Package 'gcerisk'

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Type Package

Title Generalized Competing Event Model

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Depends survival, cmprsk, ggplot2,

Imports stats

Description Generalized competing event model based on Cox PH model and Fine-Gray model. This function is designed to develop optimized risk-stratification methods for competing risks data, such as described in:
1. Carmona R, Gulaya S, Murphy JD, Rose BS, Wu J, Noticewala S,McHale MT, Yashar CM, Vaida F, and Mell LK (2014) <DOI:10.1016/j.ijrobp.2014.03.047>.
2. Carmona R, Zakeri K, Green G, Hwang L, Gulaya S, Xu B, Verma R, Williamson CW, Triplett DP, Rose BS, Shen H, Vaida F, Murphy JD, and Mell LK (2016) <DOI:10.1200/JCO.2015.65.0739>.
3. Lunn, Mary, and Don McNeil (1995) <DOI:10.2307/2532940>.

License GPL (>= 2)

LazyData TRUE

RoxygenNote 6.0.1

NeedsCompilation no

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R topics documented:

`gcecox` *Fit Generalized Competing Event Model Based on Proportional Hazards Regression*

Description

Fit a generalized competing event model by using Cox proportational hazards regression model with `coxph` function in `survival` package.

Usage

```
gcecox(formula1, formula2, formula3, formula4, survtime, surv1, surv2, data, ca,
  cm, all, N, M, t)
```

Arguments

`formula1`	a formula object for event(s) of interest, with a survival response returned by `Surv` function on the left, and the covariate terms on the right.
`formula2`	a formula object for event(s) of interest, with a survival response returned by `Surv` function on the left, and the covariate terms on the right.
`formula3`	a formula object for competing event(s), with a survival response returned by `Surv` function on the left, and the covariate terms on the right.
`formula4`	a formula object for the composite set of all events, with a survival response returned by `Surv` function on the left, and the covariate terms on the right.
`survtime`	survival time for event(s) of interest.
`surv1`	a formula object for event(s) of interest, with a survival response returned by `Surv` function on the left, and 1 on the right.
`surv2`	a formula object for competing event(s), with a survival response returned by `Surv` function on the left, and 1 on the right.
`data`	a data frame containing variables named in formula.
`ca`	the status indicator, normally 0 = alive, 1 = dead from the primary event(s) of interest.
`cm`	the status indicator, normally 0 = alive, 1 = dead from the competing event(s) of interest.
`all`	the status indicator, normally 0 = alive, 1 = dead from the all kind of event(s) of interest.
`N`	the number of bootstrap replicates
`M`	the number of bins for ω or $\omega+$ plots.
`t`	survival time point for ω or $\omega+$ plots.

Details

The **gcerisk** package is designed to help investigators optimize risk-stratification methods for competing risks data, such as described in Carmona R, Gulaya S, Murphy JD, Rose BS, Wu J, Noticewala S, McHale MT, Yashar CM, Vaida F, Mell LK. Validated competing event model for the stage I-II endometrial cancer population. Int J Radiat Oncol Biol Phys. 2014;89:888-98. Standard risk models typically estimate the effects of one or more covariates on either a single event of interest (such as overall mortality, or disease recurrence), or a composite set of events (e.g., disease-free survival, which combines events of interest with death from any cause). This method is inefficient in stratifying patients who may be simultaneously at high risk for the event of interest but low risk for competing events, and who thus stand to gain the most from strategies to modulate the event of interest. Compared to standard risk models, GCE models better stratify patients at higher (lower) risk for an event of interest and lower (higher) risk of competing events. GCE models focus on differentiating subjects based on the ratio of the cumulative hazard (or cumulative hazard of the subdistribution) for the event of interest to the cumulative hazard (or cumulative hazard of the subdistribution) for all events (ω), and the ratio of the cumulative hazard (or cumulative hazard of the subdistribution) for the event of interest to the cumulative hazard (or cumulative hazard of the subdistribution) for competing events ($\omega+$).

The `gcecox` function produces model estimates and confidence intervals from a generalized competing event model based on the Cox PH model for cause-specific hazards. The model assumes proportional hazards for the composite set of events.

The function returns ω and $\omega+$ ratio estimates for the chosen covariates, with 95% confidence intervals, and plots ω and $\omega+$ at time t within M ordered subsets of subjects as a function of increasing risk (based on the linear predictor, i.e. the inner product of a subject's data vector and the coefficient vector).

Value

`$coef1`	generalized competing event model coefficients (log (ω ratio))
`$coef2`	generalized competing event model coefficients (log ($\omega+$ ratio))
`$result1`	result table for generalized competing event model containing exponential of coefficients (ω ratio) and 95% confidence intervals
`$result2`	result table for generalized competing event model containing exponential of coefficients ($\omega+$ ratio) and 95% confidence intervals
`$omegaplot1`	ω plot for generalized competing evet model
`$omegaplot2`	$\omega+$ plot for generalized competing evet model
`$omegaplot3`	plot of ω vs time
`$omega`	predicted ω values
`$omegaplus`	predicted $\omega+$ values

Author(s)

Hanjie Shen, Ruben Carmona, Loren Mell

References

- Carmona R, Gulaya S, Murphy JD, Rose BS, Wu J, Noticewala S, McHale MT, Yashar CM, Vaida F, Mell LK. (2014) Validated competing event model for the stage I-II endometrial cancer population. Int J Radiat Oncol Biol Phys.89:888-98.
- Carmona R, Green GB, Zakeri K, Gulaya S, Xu B, Verma R, Williamson C, Rose BS, Murphy JD, Vaida F, Mell LK. (2015) Novel method to stratify elderly patients with head and neck cancer. J Clin Oncol 33 (suppl; abstr 9534).
- Carmona R, Zakeri K, Green GB, Triplett DP, Murphy JD, Mell LK. (2015) Novel method to stratify elderly patients with prostate cancer. J Clin Oncol 33 (suppl; abstr 9532).

Examples

```
# sample data to test
data(Sample)
test <- Sample
rm(list=setdiff(ls(), "test"))
test <- transform(test, LRF_OR_DF_FLAG = as.numeric(test$LRFFLAG | test$DFFLAG))
test <- transform(test, CMFLAG = as.numeric(test$OSFLAG & !test$LRFFLAG & !test$DFFLAG))
test <- transform(test, ACMFLAG = as.numeric(test$LRF_OR_DF_FLAG | test$CMFLAG))

formula1 <- Surv(survtime, status) ~ age + smoke20 + etohheavy + BMI +
dage + dsmoke20 + detohheavy + dBMI + strata(fail)
formula2 <- Surv(OSMO, LRF_OR_DF_FLAG) ~ age + smoke20 +
etohheavy + BMI
formula3 <- Surv(OSMO, CMFLAG) ~ age + smoke20 + etohheavy + BMI
formula4 <- Surv(OSMO, ACMFLAG) ~ age + smoke20 + etohheavy + BMI
surv1 <- Surv(OSMO, LRF_OR_DF_FLAG) ~ 1
surv2 <- Surv(OSMO, CMFLAG) ~ 1
survtime <- test$OSMO
ca <- test$LRF_OR_DF_FLAG
cm <- test$CMFLAG
all <- test$ACMFLAG

N <- 100
M <- 5
t <- 60

fit <- gcecox(formula1, formula2, formula3, formula4, survtime,
surv1, surv2, test, ca, cm, all, N, M, t)
```

`gcefg` *Fit Generalized Competing Event Model Based on Fine Gray Regression*

Description

Fit a generalized competing event model by using Fine Gray regression model with `crr` function in `cmprsk` package.

Usage

```
gcefg(ostime1, ostime2, ostime3, cod1, cod2, data, covnames, N, M, t)
```

Arguments

ostime1	vector of times for event(s) of interest.
ostime2	vector of times for competing event(s).
ostime3	vector of times for the composute set of all events.
cod1	vector with 1 for event(s) pf interest, 2 for competing event(s) and 0 for censored observations.
cod2	vector with 1 for the composite set of all events and 0 for censored observations.
data	a data frame containing all covariates.
covnames	vector of names for all covariates in data.
N	the number of bootstrap replicates
M	the number of bins for ω or $\omega+$ plots.
t	survival time point for ω or $\omega+$ plots.

Details

The **gcerisk** package is designed to help investigators optimize risk-stratification methods for competing risks data, such as described in Carmona R, Gulaya S, Murphy JD, Rose BS, Wu J, Noticewala S, McHale MT, Yashar CM, Vaida F, Mell LK. Validated competing event model for the stage I-II endometrial cancer population. Int J Radiat Oncol Biol Phys. 2014;89:888-98. Standard risk models typically estimate the effects of one or more covariates on either a single event of interest (such as overall mortality, or disease recurrence), or a composite set of events (e.g., disease-free survival, which combines events of interest with death from any cause). This method is inefficient in stratifying patients who may be simultaneously at high risk for the event of interest but low risk for competing events, and who thus stand to gain the most from strategies to modulate the event of interest. Compared to standard risk models, GCE models better stratify patients at higher (lower) risk for an event of interest and lower (higher) risk of competing events. GCE models focus on differentiating subjects based on the ratio of the cumulative hazard (or cumulative hazard of the subdistribution) for the event of interest to the cumulative hazard (or cumulative hazard of the subdistribution) for all events (ω), and the ratio of the cumulative hazard (or cumulative hazard of the subdistribution) for the event of interest to the cumulative hazard (or cumulative hazard of the subdistribution) for competing events ($\omega+$).

The gcefg function produces model estimates and confidence intervals from a generalized competing event model based on the Fine-Gray model for subdistribution hazards. In the subdistribution hazards model, the function H(t)= -log(1-F(t)) represents the cumulative hazard of the subdistribution for the cumulative distribution function F(t). The model assumes proportional subdistribution hazards for the composite set of events.

The function returns ω and $\omega+$ ratio estimates for the chosen covariates, with 95% confidence intervals, and plots ω and $\omega+$ at time t within M ordered subsets of subjects as a function of increasing risk (based on the linear predictor, i.e. the inner product of a subject's data vector and the coefficient vector).

Value

$coef1	generalized competing event model coefficients (log (ω ratio))
$coef2	generalized competing event model coefficients (log ($\omega+$ ratio))
$result1	result table for generalized competing event model containing exponential of coefficients (ω ratio) and 95% confidence intervals
$result2	result table for generalized competing event model containing exponential of coefficients ($\omega+$ ratio) and 95% confidence intervals
$omegaplot1	ω plot for generalized competing evet model
$omegaplot2	$\omega+$ plot for generalized competing evet model
$omegaplot3	plot of ω vs time

Author(s)

Hanjie Shen, Ruben Carmona, Loren Mell

References

- Carmona R, Gulaya S, Murphy JD, Rose BS, Wu J, Noticewala S, McHale MT, Yashar CM, Vaida F, Mell LK. (2014) Validated competing event model for the stage I-II endometrial cancer population. Int J Radiat Oncol Biol Phys.89:888-98.
- Carmona R, Green GB, Zakeri K, Gulaya S, Xu B, Verma R, Williamson C, Rose BS, Murphy JD, Vaida F, Mell LK. (2015) Novel method to stratify elderly patients with head and neck cancer. J Clin Oncol 33 (suppl; abstr 9534).
- Carmona R, Zakeri K, Green GB, Triplett DP, Murphy JD, Mell LK. (2015) Novel method to stratify elderly patients with prostate cancer. J Clin Oncol 33 (suppl; abstr 9532).

Examples

```
# sample data to test
data(Sample)
test <- Sample
d <- trunc(dim(test)[1]*0.1)
set.seed(seed=2015)
s <- sample(dim(test)[1],d,replace = FALSE)
test <- test[s,]
rm(list=setdiff(ls(), "test"))
test <- transform(test, LRF_OR_DF_FLAG = as.numeric(test$LRFFLAG | test$DFFLAG))
test <- transform(test, LRF_OR_DF_MO = pmin(test$LRFMO, test$DFMO))
test <- transform(test, CMFLAG = as.numeric(test$OSFLAG & !test$LRFFLAG & !test$DFFLAG))
test <- transform(test, ACMFLAG = as.numeric(test$LRF_OR_DF_FLAG | test$CMFLAG))
test <- transform(test, ACM_MO = pmin(test$LRF_OR_DF_MO, test$OSMO))

cod1 <- test$ACMFLAG
cod1[test$LRF_OR_DF_FLAG == 1] <- 1
cod1[test$CMFLAG == 1] <- 2
cod2 <- test$ACMFLAG
ostime1 <- test$LRF_OR_DF_MO/30
ostime2 <- test$OSMO/30
```

```
ostime3 <- test$ACM_MO/30
covnames <- c("age", "smoke20", "etohheavy", "BMI")

N <- 50
M <- 5
t <- 5

fit <- gcefg(ostime1, ostime2, ostime3, cod1, cod2, test, covnames, N, M, t)
```

`Sample` *Sample dataset*

Description

A sample dataset used to test functions in package.

Usage

```
Sample
```

Format

A data frame with 479 rows and 16 variables:

X index variable

gender covariate

smoke20 covariate

etohheavy covariate

higrade covariate

age covariate

OSFLAG status variable

LRFFLAG status variable

DFFLAG status variable

DFSFLAG status variable

OSMO time variable

LRFMO time variable

DFMO time variable

DFSMO time variable

BMI covariate

black covariate

Index