib`".
`k`	if `survdist` = "`weib`", the shape parameter `k` needs to be specified. By default `k` = 1, which refers to the exponential distribution.
`lambda0`	the scale parameter of exponential distribution or Weibull distribution for survival times of uncured patients in the control arm. The density function of Weibull distribution with shape parameter `k` and scale parameter λ_0 is given by $$f(t) = \lambda_0 k(\lambda_0 t)^{k-1} \exp(-(\lambda_0 t)^k),$$ for $t > 0$, and the corresponding survival distribution is $$S(t) = \exp(-(\lambda_0 t)^k).$$

f2 *Function Two*

Description

The second integrate function

Usage

```
f2(t, accrualtime, followuptime, accrualdist, survdist, k, lambda0)
```

Arguments

t	time variable
accrualtime	length of accrual period.
followuptime	length of follow-up time.
accrualdist	accrual pattern. It can be "uniform", "increasing" or "decreasing".
survdist	survival distribution of uncured patients. It can be "exp" or "weib".
k	if survdist = "weib", the shape parameter k needs to be specified. By default k = 1, which refers to the exponential distribution.
lambda0	the scale parameter of exponential distribution or Weibull distribution for survival times of uncured patients in the control arm. The density function of Weibull distribution with shape parameter k and scale parameter λ_0 is given by $$f(t) = \lambda_0 k(\lambda_0 t)^{k-1} \exp(-(\lambda_0 t)^k),$$ for $t > 0$, and the corresponding survival distribution is $$S(t) = \exp(-(\lambda_0 t)^k).$$

f3 *Function Three*

Description

The third integrate function

Usage

```
f3(t, beta0, gamma0, pi0, survdist, k, lambda0)
```

Arguments

t	time variable
beta0	log hazard ratio of uncured patients
gamma0	log odds ratio of cure rates between two arms
pi0	cure rate for the control arm, which is between 0 and 1.
survdist	survival distribution of uncured patients. It can be "exp" or "weib".
k	if survdist = "weib", the shape parameter k needs to be specified. By default k = 1, which refers to the exponential distribution.
lambda0	the scale parameter of exponential distribution or Weibull distribution for survival times of uncured patients in the control arm. The density function of Weibull distribution with shape parameter k and scale parameter λ_0 is given by $$f(t) = \lambda_0 k(\lambda_0 t)^{k-1} \exp(-(\lambda_0 t)^k),$$ for $t > 0$, and the corresponding survival distribution is $$S(t) = \exp(-(\lambda_0 t)^k).$$

---

f4 *Function Four*

Description

The fourth integrate function

Usage

```
f4(t, accrualtime, followuptime, accrualdist, beta0, gamma0, pi0, survdist,
 k, lambda0)
```

Arguments

t	time variable
accrualtime	length of accrual period.
followuptime	length of follow-up time.
accrualdist	accrual pattern. It can be "uniform", "increasing" or "decreasing".
beta0	log hazard ratio of uncured patients
gamma0	log odds ratio of cure rates between the two arms
pi0	cure rate for the control arm, which is between 0 and 1.
survdist	survival distribution of uncured patients. It can be "exp" or "weib".
k	if survdist = "weib", the shape parameter k needs to be specified. By default k = 1, which refers to the exponential distribution.

`lambda0` the scale parameter of exponential distribution or Weibull distribution for survival times of uncured patients in the control arm.

The density function of Weibull distribution with shape parameter `k` and scale parameter λ_0 is given by

$$f(t) = \lambda_0 k(\lambda_0 t)^{k-1} \exp(-(\lambda_0 t)^k),$$

for $t > 0$, and the corresponding survival distribution is

$$S(t) = \exp(-(\lambda_0 t)^k).$$

`H0` *Cumulative hazard function*

Description

Cumulative Hazard Function for Exponential and Weibull Distributions

Usage

```
H0(t, survdist, k, lambda0)
```

Arguments

`t`	time variable
`survdist`	survival distribution of uncured patients. It can be "`exp`" or "`weib`".
`k`	if `survdist` = "`weib`", the shape parameter `k` needs to be specified. By default `k` = 1, which refers to the exponential distribution.
`lambda0`	the scale parameter of exponential distribution or Weibull distribution for survival times of uncured patients in the control arm.

The density function of Weibull distribution with shape parameter `k` and scale parameter λ_0 is given by

$$f(t) = \lambda_0 k(\lambda_0 t)^{k-1} \exp(-(\lambda_0 t)^k),$$

for $t > 0$, and the corresponding survival distribution is

$$S(t) = \exp(-(\lambda_0 t)^k).$$

m *M Function*

Description

M integrate function

Usage

```
m(t, beta0, gamma0, pi0, survdist, k, lambda0)
```

Arguments

t	time variable
beta0	log hazard ratio of uncured patients
gamma0	log odds ratio of cure rates between two arms
pi0	cure rate for the control arm, which is between 0 and 1.
survdist	survival distribution of uncured patients. It can be "exp" or "weib".
k	if survdist = "weib", the shape parameter k needs to be specified. By default k = 1, which refers to the exponential distribution.
lambda0	the scale parameter of exponential distribution or Weibull distribution for survival times of uncured patients in the control arm. The density function of Weibull distribution with shape parameter k and scale parameter λ_0 is given by $$f(t) = \lambda_0 k(\lambda_0 t)^{k-1} \exp(-(\lambda_0 t)^k),$$ for $t > 0$, and the corresponding survival distribution is $$S(t) = \exp(-(\lambda_0 t)^k).$$

NPHMC *An R-package for Estimating Sample Size and Power of Proportional Hazards Mixture Cure Model*

Description

Estimating sample size and power of survival trial based on PH mixture cure model and standard PH model

Usage

```
NPHMC(n=NULL, power = 0.8, alpha = 0.05, accrualtime = NULL,
followuptime = NULL, p = 0.5, accrualdist = c("uniform", "increasing",
"decreasing"), hazardratio = NULL, oddsratio = NULL, pi0 = NULL,
survdist = c("exp", "weib"), k = 1, lambda0 = NULL, data = NULL)
```

Arguments

n	the sample size needed for the power calculation.
power	the power needed for sample size calculation. The default power is 80%.
alpha	the level of significance of the statistical test. The default alpha is 0.05.
accrualtime	the length of accrual period.
followuptime	the length of follow-up time.
p	the proportion of subjects in the treatment arm. The default p is 0.5.
accrualdist	the accrual pattern. It can be "uniform", "increasing" or "decreasing".
hazardratio	the hazard ratio of uncured patients between two arms, which is defined as $e^{\beta_0} = \lambda_1(t)/\lambda_0(t)$. The value must be greater than 0 but cannot be 1 because β_0 is the denominator of the sample size formula.
oddsratio	the odds ratio of cure rates between two arms, which is equivalent to $e^{\gamma_0} = \frac{\pi_1}{1-\pi_1}/\frac{\pi_0}{1-\pi_0}$. The value should be greater than 0 if there is cured fraction. When it is 0, the model is reduced to the standard proportional hazards model, which means there is no cure rate.
pi0	the cure rate for the control arm, which is between 0 and 1.
survdist	the survival distribution of uncured patients. It can be "exp" or "weib".
k	if survdist = "weib", the shape parameter k needs to be specified. By default k = 1, which refers to the exponential distribution.
lambda0	the scale parameter of exponential distribution or Weibull distribution for survival times of uncured patients in the control arm. The density function of Weibull distribution with shape parameter k and scale parameter λ_0 is given by $$f(t) = \lambda_0 k(\lambda_0 t)^{k-1}\exp(-(\lambda_0 t)^k),$$ for $t > 0$, and the corresponding survival distribution is $$S(t) = \exp(-(\lambda_0 t)^k).$$
data	if observed/historical data is avaialble, the sample size can be calculated based on the nonparametric estimators from the proportional hazards mixture model by 'smcure' package in R. The data must contain three columns with order of "Time","Status" and "X" where "Time" refers to time to event of interest, "Status" refers to censoring indicator (1=event of interest happens, and 0=censoring) and "X" refers to arm indicator (1=treatment and 0=control). By default, data=NULL.

Value

when data is not specified, the package can return the following estimated sample size (power) values:

nsize	estimated sample size based on the PH mixture cure model
nsizeph	estimated sample size based on the standard PH model

pw	estimated power based on the PH mixture cure model
pwph	estimated power based on the standard PH model

when data is specified, the package will display the estimators from the "smcure" package in R and the returned values list as follows:

f	a list of estimators from the smcure package
nonpar	estimated nonparametric sample size estimation based on the PH mixture cure model and observed data
nonparPH	estimated nonparametric sample size estimation based on the standard PH model and observed data
nonparpw	estimated nonparametric power estimation based on the PH mixture cure model and observed data
nonparpwph	estimated nonparametric power estimation based on the standard PH model and observed data

Examples

```
# parametric sample size calculation
NPHMC(power=0.90,alpha=0.05,accrualtime=3,followuptime=4,p=0.5,accrualdist="uniform",
hazardratio=2/2.5,oddsratio=2.25,pi0=0.1,survdist="exp",k=1,lambda0=0.5)

# nonparametric sample size calculation
data(e1684szdata)
NPHMC(power=0.80,alpha=0.05,accrualtime=4,followuptime=3,p=0.5,accrualdist="uniform",
data=e1684szdata)

# parametric power calculation
n=seq(100, 500, by=50)
NPHMC(n=n, alpha=0.05,accrualtime=3,followuptime=4,p=0.5,
accrualdist="uniform", hazardratio=2/2.5,oddsratio=2.25,pi0=0.1,survdist="exp",
k=1,lambda0=0.5)

# nonparametric power calculation
n=seq(100, 500, by=50)
NPHMC(n=n,alpha=0.05,accrualtime=4,followuptime=3,p=0.5,
accrualdist="uniform",data=e1684szdata)
```

S0 *S0 Function*

Description

Baseline survival function for mixture cure model

Usage

```
S0(t, pi0, survdist, k, lambda0)
```

Arguments

t	time variable
pi0	cure rate for the control arm, which is between 0 and 1.
survdist	survival distribution of uncured patients. It can be "exp" or "weib".
k	if survdist = "weib", the shape parameter k needs to be specified. By default k = 1, which refers to the exponential distribution.
lambda0	scale parameter of exponential distribution or Weibull distribution for survival times of uncured patients in the control arm. The density function of Weibull distribution with shape parameter k and scale parameter λ_0 is given by $$f(t) = \lambda_0 k(\lambda_0 t)^{k-1} \exp(-(\lambda_0 t)^k),$$ for $t > 0$, and the corresponding survival distribution is $$S(t) = \exp(-(\lambda_0 t)^k).$$

Sc *Sc Function*

Description

Survival distribution of censoring times

Usage

```
Sc(t, accrualtime, followuptime, accrualdist)
```

Arguments

t	time variable
accrualtime	length of accrual period.
followuptime	length of follow-up time.
accrualdist	accrual pattern. It can be "uniform", "increasing" or "decreasing".

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