Package ‘ClinicalTrialSummary’

January 18, 2019

Type Package
Title Summary Measures for Clinical Trials with Survival Outcomes
Version 1.1.1
Author Daewoo Pak and Song Yang
Maintainer Daewoo Pak <heavyrain.pak@gmail.com>
Description Provides estimates of several summary measures for clinical trials including
the average hazard ratio, the weighted average hazard ratio, the restricted
superiority probability ratio, the restricted mean survival difference and
the ratio of restricted mean times lost, based on the short-term and
long-term hazard ratio model (Yang, 2005 <doi:10.1093/biomet/92.1.1>)
which accommodates various non-proportional hazards scenarios. The inference
procedures and the asymptotic results for the summary measures are discussed
License GPL (>= 3)
Encoding UTF-8
LazyData true
RoxygenNote 6.1.1
Imports Rcpp
LinkingTo Rcpp
NeedsCompilation yes
Repository CRAN
Date/Publication 2019-01-18 21:40:04 UTC

R topics documented:

ClinicalTrialSummary-package ........................................... 2
ClinicalTrialSummary-internal ........................................... 3
ggas ................................................................. 3
ypsummary ............................................................ 4

Index 7
ClinicalTrialSummary-package

Summary Measures for Clinical Trials with Survival Outcomes

Description

ClinicalTrialSummary provides estimates of several summary measures of the treatment effect for design and analysis of clinical trials with survival outcomes, introduced in Yang (2018). These estimates are obtained under the short-term and long-term hazard ratio model (Yang and Prentice, 2005) which allows a range of time-varying hazard ratio shapes including crossing hazards situations.

Let $hr(x) = \lambda_t(x)/\lambda_c(x)$ be the hazard ratio function, where $\lambda_t(x)$ and $\lambda_c(x)$ are the hazard functions for the treatment group and the control group, respectively. The main function of the package, `ypsummary`, provides following five summary measures:

- the average hazard ratio (AHR): $\int hr(x)dx$
- the weighted average hazard ratio (WAHR): $\int hr(x)dw(x)$ where $dw(x) = dF_c(x)/F_c(\tau)$
- the restricted superiority probability ratio (RSPR): $\frac{\int S_c(x)dF_t(x)}{\int S_t(x)dF_c(x)}$
- the restricted mean survival difference (RMSD): $\int S_t(x)dx - \int S_c(x)dx$
- the ratio of restricted mean times lost (RRMTL): $\frac{\tau - \int S_t(x)dx}{\tau - \int S_c(x)dx}$

Note that all integrals are taken over $(0, \tau)$ for $\tau$ less than or equal to the maximum follow-up duration of the trial. The asymptotic results for the average hazard ratio and the restricted mean survival difference were established in Yang and Prentice (2011) and Yang (2013), respectively. For other measures, the asymptotic results were established in Yang (2018).

The data used as an example in this package was from Gastrointestinal Tumor Study Group (1982) and the object returned by `ypsummary` can be formatted to a table using the function `summary`.

Details

<table>
<thead>
<tr>
<th>Package</th>
<th>ClinicalTrialSummary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Package</td>
</tr>
<tr>
<td>Version</td>
<td>1.0.0</td>
</tr>
<tr>
<td>Date</td>
<td>2018-12-19</td>
</tr>
<tr>
<td>License</td>
<td>GPL (&gt;= 3)</td>
</tr>
</tbody>
</table>

Author(s)

Daewoo Pak and Song Yang
References


See Also

ypsummary

Examples

library(ClinicalTrialSummary)
data(ggas)
result <- ypsummertime=ggas$time, event=ggas$event, group=ggas$group, tau = 8.2)
print(result)
summary(result)
ypsummary

Usage

data(ggas)

Format

The data has the following information for the ninety subjects:

time the vector for the pooled lifetimes of the two groups
event the numeric vector of the right-censoring indicator (event = 1, censored = 0)
group the numeric vector of the group indicator (treatment = 1, control = 0)

References


See Also

ypsummary

Examples

library(ClinicalTrialSummary)
data(ggas)

ypsummary

The main function of the package provides five summary measures of the treatment effect for clinical trials.

Description

ypsummary provides estimates of several summary measures of the treatment effect for design and analysis of clinical trials with survival outcomes, introduced in Yang (2018). The function utilizes the short-term and long-term hazard ratio model proposed in Yang and Prentice (2005), which can accommodate various nonproportional hazard scenarios. The asymptotic properties of the summary measures are also discussed in Yang and Prentice (2011), Yang (2013), and Yang (2018).

Usage

## Default S3 method:
ypsummary(time, event, group, tau, alpha = 0.05, tie = TRUE,
    bound = 50, repnum = 2000, ...)
Arguments

... for S4 method only.

time
A numeric vector of observations pooled from the two groups

event
A numeric vector of the right-censoring indicator (event = 1, censored = 0)

group
A numeric vector of the group indicator (treatment = 1, control = 0)

tau
the upper end of the range used in defining the summary measures. Must be user-specified.

alpha
Significance level. The default value is 0.05.

tie
The default is TRUE. Add very tiny values to the observations when sorting them to avoid ties.

bound
A boundary (~bound, bound) for estimating the parameters in the short-term and long-term hazard ratio model (Yang and Prentice, 2005). These parameters are \( \beta_1 \) and \( \beta_2 \) in their notations. The default boundary is \((-50, 50)\).

replnum
the number of replications for the resampling method in obtaining the limiting variance estimators of the measures. The default value is 2000.

Details

The function `ypsummary` provides five summary measures of the treatment effect (see, Yang 2018), which can be utilized for various nonproportional haards scenarios:

- the average hazard ratio (AHR): \( \int hr(x)dx \)
- the weighted average hazard ratio (WAHR): \( \int hr(x)dw(x) \) where \( dw(x) = dF_c(x)/F_c(\tau) \)
- the restricted superiority probability ratio (RSPR): \( \int Sc(x)dF_t(x) / \int St(x)dF_t(x) \)
- the restricted mean survival difference (RMSD): \( \int St(x)dx - \int Sc(x)dx \)
- the ratio of restricted mean times lost (RRMTL): \( \frac{\tau - \int St(x)dx}{\tau - \int Sc(x)dx} \)

where \( hr(x) \) is the hazard ratio of the treatment group over the control group, \( F_t(x) \) and \( F_c(x) \) are the distribution functions for the treatment group and control group, respectively, and \( S_t(x) = 1 - F_t(x) \) and \( S_c(x) = 1 - F_c(x) \). Note that all integrals are taken from 0 to \( \tau \).

Value

| Estimate | The point estimate for the corresponding summary measure |
| CI | The confidence interval constructed by a re-sampling method. If the measure is a ratio, the z-value is the standardized log of the estimate. If the measure is a difference, the z-value is the standardized estimate. |
| z-value | Normally distributed value derived from the asymptotic results |
| p-value | the (two-sided) p-value using z-value |
References


Examples

```r
library(ClinicalTrialSummary)
data(ggas)
time <- ggas$time
event <- ggas$event
group <- ggas$group
result <- ypsummary(time, event, group, tau=8.2) # tau must be supplied.
result
summary(result)
```
Index

*Topic **Data**
  ggas, 3

*Topic **Survival analysis, Clinical trials, Hazard ratio, Yang and Prentice model**
  ClinicalTrialSummary-package, 2

ClinicalTrialSummary-internal, 3
ClinicalTrialSummary-package, 2

fun_ahrf
  (ClinicalTrialSummary-internal), 3
fun_ahrypt
  (ClinicalTrialSummary-internal), 3
fun_ahryptwo
  (ClinicalTrialSummary-internal), 3
fun_digit
  (ClinicalTrialSummary-internal), 3
fun_estimate
  (ClinicalTrialSummary-internal), 3
fun_less
  (ClinicalTrialSummary-internal), 3
fun_mdypt
  (ClinicalTrialSummary-internal), 3
fun_mrypt
  (ClinicalTrialSummary-internal), 3
fun_rspypyt
  (ClinicalTrialSummary-internal), 3

ggas, 3
print.ypsummary (ypsummary), 4

ransamf
  (ClinicalTrialSummary-internal), 3

summary, 2
summary.ypsummary (ypsummary), 4

ypsummary, 2–4, 4