

Package: gcemod (via r-universe)

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Type Package

Title Generalized Competing Event Models with Lunn-McNeil Testing

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Description Tools for fitting generalized competing event (GCE) models and estimating covariate effects on omega-plus, the ratio of the hazard for an event of interest to the hazard for a competing event, on both the cause-specific (Cox) and subdistribution (Fine-Gray) hazard scales. Confidence intervals and p-values are obtained from the Lunn-McNeil (1995) stacked (augmented) data approach. The package builds GCE risk scores from the model linear predictor, identifies risk-score cutpoints that maximize the separation in omega-plus between groups, and produces cumulative incidence ("alligator") plots by risk group and calibration plots of predicted versus observed omega-plus. Methods follow Carmona et al. (2014) [doi:10.1016/j.ijrobp.2014.03.047](https://doi.org/10.1016/j.ijrobp.2014.03.047), Mell et al. (2024) [doi:10.1016/j.eururo.2023.01.020](https://doi.org/10.1016/j.eururo.2023.01.020), and Lunn and McNeil (1995) [doi:10.2307/2532940](https://doi.org/10.2307/2532940).

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gce_alligator	<i>Alligator plot: cumulative incidence by risk group and event type</i>
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Description

Plots the cause-specific cumulative incidence functions (CIFs) of the event of interest and the competing event over time on a single panel, with risk groups distinguished by colour and event types by line type (event of interest solid, competing event dashed). In higher-risk groups the event-of-interest CIF rises above the competing-event CIF and the curves separate like an alligator’s open jaws.

The x-axis is truncated at the model’s readout time *t*, with tick marks at 1-unit (e.g. 1-year) intervals. The y-axis auto-scales its cap to the smallest of 25/50/75/100% that covers the peak cumulative incidence (so low-incidence settings are not compressed), with ticks at 10% (or 5% when capped at 25%). Numbers at risk for each group are shown in an aligned panel below the plot. Gray’s test across groups is attached.

Usage

```
gce_alligator(  
  object,  
  groups = 2,  
  method = c("optimal", "quantile"),  
  criterion = c("omegaplus", "cif"),  
  xlab = "Time (years)",  
  ylab = "Cumulative incidence",  
  group.lab = "Risk group",
```

```

    risk.table = TRUE,
    ymax = NULL
  )

```

Arguments

object	a "gcmmod" object from gcecox or gcefg .
groups	a gce_cutpoints result, a grouping factor of length n, or a single integer giving the number of risk groups (default 2). When an integer is given, the groups are derived with gce_cutpoints using method.
method	grouping rule used when groups is an integer: "optimal" (default) or "quantile" (equal-sized groups). Ignored when groups is a cutpoints object or a factor.
criterion	optimal-search criterion when groups is an integer and method = "optimal": "omegaplus" (default, $\log\omega^+$ separation; not tail-sensitive) or "cif" (joint Gray statistic on the observed cumulative incidence of both events). See gce_cutpoints .
xlab, ylab	axis labels.
group.lab	legend title for the risk groups (default "Risk group").
risk.table	logical; show numbers at risk in an aligned panel below the plot (default TRUE).
ymax	optional numeric upper cap for the y-axis (0-1). If NULL (default) the cap auto-scales to 25/50/75/100% based on the peak incidence.

Value

A ggplot/patchwork object. The Gray's-test result, the plotted CIF data, the numbers-at-risk table, and the cutpoints are attached as attributes "grays_test", "data", "n.risk", and "cutpoints".

Examples

```

data(hn)
Ind <- data.frame(event = as.integer(hn$status == 1),
                  competing = as.integer(hn$status == 2))
fit <- gcecox(hn$time, Ind, hn[, c("age", "t_cat", "p16")], M = 5, t = 5)
gce_alligator(fit, groups = 2)

```

gce_calibration	<i>Calibration of predicted vs. observed omega+ by risk rank</i>
-----------------	--

Description

Groups subjects into equal-sized rank groups on the GCE risk score and compares the model-predicted ω^+ (or ω) with an observed estimate in each group. Observed values use cause-specific Nelson-Aalen cumulative hazards within the group at time t : $\omega_{obs}^+ = H_1(t)/H_2(t)$ and $\omega_{obs} = H_1(t)/(H_1(t) + H_2(t))$. A calibration plot (predicted vs. observed with the identity line) and the underlying table are returned.

Usage

```
gce_calibration(object, which = c("omegaplus", "omega"), groups = 5)
```

Arguments

object	a "gcmmod" object from gcecox or gcefg .
which	"omegaplus" (default) or "omega".
groups	number of rank groups (default 5).

Value

A ggplot object (predicted vs. observed). The calibration table is attached as attribute "data".

Examples

```
data(hn)
Ind <- data.frame(event = as.integer(hn$status == 1),
                  competing = as.integer(hn$status == 2))
fit <- gcecox(hn$time, Ind, hn[, c("age", "t_cat", "p16")], M = 5, t = 5)
gce_calibration(fit, which = "omegaplus", groups = 5)
```

gce_cutpoints

Risk-score cutpoints for GCE risk stratification

Description

Splits subjects into ordered risk groups on the GCE risk score. With method = "optimal" the cutpoint(s) maximize a separation criterion by a greedy forward search; with method = "quantile" equal-sized groups are used.

The default criterion, "omegaplus", maximizes the between-group separation in $\log \omega^+$ (equivalently, the risk score / linear predictor). This is the additive scale on which the joint event-of-interest-vs-competing ω^+ contrast is defined, and – unlike separation measured on the exponential ω^+ scale – it is **not** sensitive to a few extreme high-risk subjects, so the search does not chase high-risk tails and tends to return balanced, well-separated groups. The alternative "cif" maximizes a joint Gray's test statistic (summed across both competing events) on the observed cumulative incidence.

Usage

```
gce_cutpoints(
  object,
  groups = 2,
  method = c("optimal", "quantile"),
  criterion = c("omegaplus", "cif"),
  min.prop = 0.1,
  nperm = 0,
  labels = NULL
)
```

Arguments

object	a "gcmmod" object from gcecox or gcefg .
groups	number of groups (default 2).
method	"optimal" (default) or "quantile".
criterion	optimal-search criterion: "omegaplus" (default, log- ω^+ separation) or "cif" (joint Gray statistic on observed cumulative incidence of both events).
min.prop	minimum proportion of subjects per group (default 0.1).
nperm	number of permutations for the selection-adjusted p-value (default 0 = not computed). When <code>nperm > 0</code> , the maximally-selected joint Gray statistic is permuted (risk score vs. outcome) to give a p-value accounting for the data-driven choice of cutpoint.
labels	optional character labels for the groups (low to high risk).

Value

A list with: groups (ordered factor), cutpoints (on the risk-score scale), summary (per-group n, events, mean ω^+ / ω), and test. The test element reports the Lunn-McNeil ω^+ contrast between groups – a test that the ratio of cause-specific (or subdistribution) hazards differs across groups – with the univariable ω^+ ratio estimate and CI (`$omegaplus`), the joint test (`$statistic`, `$df`, `$p.value`), the per-event Gray tests for comparison (`$individual_gray`), and a selection-adjusted `$p.perm` when `nperm > 0`.

Examples

```
data(hn)
Ind <- data.frame(event = as.integer(hn$status == 1),
                  competing = as.integer(hn$status == 2))
fit <- gcecox(hn$time, Ind, hn[, c("age", "t_cat", "p16")], M = 5, t = 5)
gce_cutpoints(fit, groups = 2, nperm = 200)
```

<code>gce_performance</code>	<i>Discrimination (C-index) for a GCE model</i>
------------------------------	---

Description

Reports the cause-specific concordance (C-index) of the GCE risk score for the event of interest. For calibration (predicted vs. observed ω^+), see [gce_calibration](#).

Usage

```
gce_performance(object, conf.level = 0.95)
```

Arguments

object	a "gcmmod" object.
conf.level	confidence level for the C-index interval (default 0.95).

Details

The C-index is computed with [concordance](#) using the event of interest as the outcome and the GCE risk score as the predictor. Higher risk scores denote higher risk; the statistic is oriented so that values above 0.5 indicate discrimination in the expected direction.

Value

Invisibly, a named numeric vector `cindex` (estimate, se, lower, upper). The value is also printed.

See Also

[gce_calibration](#)

Examples

```
data(hn)
Ind <- data.frame(event = as.integer(hn$status == 1),
                  competing = as.integer(hn$status == 2))
fit <- gcecox(hn$time, Ind, hn[, c("age", "t_cat", "p16")], M = 5, t = 5)
gce_performance(fit)
```

<code>gce_riskscore</code>	<i>Normalized risk score and relative omega+ for new subjects</i>
----------------------------	---

Description

Computes the GCE risk score for new subjects using the covariate means/SDs and coefficients stored in a fitted model. The score is the normalized (mean-centered) linear predictor, so `exp(riskscore)` is the subject's omega+ relative to the *average* subject in the fitting data (a value of 1 = same as average, 2 = twice the average omega+). For cause-specific ([gcecox](#)) models the absolute predicted omega+ and omega at the model's time `t` are also returned.

Usage

```
gce_riskscore(object, newdata)
```

Arguments

<code>object</code>	a "gcemod" object.
<code>newdata</code>	a data frame containing the covariates used to fit <code>object</code> (same column names). Factor levels not seen in the fitting data are treated as the reference level.

Value

A data frame with `riskscore`, `omegaplus_rel` (`= exp(riskscore)`), and, for cause-specific models, `omegaplus` and `omega` (absolute, at time `t`).

See Also[gce_scaling](#)**Examples**

```
data(prostate)
Ind <- data.frame(as.integer(prostate$status == 1), as.integer(prostate$status == 2))
fit <- gcecox(prostate$time, Ind, prostate[, c("age", "psa", "gleason")], M = 5, t = 10)
gce_riskscore(fit, newdata = prostate[1:5, ])
```

gce_scaling

*Covariate scaling (means and SDs) used by the GCE risk score***Description**

Returns each covariate's mean and standard deviation (from the data used to fit the model), together with the per-SD log-omega+ coefficient and omega+ ratio. These are the quantities needed to reproduce the normalized risk score for new subjects (see [gce_riskscore](#)) and to interpret how far a subject sits from the average patient.

Usage

```
gce_scaling(object)
```

Arguments

object a "gcmmod" object from [gcecox](#) or [gcefg](#).

Value

A data frame with columns term, mean, sd, coef_perSD (log-omega+ ratio per 1 SD) and omegaplus_ratio_perSD.

See Also[gce_riskscore](#)**Examples**

```
data(prostate)
Ind <- data.frame(as.integer(prostate$status == 1), as.integer(prostate$status == 2))
fit <- gcecox(prostate$time, Ind, prostate[, c("age", "psa", "gleason")], M = 5, t = 10)
gce_scaling(fit)
```

gce_tidy

*Tidy a GCE model into a data frame of estimates***Description**

With `effects = FALSE` (the default) the omega+ ratio estimates are returned. With `effects = TRUE` a covariate-effects comparison table is returned that juxtaposes, for each covariate, the hazard ratio for the primary (event-of-interest) hazard, the competing-event hazard, the total (composite, any-event) hazard, and the relative hazard ratio (the omega+ ratio) from the GCE model, each with a confidence interval. This lets the investigator see whether a covariate acts mainly on the event of interest, the competing event, both, or on their balance.

Usage

```
gce_tidy(object, effects = FALSE, ...)
```

Arguments

<code>object</code>	a "gcmmod" object from gcecox or gcefg .
<code>effects</code>	logical; if TRUE, return the primary/competing/total/ relative effects comparison table instead of the omega+ ratio table. Requires an object fit with gcmmod >= 0.3.0 (which stores the design matrix). Default FALSE.
<code>...</code>	unused.

Details

The individual- and total-event columns are estimated on the same hazard scale as the fitted model: cause-specific Cox models for a [gcecox](#) fit, and Fine-Gray subdistribution models for a [gcefg](#) fit. The total (composite) event has no competing event, so its subdistribution and cause-specific hazards coincide and a Cox model on the composite endpoint is used in both cases.

Value

If `effects = FALSE`, a data frame with columns `term`, `log_ratio`, `ratio`, `conf.low`, `conf.high`, `p.value`. If `effects = TRUE`, a data frame with columns `term`, `primary`, `competing`, `total`, and `relative`, each a formatted "HR (low, high)" string.

Examples

```
data(hn)
Ind <- data.frame(event = as.integer(hn$status == 1),
                  competing = as.integer(hn$status == 2))
fit <- gcecox(hn$time, Ind, hn[, c("age", "t_cat", "p16")], M = 5, t = 5)
gce_tidy(fit)
gce_tidy(fit, effects = TRUE)
```

gcecox

*Generalized competing event model via cause-specific Cox regression***Description**

Fits a generalized competing event (GCE) model on the cause-specific hazard scale and estimates covariate effects on ω^+ (event of interest vs. competing event) using the Lunn-McNeil stacked model (see [lunnmcneil](#)), with 95% confidence intervals, Wald p-values, and an omnibus test. A GCE risk score is formed from the model linear predictor, and per-subject $\omega = \omega^+ / (1 + \omega^+)$ is returned for comparison with observed values.

Usage

```
gcecox(
  Time,
  Ind,
  Cov,
  M = 5,
  t,
  conf.level = 0.95,
  cluster.se = TRUE,
  standardize = FALSE
)
```

Arguments

Time	numeric vector of follow-up times.
Ind	a data frame of event indicators. Column 1 = event of interest, column 2 = competing event (0/1). A third column, if present, is ignored.
Cov	a data frame of covariates.
M	number of bins for the ω^+ risk plot (default 5).
t	time point at which per-subject ω / ω^+ are evaluated.
conf.level	confidence level (default 0.95).
cluster.se	logical; cluster-robust SEs in the Lunn-McNeil model (default TRUE).
standardize	logical; controls only the <i>reported</i> omega+ ratio scale (default FALSE = per natural covariate unit; TRUE = per 1 SD). The risk score is <i>always</i> the normalized (mean-centered) linear predictor regardless of this setting, so cutpoints, plots, and the predicted-vs-observed omega calibration are unaffected. Covariate means/SDs are available in \$scaling (see gce_scaling).

Value

An object of class "gcemod" (subclass "gcecox") with: coef (log ω^+ ratios), result (ratio table with CIs and p-values), omnibus (Lunn-McNeil global test), riskscore (linear predictor), omega / omegaplus (per-subject values at t), omegaplot and omegatimeplot (ggplot objects), and the fitted Lunn-McNeil model.

See Also

[gcefg](#), [lunmcneil](#), [gce_cutpoints](#)

Examples

```
data(hn)
Ind <- data.frame(event = as.integer(hn$status == 1),
                  competing = as.integer(hn$status == 2))
Cov <- hn[, c("age", "smoker", "t_cat", "n_cat", "p16")]
fit <- gcecox(hn$time, Ind, Cov, M = 5, t = 5)
summary(fit)
```

gcefg

Generalized competing event model via Fine-Gray regression

Description

Fits a generalized competing event (GCE) model on the subdistribution hazard scale and estimates covariate effects on ω^+ using a Lunn-McNeil-style stacked Fine-Gray model (see [lunmcneil](#) with `type = "finegray"`), giving 95% confidence intervals, Wald p-values, and an omnibus test from one joint model. A GCE risk score is formed from the model linear predictor, and per-subject ω^+ / ω at time `t` are returned for comparison with observed values.

Usage

```
gcefg(Time, Ind, Cov, M = 5, t, conf.level = 0.95, standardize = FALSE)
```

Arguments

Time	numeric vector of follow-up times.
Ind	a data frame of event indicators. Column 1 = event of interest, column 2 = competing event (0/1).
Cov	a data frame of covariates (factors are expanded to indicators).
M	number of bins for the ω^+ risk plot (default 5).
t	time point at which per-subject ω^+ / ω are evaluated.
conf.level	confidence level (default 0.95).
standardize	logical; controls only the <i>reported</i> omega+ ratio scale (default FALSE = per natural covariate unit; TRUE = per 1 SD). The risk score is always the normalized (mean-centered) linear predictor. Covariate means/SDs are in <code>\$scaling</code> (see gce_scaling).

Value

An object of class "gcemod" (subclass "gcefg") with the same components as [gcecox](#) on the sub-distribution scale.

See Also

[gcecox](#), [lunmcneil](#)

Examples

```
data(hn)
Ind <- data.frame(event = as.integer(hn$status == 1),
                  competing = as.integer(hn$status == 2))
Cov <- hn[, c("age", "smoker", "t_cat", "n_cat", "p16")]
fit <- gcefg(hn$time, Ind, Cov, M = 5, t = 5)
summary(fit)
```

hn	<i>Head-and-neck cancer competing-risks example dataset</i>
----	---

Description

An example head-and-neck cancer competing-risks dataset used to illustrate the **gcemod** functions. The data are provided for illustration only and do not represent real patients. The event of interest is cancer recurrence and the competing event is death without recurrence; recurrence is the more frequent event (recurrence-dominant, $\omega^+ > 1$). Contrast with [prostate](#).

Usage

```
hn
```

Format

A data frame with 1000 rows and 11 variables:

id sequential subject identifier

time follow-up time in years

status competing-risks status: 0 = censored, 1 = cancer recurrence (event of interest), 2 = death without recurrence (competing event)

age age at diagnosis (years)

ps ECOG performance status (factor: 0, 1, 2)

female sex indicator (1 = female)

smoker smoking indicator (1 = more than 10 pack-years)

t_cat T category (factor: 1-4)

n_cat N category (factor: 0-3)

p16 p16 status (1 = positive)

site primary site (factor: oropharynx, larynx, hypopharynx, oralcavity)

lunnmcneil

*Lunn-McNeil stacked-model estimation of omega+ ratios***Description**

Estimates covariate effects on ω^+ (the ratio of the hazard for the event of interest to the hazard for the competing event) from a single stacked ("augmented") model, following Lunn and McNeil (1995). Each subject contributes one record per event type; the model is stratified by event type and the covariate-by-event-type interaction estimates $\log(\omega^+ \text{ ratio})$ with model-based standard errors, per-covariate Wald tests, and an omnibus multivariate Wald test.

Usage

```
lunnmcneil(
  Time,
  cause,
  Cov,
  event = 1,
  competing = 2,
  type = c("coxph", "finegray"),
  cluster.se = TRUE,
  conf.level = 0.95,
  standardize = FALSE,
  ...
)
```

Arguments

Time	numeric vector of follow-up times.
cause	event indicator per subject: 0 = censored, and the codes in event and competing for the two event types.
Cov	a data frame of covariates (factors are expanded to indicators).
event	code marking the event of interest (default 1).
competing	code marking the competing event (default 2).
type	"coxph" (cause-specific, default) or "finegray" (subdistribution).
cluster.se	logical; cluster-robust (subject) SEs (default TRUE).
conf.level	confidence level (default 0.95).
standardize	logical; controls only the <i>reported</i> coefficient scale (default FALSE). FALSE reports omega+ ratios per natural covariate unit; TRUE reports them per 1 SD. This is a reparameterization, so Wald tests, p-values, and the omnibus test are identical either way. The covariate means/SDs (\$center, \$scale) are always returned.
...	passed to coxph .

Details

Two hazard scales are supported:

`type = "coxph"` Cause-specific hazards. The augmented data set duplicates each subject into an "event" stratum and a "competing" stratum; the interaction coefficient is exactly the difference in cause-specific log-hazards, i.e. $\log(\omega^+)$. This is the original Lunn-McNeil construction and the interaction MLE equals the difference of two separate cause-specific Cox fits.

`type = "finegray"` Subdistribution hazards. Risk-set-weighted data are generated for each event type with [finegray](#), stacked, and fit with a single weighted, event-type-stratified [coxph](#). The interaction estimates the difference in subdistribution log-hazards. Because subjects recur across the weighted risk sets, cluster-robust (subject) standard errors are used. This is an extension of Lunn-McNeil to the subdistribution scale.

Subject records are duplicated in both cases, so cluster-robust standard errors (clustered on subject) are the default.

Value

An object of class "gce_lunmneil": a list with the fitted model (`$fit`), the omega+ coefficient table (`$omegaplus`), the reference (competing-event) coefficients (`$beta_competing`), the omnibus test (`$omnibus`), the design column names (`$terms`), and the hazard scale (`$type`).

References

Lunn M, McNeil D (1995) Applying Cox regression to competing risks. *Biometrics* 51:524-32.

Examples

```
data(hn)
Cov <- hn[, c("age", "smoker", "t_cat", "n_cat", "p16")]
lunmneil(hn$time, hn$status, Cov, type = "coxph")
lunmneil(hn$time, hn$status, Cov, type = "finegray")
```

prostate

Prostate cancer competing-risks example dataset

Description

An example prostate cancer competing-risks dataset used to illustrate the **gcemod** functions. The data are provided for illustration only and do not represent real patients. The event of interest is distant metastasis or prostate-cancer death and the competing event is death from other causes; the competing event is the more frequent (competing-death-dominant, $\omega^+ < 1$). Contrast with [hn](#).

Usage

prostate

Format

A data frame with 1000 rows and 9 variables:

id sequential subject identifier

time follow-up time in years

status competing-risks status: 0 = censored, 1 = distant metastasis or prostate-cancer death (event of interest), 2 = death from other causes (competing event)

age age at diagnosis (years)

ps performance status (factor: 0, 1)

psa pre-treatment PSA (ng/mL, capped at 20)

gleason Gleason grade group (factor: "<=6", "3+4", "4+3", ">=8")

t2b stage indicator (1 = T2b or higher)

comorbidity significant comorbidity indicator (1 = yes)

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