Package 'PBIR'

January 20, 2025

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

Contents

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

```
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

Gray, RJ. (1988) A class of K-sample tests for comparing the cumulative incidence of a competing risk, ANNALS OF STATISTICS, 16:1141-1154.

Aalen, O. (1978) Nonparametric estimation of partial transition probabilities in multiple decrement models, ANNALS OF STATISTICS, 6:534-545.

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[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

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",
     main="black: group 0; red: group 1", type="n")
```

```
lines(tt0, CRR0, col=1)
lines(tt1, CRR1, col=2)
```

`mduration` *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 esimated DOR
- time.truncation: the truncation time point used in DOR.

References

Huang, B., Tian, L., Talukder, E., Rothenberg, M., Kim, DY., and Wei, LJ. (2018) Evaluating Treatment Effect Based on Duration of Response for a Comparative Oncology Study. JAMA Oncol, doi: 10.1001/jamaoncol.2018.0275

Huang, B., Tian, L., McCaw, Z., Luo, Talukder, E., X., Rothenberg, M., Xie, W., Choueiri, T., Kim, DY., & Wei, LJ. (2020). Analysis of Response Data for Assessing Treatment Effects in Comparative Clinical Studies. Ann Intern Med, doi: 10.7326/M20-0104.

Examples

```
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

```
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

Huang, B., Tian, L., Talukder, E., Rothenberg, M., Kim, DY., and Wei, LJ. (2018) Evaluating Treatment Effect Based on Duration of Response for a Comparative Oncology Study. JAMA Oncol, doi: 10.1001/jamaoncol.2018.0275

Huang, B., Tian, L., McCaw, Z., Luo, Talukder, E., X., Rothenberg, M., Xie, W., Choueiri, T., Kim, DY., & Wei, LJ. (2020). Analysis of Response Data for Assessing Treatment Effects in Comparative Clinical Studies. Ann Intern Med, doi: 10.7326/M20-0104.

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$time)
PBIR1=c(0, fit1$PBIR)
B1=length(tt1)
tt1=rep(tt1, rep(2, B1))[-1]
PBIR1=rep(PBIR1, rep(2, B1))[-(2*B1)]
tt0=c(0, fit0$time)
PBIR0=c(0, fit0$PBIR)
B0=length(tt0)
tt0=rep(tt0, rep(2, B0))[-1]
PBIR0=rep(PBIR0, 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, PBIR0, col=1)
lines(tt1, PBIR1, 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

Huang, B., Tian, L., Talukder, E., Rothenberg, M., Kim, DY., and Wei, LJ. (2018) Evaluating Treatment Effect Based on Duration of Response for a Comparative Oncology Study. JAMA Oncol, doi: 10.1001/jamaoncol.2018.0275

Huang, B., Tian, L., McCaw, Z., Luo, Talukder, E., X., Rothenberg, M., Xie, W., Choueiri, T., Kim, DY., & Wei, LJ. (2020). Analysis of Response Data for Assessing Treatment Effects in Comparative Clinical Studies. Ann Intern Med, doi: 10.7326/M20-0104.

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)
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 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 differnece 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)
```

Index