

# 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, Notice-wala S,McHale MT, Yashar CM, Vaida F, and Mell LK.(2014) <DOI:10.1016/j.ijrobp.2014.03.047>. Validated competing event model for thestage I-II endometrial cancer population. Int J Radiat Oncol Biol Phys.89:888-98.  
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>. Improved method to stratify elderly cancer patients at risk for competing events. J Clin Oncol.in press.

**License** GPL (>= 2)

**LazyData** TRUE

**RoxygenNote** 5.0.1

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gcecox	<i>Fit Generalized Competing Event Model Based on Proportional Hazards Regression</i>
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Description

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

Usage

```
gcecox(formula1, formula2, formula3, surv1, surv2, data, 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 competing event(s), with a survival response returned by Surv function on the left, and the covariate terms on the right.
formula3	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.
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.
N	the number of bootstrap replicates
M	the number of bins for $\omega$ or $\omega+$ plots.
t	survival time point for $\omega$ 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 ( $\omega$ ), 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  $\omega$  and  $\omega+$  ratio estimates for the chosen covariates, with 95% confidence intervals, and plots  $\omega$  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 ( $\omega$ ratio))
\$coef2	generalized competing event model coefficients (log ( $\omega+$ ratio))
\$result1	result table for generalized competing event model containing exponential of coefficients ( $\omega$ ratio) and 95% confidence intervals
\$result2	result table for generalized competing event model containing exponential of coefficients ( $\omega+$ ratio) and 95% confidence intervals
\$omegaplot1	$\omega$ plot for generalized competing event model
\$omegaplot2	$\omega+$ plot for generalized competing event model
\$omegaplot3	plot of $\omega$ 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
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$LRFM0, test$DFM0))
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$OSM0))

formula1 <- Surv(LRF_OR_DF_MO, LRF_OR_DF_FLAG) ~ age + gender + smoke20 +
etohheavy + higrade + BMI + black
formula2 <- Surv(OSM0, CMFLAG) ~ age + gender + smoke20 + etohheavy + higrade + BMI + black
formula3 <- Surv(ACM_MO, ACMFLAG) ~ age + gender + smoke20 + etohheavy + higrade + BMI + black
surv1 <- Surv(LRF_OR_DF_MO, LRF_OR_DF_FLAG) ~ 1
surv2 <- Surv(OSM0, CMFLAG) ~ 1
N <- 100
M <- 5
t <- 60

fitgce.cox <- gcecox(formula1, formula2, formula3, surv1, surv2, test, N, M, t)
```

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gcefg

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


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## 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

<code>ostime1</code>	vector of times for event(s) of interest.
<code>ostime2</code>	vector of times for competing event(s).
<code>ostime3</code>	vector of times for the composite set of all events.
<code>cod1</code>	vector with 1 for event(s) of interest, 2 for competing event(s) and 0 for censored observations.
<code>cod2</code>	vector with 1 for the composite set of all events and 0 for censored observations.
<code>data</code>	a data frame containing all covariates.
<code>covnames</code>	vector of names for all covariates in data.

N	the number of bootstrap replicates
M	the number of bins for $\omega$ or $\omega+$ plots.
t	survival time point for $\omega$ 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 ( $\omega$ ), 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  $\omega$  and  $\omega+$  ratio estimates for the chosen covariates, with 95% confidence intervals, and plots  $\omega$  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

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

## Author(s)

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## 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$LRFM0, test$DFM0))
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$LRF_OR_DF_MO
ostime2 <- test$OSMO
ostime3 <- test$ACM_MO
covnames <- c("age", "gender", "smoke20", "etohheavy", "higrade", "BMI", "black")

N <- 50
M <- 5
t <- 60

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

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Sample

*Sample dataset*

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## 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

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