

Package ‘cox.rvph’

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Type Package

Title Remedy for Violations of the Proportional Hazards Assumption in
Cox Proportional Hazards Models

Version 0.2.1

Description Remediating proportional hazards
assumption violations of a Cox proportional hazards model using
stepwise split-point and time-varying coefficient methods based on
Cox (1972) <doi:10.1111/j.2517-6161.1972.tb00899.x> and Klein
and Moeschberger (1997) <doi:10.1007/978-1-4757-2728-9>.

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Imports survival

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cox.rvph

Remedy for Violations of the Proportional Hazards Assumption in Cox Proportional Hazards Models

Description

Stepwise or time-varying remedies for proportional hazards assumption violations in Cox Proportional Hazards Models

Usage

```
cox.rvph(
  data,
  time,
  event,
  covariate,
  adjust_vars = NULL,
  method = c("step", "timev"),
  g_candidates = NULL,
  max_K = 4,
  p_threshold = 0.05,
  verbose = TRUE
)
```

Arguments

data	a data frame
time	the survival time variable
event	the event indicator variable coded as 0 = right-censored and 1 = event
covariate	the covariate that violates the proportional hazards assumption
adjust_vars	the variables to be included as adjustment covariates
method	the method to be applied ("step" or "timev")
g_candidates	a list of candidate time functions used in the time-varying coefficient method If NULL, a default set of candidate functions (linear, log, sqrt, quadratic and inverse) is used. Users may also supply custom transformation functions. If supplied, the user-provided functions replace the default candidate set.
max_K	the maximum number of segments The actual number of searchable segments may be limited by the number of distinct candidate split points.
p_threshold	The significance threshold used for the PH test
verbose	logical; whether to print progress messages

Details

The event indicator specified by `event` must be binary, with 0 indicating a right-censored observation and 1 indicating that the event of interest occurred. Other event codings must be recoded before using `cox.rvph()`.

Additionally, users should verify that the survival time variable does not contain negative values. For the `step` method, observations with a survival time of 0 should be handled using an appropriate preprocessing strategy based on the scientific context. For the `timev` method, the specified time-transformation functions should be defined over the observed range of survival times.

Users should first assess the proportional hazards (PH) assumption using `cox.zph()` before applying `cox.rvph()`. Variables showing evidence of non-proportional hazards may then be modeled using stepwise or time-varying remedies.

Currently, only a single continuous variable can be specified in `covariate`. Categorical variables may still be included in `adjust_vars` as adjustment covariates.

The `step` method performs segmented modeling by searching for optimal split points in time by maximizing the partial likelihood. The selected split points are incorporated into the Cox model through time-dependent interval-specific covariates using the counting-process formulation. For each number of segments, the PH assumption is assessed using the global test from `cox.zph()`. The search stops at the first model for which the global p-value exceeds `p_threshold`. If the resulting model satisfies the PH assumption with relatively few split points, hazard ratios (HRs) may be interpreted within each estimated time interval.

The resulting hazard ratio within each time interval k is given by:

$$HR(t) = \exp(\beta_k), \quad t \in I_k$$

However, if many split points are required or PH violations persist, a smooth time-varying effect may be more appropriate. In such cases, the `timev` method compares the base Cox model with several time-varying alternatives based on candidate time-transformation functions using AIC, and selects the one with the smallest AIC. By default, the following candidate functions are evaluated: linear (t), logarithmic ($\log(\log(t + 1))$), square-root ($\text{sqrt}(\sqrt{t})$), quadratic (t^2) and inverse ($1/(t + 1)$). Users may alternatively provide their own candidate functions through the `g_candidates` argument.

The resulting hazard ratio at time t is given by:

$$HR(t) = \exp(\beta + \gamma g(t))$$

where β is the coefficient of the covariate and γ represents the time-varying interaction effect. Users may evaluate this expression at clinically relevant time points to interpret how the hazard ratio changes over time.

Example output from `print()` (method: `step`):

```
cox.rvph fit
Method: step
Number of segments: 2
Split point(s): 24.8
Global PH test p-value: 0.2529169
```

PH assumption satisfied ($p > 0.05$)

Coefficients:

```
age_seg1 age_seg2    sex2
  0.2705   0.0555  -0.4791
```

Interpretation (method: step):

For the step method, hazard ratios are interpreted separately within each estimated time interval.

$$HR(t) = \begin{cases} \exp(0.27052) = 1.31, & t \leq 24.8, \\ \exp(0.05550) = 1.06, & t > 24.8. \end{cases}$$

If the estimated split point is $\tau = 24.8$, this indicates that the hazard ratio associated with a one-unit increase in age is approximately 1.31 before time 24.8 and decreases to approximately 1.06 after time 24.8.

Example output from `print()` (method: timev):

```
cox.rvph fit
Method: time-varying coefficient
Selected time function: quadratic
```

Coefficients:

```
      bili  tt(bili) ascites1      edema  protime
8.036e-02 3.563e-08 1.153e+00 1.128e+00 2.670e-01
```

Interpretation (method: timev):

For the timev method, hazard ratios vary continuously over time.

$$HR(t) = \exp(0.08036 + 3.563 \times 10^{-8}t^2)$$

In this example, the quadratic time transformation indicates that the effect of `bili` changes continuously over time. Users may substitute clinically meaningful values of t to estimate hazard ratios at specific time points.

Value

An object of class `"cox.rvph"` containing the fitted model and method-specific results.

Examples

```
if (requireNamespace("KMSurv", quietly = TRUE)) {
  data(psych, package = "KMSurv")

  psych$sex <- factor(psych$sex)

  fit_step <- cox.rvph(
    data = psych,
    time = "time",
```

```
    event = "death",
    covariate = "age",
    adjust_vars = "sex",
    method = "step"
  )

  print(fit_step)
  summary(fit_step)
}

data(pbc, package = "survival")

pbc$status2 <- ifelse(pbc$status == 2, 1, 0)
pbc$ascites <- factor(pbc$ascites)

fit_timev <- cox.rvph(
  data = pbc,
  time = "time",
  event = "status2",
  covariate = "bili",
  adjust_vars = c("ascites", "edema", "protime"),
  method = "timev"
)

print(fit_timev)
summary(fit_timev)
```

print.cox.rvph	<i>Print a cox.rvph Object</i>
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Description

Print a cox.rvph Object

Usage

```
## S3 method for class 'cox.rvph'
print(x, ...)
```

Arguments

x	An object of class "cox.rvph".
...	Additional arguments, currently unused.

summary.cox.rvph	<i>Summarize a cox.rvph Object</i>
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Description

Summarize a cox.rvph Object

Usage

```
## S3 method for class 'cox.rvph'  
summary(object, ...)
```

Arguments

object	An object of class "cox.rvph".
...	Additional arguments, currently unused.

Value

The input "cox.rvph" object, returned invisibly.

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