Package ‘intcure’

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Title Mixture Cure Models with Random Effects

Version 2.1

Description Mixture cure models with random effects to survival data as described in Peng and Taylor (2011) <doi:10.1002/sim.4098>.

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Imports mvtnorm, cubature

License GPL-3

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R topics documented:

intcure-package *Random effects mixture cure models*

Description

Fit random effects mixture cure models

Details

This package fits a mixture cure model with random effects in both latency and incidence parts of the model. The random effects in the two parts can be correlated.

Author(s)

Yingwei Peng

References

Peng, Y. and Taylor, J. M. G. Mixture cure model with random effects for the analysis of a multi-centre tonsil cancer study. Statistics in Medicine, 30:211-223, 2011

basesurvfun *Estimated baseline survival function*

Description

Estimate the baseline survival probabilities at specified time points

Usage

```
basesurvfun(time, intcureobj)
```

Arguments

`time` a vector of time points at which survival probabilities will be calculated.

`intcureobj` an object from `intcure` function

Details

The estimated baseline survival function should be a continuous function and will be smooth if the `basedist = "exponential"` or `"Weibull"`

Value

a vector of the same length as `time` containing the survival probabilities at `time`

Author(s)

Yingwei Peng

See Also

`intcure`

Examples

```
data(bmtfit)
# Estimated baseline survival at 1 year
basesurvfun(1, bmtfit)
plot(function(x)basesurvfun(x, intcureobj = bmtfit), from = 0, to = 6, type = "l")
```

`bmt` *Data from bone marrow transplant patients*

Description

This data set is used in the examples of this package.

Usage

```
data(bmt)
```

Format

A data.frame object with columns:

`time`**:** Disease Free Survival Time (Time To Relapse, Death Or End Of Study).

`cens`**:** Relapse Indicator with 1-Relapsed, 0-Disease Free.

`g`**:** Disease Group with 1-ALL, 2-AML Low Risk, 3-AML High Risk.

`FAB`**:** 1-FAB Grade 4 Or 5 and AML, 0-Otherwise.

`inst`**:** Hospital with 1-The Ohio State University, 2-Alferd , 3-St. Vincent, 4-Hahnemann.

Source

Klein, J. P. & Moeschberger, M. L. Survival Analysis, Techniques for Censored and Truncated Data Spinger-Verlag, 2003

Examples

```
data(bmt)
```

bmtfit *Model fit from a mixture cure model with random effects to bmt data*

Description

This is the result of the model fit `intcure` as shown below

Usage

```
data(bmtfit)
```

Format

A list of class `intcure`

Examples

```
# bmtfit = intcure(Surv(time, cens) ~ g + FAB + cluster(inst), ~ g + FAB,
# data = bmt, basedist = "weibull", sigma = c(-1, NA, NA),
# optimcfg = list(method = "BFGS", hessian = TRUE, maxit = 2000)).
data(bmtfit)
```

coef.intcure *Retrieve coefficients from a fitted mixture cure model with random effects*

Description

It collects all the estimates from a fitted mixture cure model with random effects and forms a long vector.

Usage

```
## S3 method for class 'intcure'
coef(object, ...)
```

Arguments

`object`	an `intcure` object obtained from `intcure`
`...`	inherited but not used here

Value

a vector consists of `bt`, `gm`, `basepara` and `sigma`

Author(s)

Yingwei Peng

See Also

intcure

Examples

```
data(bmtfit)
coef(bmtfit)
```

intcure *Mixture cure models with random effects*

Description

Fit mixture cure models with random effects based on numerical integration.

Usage

```
intcure(
  formula = formula(data),
  cureform = NULL,
  data = sys.parent(),
  subset,
  na.action,
  bt = NULL,
  gm = NULL,
  basepara = NULL,
  sigma = c(0, 0, 0),
 optimcfg = list(ndeps = 0.001, maxit = 1000, reltol = 1e-05, method = "Nelder-Mead",
    hessian = FALSE),
  intcfg = list(eps = 1e-04, lower = c(-5, -5), upper = c(5, 5)),
  basedist = c("exponential", "weibull", "piecewise"),
  npiece = 3,
  piececut = NULL,
  piececuttype = c("quantile", "even"),
  model = FALSE,
  y = TRUE,
  x = FALSE,
  z = FALSE,
  funval = FALSE,
  debug = c("intcure", "integration", "optim")
)
```

Arguments

formula — a formula expression similar to the one used in survreg and coxph. The response is a survival object returned by the Surv() function. It is used to specify the time (and censoring variable) variable and covariates in the model for uncured patients. A covariate that defines clusters in data will be in cluster function. See coxph() for details If random effects are specified in sigma and cluster is not specified, every subject forms its own cluster.

cureform — a formula expression similar to formula except that it does not contain a response. It is used to specify the effects of covariates on the cure rate. A covariate that defines clusters in data will be in cluster function as in formula. However, currently it is not used in the function because we assume that both components in cure model use the same cluster structure If random effects are specified in sigma and cluster is not specified, every subject forms its own cluster.

data, subset, na.action — standard arguments for R model functions

bt — a vector of initial value of beta in the latency model. It is optional. If survreg is used to get initial values, -survreg's bt/survreg's scale = bt

gm — a vector of initial value of gamma in the incidence model. It is optional

basepara — a vector of initial values of the parameters in the baseline distribution. They are the log rate if baseline = "exponential", log shape and log rate if baseline = "weibull", and log hazard if baseline = "piecewise". It is optional. If survreg is used to get initial values, then survreg's scale = 1/weibull shape and survreg's intercept = -log(weibull rate)/weibull shape if basedist = "weibull", and survreg's intercept = -log(rate) if basedist = "exponential". Inappropriate initial values can cause some problems in adaptIntegrate function.

sigma — a vector of 3 corresponding to log standard deviation of u and v, and a Fisher's z-transformed correlation coefficient of u and v. If any of the value is set to NA, the corresponding effects will not be present in the model

optimcfg — a list of method, maxit, reltol, hessian, ndeps arguments for R function optim(). The default optimization method is Nelder-Mead.

intcfg — a list of lower, upper, eps to be passed onto an R integration function. If one random effect is specified, the built-in R integration function integrate is used. If two random effects are specified, R function adaptIntegrate from package cubature is used to do the integration.

basedist — type of baseline distribution. It can be one of "exponential", "weibull", or "piecewise", where "piecewise" stands for piecewise constant hazard distribution. The default is "exponential".

npiece, piececut, piececuttype — arguments for baseline distribution when it is piecewise constant hazard distribution. They are respectively the number of pieces, the cut points to form the pieces and how the pieces are formed. piececut should only include the interior time points and the length of piececut should be equal to npiece -1. There are two ways to specify the piecewise constant hazard distribution: specify piececut or specify npiece and piececuttype. There are two possible types for `piececuttype`: `"quantile"` and `"even"`. `"quantile"` is the default if not specified.

`model` if TRUE, output model matrix instead of fitting the model

`y, x, z` if TRUE, output corresponding matrix in the model matrix

`funval` a logical value. If TRUE, evaluate the likelihood function at initial values instead of fitting the model

`debug` for debug purpose

Details

This package depends on `cubature` package for numerical integration and `mvtnorm` package. Better initial values for `bt`, `gm` and `basepara` obtained from a mixture cure model without random effects may help speed up the program or finding the best estimates.

Value

an object of class `intcure` is returned. It includes all the values returned from `optim()` in addition to the following values:

`call` The call to `intcure`

`basedist` The baseline distribution fitted

`method` The optimization method used

`n` Sample size

Author(s)

Yingwei Peng

References

Peng, Y. and Taylor, J. M. G. Mixture cure model with random effects for the analysis of a multicentre tonsil cancer study. Statistics in Medicine, 30:211-223, 2011

See Also

`survreg`, `coxph`, `glm`

Examples

```
data(simdata)
intcure(Surv(time, cens) ~ rx + cluster(id), ~ rx, data = simdata,
basedist = "weibull", sigma = c(-1, NA, NA), optimcfg = list(maxit = 1000))
```

`print.intcure` *Print method for fitted mixture cure models with random effects*

Description

It prints the estimates of the parameters in the model and the maximum likelihood value.

Usage

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

Arguments

`x`	an `intcure` object obtained from `intcure`
`...`	other standard printing arguments

Value

It will return the object in `x`. This function is called for side effects

Author(s)

Yingwei Peng

See Also

`intcure`

Examples

```
data(bmtfit)
print(bmtfit)
```

`print.summary.intcure` *Print method for summary of fitted mixture cure models with random effects*

Description

It prints the estimates of the parameters, standard errors, z-values, p-values, and the maximum likelihood value from a fitted mixture cure model with random effects.

Usage

```
## S3 method for class 'summary.intcure'
print(x, ...)
```

Arguments

`x`	an `summary.intcure` object obtained from `summary()`
`...`	other standard printing arguments

Value

It will return the object in `x`. This function is called for side effects

Author(s)

Yingwei Peng

See Also

`intcure`

Examples

```
data(bmtfit)
print(summary(bmtfit))
```

`simdata` *Simulated Data*

Description

This is a simulated data set for a testing purpose

Usage

```
data(simdata)
```

Format

A data.frame object with columns:

`time`: Survival time

`cens`: Censoring indicator

`rx`: A binary treatment variable

`id`: Cluster indicator

Examples

```
data(simdata)
```

summary.intcure *Summary of fitted mixture cure models with random effects*

Description

It calculates standard errors, z-values, and p-values of estimates from a fitted mixture cure model with random effects

Usage

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

Arguments

object	an intcure object obtained from intcure
...	inherited but not used here

Value

An object of class summary.intcure is returned. It is a list that includes all the components of class intcure plus an additional component statistics, which is a list of following components:

bt	a matrix with column Estimate, Stderr, zvalue, and pvalue for the estimated value of beta in the latency model
gm	a matrix with column Estimate, Stderr, zvalue, and pvalue for the estimated value of gamma in the incidence model
basepara	a matrix with column Estimate, Stderr, zvalue, and pvalue for the estimated value of the parameters in the baseline distribution
sigma	a matrix with column Estimate and Stderr for the random effects in the model

Author(s)

Yingwei Peng

See Also

intcure

Examples

```
data(bmtfit)
summary(bmtfit)
```

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