

Package ‘cohetsurr’

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Type Package

Title Assessing Complex Heterogeneity in Surrogacy

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Description Provides functions to assess and test for complex heterogeneity in the utility of a surrogate marker with respect to multiple baseline covariates, using both a parametric model and a semiparametric two-step model. More details are available in: Knowlton, R., Tian, L., & Parast, L. (2025). ``A General Framework to Assess Complex Heterogeneity in the Strength of a Surrogate Marker," Statistics in Medicine, 44(5), e70001 <doi:10.1002/sim.70001>. A tutorial for this package can be found at <<https://laylaparast.com/home/cohetsurr.html>>.

License GPL

Imports stats, matrixStats, mvtnorm

NeedsCompilation no

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boot.var	<i>Performs bootstrap estimation procedures for the variance of the proportion of treatment effect explained, the omnibus test, and identifying a region above a threshold</i>
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Description

Performs bootstrap estimation procedures for the variance of the proportion of treatment effect explained, the omnibus test, and identifying a region above a threshold

Usage

```
boot.var(data.control, data.treat, W.grid.expand, type, test = FALSE,
data.all = NULL, num.cov = NULL, results.for.test = NULL, threshold = NULL)
```

Arguments

<code>data.control</code>	dataframe containing data from the control group, specifically the outcome Y, the surrogate S, and the baseline covariates W
<code>data.treat</code>	dataframe containing data from the treatment group, specifically the outcome Y, the surrogate S, and the baseline covariates W
<code>W.grid.expand</code>	expanded version of the W grid of baseline covariates, where each row is a specific combination of the covariates for which the estimates should be provided
<code>type</code>	options are "model", "two step", or "both"; specifies the estimation method that should be used for the proportion of treatment effect explained
<code>test</code>	TRUE or FALSE, if test for heterogeneity is wanted
<code>data.all</code>	dataframe containing data from the control and treatment groups, specifically the outcome Y, the surrogate S, and the baseline covariates W
<code>num.cov</code>	number of baseline covariates in the matrix W
<code>results.for.test</code>	the grid of estimates for the proportion of treatment effect explained obtained prior to bootstrapping, needed for the omnibus test
<code>threshold</code>	threshold to flag regions where the estimated proportion of the treatment effect explained is at least that high

Value

A list is returned:

<code>return.grid</code>	grid of variance estimates for the overall treatment effect, the residual treatment effect, and the proportion of treatment effect explained as a function of the baseline covariates, W. If requested by user, includes regions flagged above the threshold.
<code>pval</code>	p-value(s) from the F test and the two step omnibus test for heterogeneity, depending on type argument

`complex.heterogeneity` *Estimates the proportion of treatment effect explained by the surrogate marker as a function of multiple baseline covariates.*

Description

Assesses complex heterogeneity in the utility of a surrogate marker by estimating the proportion of treatment effect explained by the surrogate marker as a function of multiple baseline covariates. Optionally, tests for evidence of heterogeneity overall and flags regions where the proportion of treatment effect explained is above a given threshold.

Usage

```
complex.heterogeneity(y, s, a, W.mat, type = "model", variance = FALSE,
test = FALSE, W.grid = NULL, grid.size = 4, threshold = NULL)
```

Arguments

y	y, the outcome
s	s, the surrogate marker
a	a, the treatment assignment with 1 indicating the treatment group and 0 indicating the control group
W.mat	matrix of baseline covariate observations, where the first column is W1, second columns is W2, and so on.
type	options are "model", "two step", or "both"; specifies the estimation method that should be used for the proportion of treatment effect explained
variance	TRUE or FALSE, if variance/standard error estimates are wanted
test	TRUE or FALSE, if test for heterogeneity is wanted
W.grid	grid for the baseline covariates W where estimation will be provided
grid.size	number of measures for each baseline covariate to include in the estimation grid, if one is not provided by the user directly
threshold	threshold to flag regions where the estimated proportion of the treatment effect explained is at least that high

Value

A list is returned:

return.grid	grid of estimates for the overall treatment effect, the residual treatment effect, and the proportion of treatment effect explained as a function of the baseline covariates, W. Includes variance estimates and regions flagged above the threshold, if specified by the user.
pval	p-value(s) from the F test and the two step omnibus test for heterogeneity, depending on type argument

Author(s)

Rebecca Knowlton

References

Knowlton, R., Tian, L., & Parast, L. (2025). A General Framework to Assess Complex Heterogeneity in the Strength of a Surrogate Marker. *Statistics in Medicine*, 44(5), e70001

Examples

```
data(exampladata)
names(exampladata)
complex.heterogeneity(y = exampladata$y,
                      s = exampladata$s,
                      a = exampladata$a,
                      W.mat = matrix(cbind(exampladata$w1, exampladata$w2), ncol = 2),
                      type = "model",
                      W.grid = matrix(cbind(exampladata$w1.grid, exampladata$w2.grid), ncol=2))
#computationally intensive

complex.heterogeneity(y = exampladata$y,
                      s = exampladata$s,
```

```

a = exampledata$a,
W.mat = matrix(cbind(exampledata$w1,
exampledata$w2), ncol = 2),
type = "both",
variance = TRUE,
test = TRUE,
W.grid = matrix(cbind(exampledata$w1.grid,
exampledata$w2.grid), ncol = 2),
threshold = 0.75)

```

exampledata

Example data

Description

Example data

Usage

```
data("exampledata")
```

Format

A list with 7 elements representing 1000 observations from a treatment group and 1000 observations from a control group, and a grid of baseline covariate values at which to calculate estimates:

y the outcome

s the surrogate marker

a the treatment assignment, where 1 indicates treatment and 0 indicates control

w1 the first baseline covariate of interest

w2 the second baseline covariate of interest

w1.grid the grid of first baseline covariate values to provide estimates for

w2.grid the grid of second baseline covariate values to provide estimates for

Examples

```

data(exampledata)
names(exampledata)

```

parametric.est	<i>Estimates the proportion of treatment effect explained as a function of multiple baseline covariates, W, using a parametric model</i>
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Description

Estimates the proportion of treatment effect explained as a function of multiple baseline covariates, W, using a parametric model

Usage

```
parametric.est(data.control, data.treat, W.grid.expand)
```

Arguments

data.control	dataframe containing data from the control group, specifically the outcome Y, the surrogate S, and the baseline covariates W
data.treat	dataframe containing data from the treatment group, specifically the outcome Y, the surrogate S, and the baseline covariates W
W.grid.expand	expanded version of the W grid of baseline covariates, where each row is a specific combination of the covariates for which the estimates should be provided

Value

grid of estimates of the proportion of treatment effect explained, the overall treatment effect, and the residual treatment effect for the given baseline covariate combinations

two.step.est	<i>Estimates the proportion of treatment effect explained as a function of multiple baseline covariates, W, using a two step, semiparametric model</i>
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Description

Estimates the proportion of treatment effect explained as a function of multiple baseline covariates, W, using a two step, semiparametric model

Usage

```
two.step.est(data.control, data.treat, W.grid.expand.function)
```

Arguments

data.control	dataframe containing data from the control group, specifically the outcome Y, the surrogate S, and the baseline covariates W
data.treat	dataframe containing data from the treatment group, specifically the outcome Y, the surrogate S, and the baseline covariates W
W.grid.expand.function	expanded version of the W grid of baseline covariates, where each row is a specific combination of the covariates for which the estimates should be provided

Value

grid of estimates of the proportion of treatment effect explained, the overall treatment effect, and the residual treatment effect for the given baseline covariate combinations

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