Package ‘PBIR’

October 12, 2022

Type Package

Title Estimating the Probability of Being in Response and Related Outcomes

Version 0.1-0

Author Xiaodong Luo [aut], Bo Huang [aut], Lu Tian [aut, cre](<https://orcid.org/0000-0002-5893-0169>)

Maintainer Lu Tian <lutian@stanford.edu>

Description Make statistical inference on the probability of being in response, the duration of response, and the cumulative response rate up to a given time point. The method can be applied to analyze phase II randomized clinical trials with the endpoints being time to treatment response and time to progression or death.

License GPL (>= 2)

Imports survival, stats, cmprsk

Encoding UTF-8

LazyData true

VignetteBuilder knitr

Suggests knitr, rmarkdown

Repository CRAN

RoxygenNote 7.1.0

NeedsCompilation no

Date/Publication 2020-09-17 09:10:12 UTC

R topics documented:

CRR ................................................................. 2
mduration ....................................................... 4
PBIR1 .............................................................. 5
PBIR2 .............................................................. 7

Index 10
CRR

Estimate cumulative response rates (CRR) and test their equality between two groups

Description

Estimate cumulative response rates (CRR) and test their equality between two groups

Usage

```r
CRR(
    t2PROGRESSION,
    STATUS_PROGRESSION,
    t2RESPONSE,
    STATUS_RESPONSE,
    TRT,
    time = NULL,
    alpha = 0.95
)
```

Arguments

t2PROGRESSION: time to progression/death or censoring

STATUS_PROGRESSION: binary indicator for progression status: 1 for progression/death; 0 for censoring

t2RESPONSE: time to response or censoring

STATUS_RESPONSE: binary indicator for response status: 1 for response; 0 for censoring

TRT: binary indicator for treatment assignment: 1 for treatment arm and 0 for control arm

time: user-selected time points at which the cumulative response rate is to be estimated; the default value is "NULL" and the cumulative response rate will be estimated at all observed time points

alpha: coverage level of the point-wise confidence interval for the cumulative response rate; the default value is 0.95

Value

A list with following elements

- result0: a data matrix containing "time", "CRR estimates (group 0)"; "standard error of CRR estimates (group 0)"; "confidence interval of CRR (group 0)"
- result1: a data matrix containing "time", "CRR estimates (group 1)"; "standard error of CRR estimates (group 1)"; "confidence interval of CRR (group 1)"
- pvalue: the p-value from two group comparison
References


Examples

library(cmprsk)
n=100
set.seed(10)

# Generate the data
trt=rbinom(n, 1, 0.5)
error=rnorm(n)
tr=exp(rnorm(n)+error-trt*0.5+0.5)
tp=exp(rnorm(n)+error+trt*0.25)
tr[tr<tr]=Inf
tc=runif(n, 3, 8.5)
t2response=pmin(tr, tc)
delta_response=1*(tr<tc)
t2progression=pmin(tp, tc)
delta_progression=1*(tp<tc)

# Estimate the PBIR in two groups
fit=CRR(t2PROGRESSION=t2progression,
STATUS_PROGRESSION=delta_progression,
t2RESPONSE=t2response,
STATUS_RESPONSE=delta_response,
TRT=trt)

fit

# Plot the estimated PBIR by group

tt1=c(0, fit$result1$time)
CRR1=c(0, fit$result1$CRR)
B1=length(tt1)
tt1=rep(tt1, rep(2, B1))[-1]
CRR1=rep(CRR1, rep(2, B1))[-(2*B1)]
tt0=c(0, fit$result0$time)
CRR0=c(0, fit$result0$CRR)
B0=length(tt0)
tt0=rep(tt0, rep(2, B0))[-1]
CRR0=rep(CRR0, rep(2, B0))[-(2*B0)]
plot(range(c(fit$result1$time, fit$result0$time)),
range(c(fit$result1$CRR, fit$result0$CRR)),
xlab="time", ylab="CRR",
...
**Description**

Estimate mean duration of response

**Usage**

```r
duration(
  t2PROGRESSION,
  STATUS_PROGRESSION,
  t2RESPONSE,
  STATUS_RESPONSE,
  time.max = -1
)
```

**Arguments**

- `t2PROGRESSION`: time to progression/death or censoring
- `STATUS_PROGRESSION`: binary indicator for progression/death status: 1 for progression/death; 0 for censoring
- `t2RESPONSE`: time to response or censoring
- `STATUS_RESPONSE`: binary indicator for response status: 1 for response; 0 for censoring
- `time.max`: maximum time point, up to which the mean DOR is to be estimated; the default value corresponds to the maximum time window in which the mean DOR is estimable

**Details**

The mean duration of response restricted within a time window is also the area under the PBIR curve over the same time window. The estimated mean duration can be viewed as a global summary of the PBIR curve. One may compare the mean duration of response between two groups, which is also a global comparison between two PBIR curves.

**Value**

A list with following elements

- `meandor.est`: the restricted mean DOR estimate
- `meandor.se`: the standard error of the estimated DOR
- `time.truncation`: the truncation time point used in DOR.
References

Examples

library(survival)
n=100
set.seed(10)

# Generate the data
error=rnorm(n)
tr=exp(rnorm(n)+error+0.5)
kp=exp(rnorm(n)+error)
tr[tp<tr]=Inf
tc=runif(n, 3, 8.5)
t2response=pmin(tr, tc)
delta_response=1*(tr<tc)
t2progression=pmin(tp, tc)
delta_progression=1*(tp<tc)

# Estimate the mean duration of response (point estimator and its standard error)
fit=mduration(t2PROGRESSION=t2progression,
STATUS_PROGRESSION=delta_progression,
t2RESPONSE=t2response,
STATUS_RESPONSE=delta_response,
time.max=8)
fit

PBIR1

Estimate the PBIR curve over a time window

Description
Estimate the PBIR curve over a time window

Usage

PBIR1(  
t2PROGRESSION,  
STATUS_PROGRESSION,
t2RESPONSE,
STATUS_RESPONSE,
time = NULL,
alpha = 0.95
)

Arguments

t2PROGRESSION time to progression/death or censoring
STATUS_PROGRESSION binary indicator for progression status: 1 for progression/death; 0 for censoring
t2RESPONSE time to response or censoring
STATUS_RESPONSE binary indicator for response status: 1 for response; 0 for censoring
time user-selected time points at which the PBIR is estimated; the default value is "NULL" and the PBIR will be estimated at all observed time points
alpha coverage level of the point-wise confidence interval for PBIR curve; the default value is 0.95

Value

da data matrix containing "time", "PBIR estimates", "standard errors of PBIR estimates", "confidence intervals of the PBIR"

References


Examples

library(survival)
n=100
set.seed(10)

# Generate the data
trt=rbinom(n, 1, 0.5)
error=rnorm(n)
tr=exp(rnorm(n)+error-trt*0.5+0.5)
trn=exp(rnorm(n)+error+trt*0.25)
tr[trn<tr]=Inf

#time=runif(n, 3, 8.5)
t2response=pmin(tr, tc)
PBIR2

Estimate and compare PBIR curves from two groups over a time window

Description

Estimate and compare PBIR curves from two groups over a time window

Usage

PBIR2(
  t2PROGRESSION,
  STATUS_PROGRESSION,
  t2RESPONSE,
  STATUS_RESPONSE,
)
TRT,
  time = NULL,
  alpha = 0.95
)

Arguments

t2PROGRESSION time to progression/death or censoring
STATUS_PROGRESSION binary indicator for progression status: 1 for progression/death; 0 for censoring
t2RESPONSE time to response or censoring
STATUS_RESPONSE binary indicator for response status: 1 for response; 0 for censoring
TRT treatment indicator: 1 for treatment arm; 0 for control arm
time user-selected time points at which PBIRs are to be compared; the default value is "NULL" and PBIRs at all observed time points are compared
alpha coverage level of the point-wise confidence interval for the difference in the PBIR, the default value is 0.95

Value

a data matrix containing "time", "estimated differences in PBIR (treatment-control)", "standard errors of estimated PBIR differences", "confidence intervals of the PBIR difference"

References


Examples

library(survival)
n=100
set.seed(10)

# Generate the data
TRT=trt=rbinom(n, 1, 0.5)
error=rnorm(n)
tr=exp(rnorm(n)+error-trt*0.5+0.5)
tr[tr<tc]=Inf
tc=runif(n, 3, 8.5)
PBIR2

\[ t_2\text{response} = \text{pmin}(tr, tc) \]
\[ \text{delta.response} = 1 \times (tr < tc) \]
\[ t_2\text{progression} = \text{pmin}(tp, tc) \]
\[ \text{delta.progression} = 1 \times (tp < tc) \]

# Estimate the difference in PBIR
# the analysis is truncated at time 8, which is slightly smaller than the largest follow-up time

\[
\text{fit} = \text{PBIR2}(t_2\text{PROGRESSION} = t_2\text{progression},
\text{STATUS_PROGRESSION} = \text{delta.progression},
\text{t2RESPONSE} = t_2\text{response},
\text{STATUS_RESPONSE} = \text{delta.response},
\text{TRT} = \text{trt})
\]

# Plot the estimated difference in PBIR

\[
\text{tt} = \text{fit}$\text{time}
\]
\[
\text{diff} = \text{fit}$\text{diff}
\]
\[
\text{low} = \text{fit}$\text{ci.low}
\]
\[
\text{up} = \text{fit}$\text{ci.up}
\]

\[
\text{tt} = \text{c}(0, \text{tt})
\]
\[
\text{diff} = \text{c}(0, \text{diff})
\]
\[
\text{low} = \text{c}(0, \text{low})
\]
\[
\text{up} = \text{c}(0, \text{up})
\]
\[
B = \text{length(tt)}
\]

\[
\text{tt} = \text{rep}(\text{tt}, \text{rep}(2, B))[-1]
\]
\[
\text{diff} = \text{rep}(\text{diff}, \text{rep}(2, B))[-(2 \times B)]
\]
\[
\text{low} = \text{rep}(\text{low}, \text{rep}(2, B))[-(2 \times B)]
\]
\[
\text{up} = \text{rep}(\text{up}, \text{rep}(2, B))[-(2 \times B)]
\]

\[
\text{plot}(\text{range(c(\text{fit}$\text{time}, 0))}, \text{range(c(\text{low}, \text{up}))},
\text{xlab} = "\text{time}" , \text{ylab} = "\text{difference in PBIR},
\text{lwd} = 2, \text{type} = "n"
\text{lines}(\text{tt}, \text{diff}, \text{lwd} = 2, \text{col} = 3)
\text{lines}(\text{tt}, \text{low}, \text{col} = 2)
\text{lines}(\text{tt}, \text{up}, \text{col} = 2)
\text{lines}(\text{range(\text{fit}$\text{time}), \text{rep}(0, 2)) , \text{col} = 4, \text{lt} = 4)\]
Index

CRR, 2
mduration, 4
PBIR1, 5
PBIR2, 7