

# Package: PBIR (via r-universe)

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**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

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## Contents

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

<b>Index</b>	<b>10</b>
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CRR	<i>Estimate cumulative response rates (CRR) and test their equality between two groups</i>
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### 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)
```

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mduration	<i>Estimate mean duration of response</i>
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### 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

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=rnorm(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*


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### 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 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)

```

# Index

CRR, [2](#)

mduration, [4](#)

PBIR1, [5](#)

PBIR2, [7](#)