Package ‘PBIR’

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Type Package
Title Estimating the Probability of Being in Response and Related Outcomes
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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.
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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

```r
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)
tr[tr<0]=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)

CRR1=rep(CRR1, rep(2, B1))[-1]
tt0=c(0, fit$result0$time)
CRR0=c(0, fit$result0$CRR)
B0=length(tt0)

plot(range(c(fit$result1$time, fit$result0$time)),
     range(c(fit$result1$CRR, fit$result0$CRR)),
     xlab="time", ylab="CRR",
     # Add more plot arguments if needed
```

mduration

main="black: group 0; red: group 1", type="n")
lines(tt0, CRR0, col=1)
lines(tt1, CRR1, col=2)

---

duration

Estimate mean duration of response

Description

Estimate mean duration of response

Usage

mduration(
  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

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

# Generate the data
error=rnorm(n)
tr=exp(rnorm(n)+error+0.5)
 tp=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**

```r
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

a 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)
tp=exp(rnorm(n)+error+trt*0.25)
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 PBIR in two groups

fit1=PBIR1(t2PROGRESSION=t2progression[trt==1],
            STATUS_PROGRESSION=delta_progression[trt==1],
            t2RESPONSE=t2response[trt==1],
            STATUS_RESPONSE=delta_response[trt==1])

fit0=PBIR1(t2PROGRESSION=t2progression[trt==0],
            STATUS_PROGRESSION=delta_progression[trt==0],
            t2RESPONSE=t2response[trt==0],
            STATUS_RESPONSE=delta_response[trt==0])

# Plot the estimated PBIR by group

tt1=c(0, fit1$time)
PBI1=c(0, fit1$PBIR)
B1=length(tt1)

b1=rep(tt1, rep(2, B1))[-1]
PBI1=rep(PBI1, rep(2, B1))[-(2*B1)]

b0=rep(tt0, rep(2, B0))[-1]
PBI0=rep(PBI0, rep(2, B0))[-(2*B0)]

plot(range(c(fit1$time, fit0$time)), range(c(fit1$PBIR, fit0$PBIR)),
     xlab="time", ylab="PBIR",
     main="black: group 0; red: group 1", type="n")
lines(tt0, PBI0, col=1)
lines(tt1, PBI1, col=2)

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)
t2response=pmin(tr, tc)
delta_response=1*(tr<tc)
t2progression=pmin(tp, tc)
delta_progression=1*(tp<tc)

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

fit=PBIR2(t2PROGRESSION=t2progression,
STATUS_PROGRESSION=delta_progression,
t2RESPONSE=t2response,
STATUS_RESPONSE=delta_response,
TRT=trt)

# Plot the estimated difference in PBIR

tt=fit$time
diff=fit$diff
low=fit$ci.low
up=fit$ci.up

tt=c(0, tt)
diff=c(0, diff)
low=c(0, low)
up=c(0, up)
B=length(tt)

tt=rep(tt, rep(2, B))[-1]
diff=rep(diff, rep(2, B))[-(2*B)]
low=rep(low, rep(2, B))[-(2*B)]
up=rep(up, rep(2, B))[-(2*B)]

plot(range(c(fit$time, 0)), range(c(low, up)),
xlab="time", ylab="difference in PBIR",
  lwd=2, type="n")
lines(tt, diff, lwd=2, col=3)
lines(tt, low, col=2)
lines(tt, up, col=2)
lines(range(fit$time), rep(0, 2), col=4, lty=4)
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