

Package ‘quint’

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Type Package

Title Qualitative Interaction Trees

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Description Grows a qualitative interaction tree. Quint is a tool for subgroup analysis, suitable for data from a two-arm randomized controlled trial.

URL http://www.elisedusseldorp.nl/pdf/Dusseldorpetal2015BRM_QUINT.pdf

Depends R (>= 3.0.2), partykit, Formula, rpart, stats

License GPL-2

LazyData TRUE

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`quint-package`*R package for Qualitative Treatment-Subgroup Interactions*

Description

When two treatment alternatives (say A and B) are available for some problem, one may be interested in qualitative treatment-subgroup interactions. Such interactions imply the existence of subgroups of persons (patients) which are such that in one subgroup Treatment A outperforms Treatment B, whereas the reverse holds in another subgroup. Obviously, this type of interactions is crucial for optimal treatment assignment of future patients. Given baseline characteristics and outcome data from a two-arm Randomized Controlled Trial (RCT), QQualitative INteraction Trees (QUINT) is a tool to identify subgroups that are involved in meaningful qualitative treatment-subgroup interactions. The result of QUINT is a tree that partitions the total group of participants (patients) on the basis of their baseline characteristics into three subgroups (i.e., partition classes): Subgroup 1: Those for whom Treatment A is better than Treatment B (P1), Subgroup 2: Those for whom Treatment B is better than Treatment A (P2), and Subgroup 3: Those for whom it does not make any difference (P3).

Details

Package: `quint`
Type: `Package`
Version: `1.2`
Date: `2016-22-04`
License: `GPL`

This method is suitable for a continuous outcome variable. From version 1.2 onwards the baseline variables for growing a tree may have numerical or integer values (such as continuous, ordinal or dichotomous variables) or may be nominal (categorical variables with factors). Previously only numerical or dichotomous variables were supported. Another new feature of this version is that the output of a `quint` object can now also display results for either the raw difference in means or the effect size with corresponding standard error. This depends on the criterion specified. Furthermore a `predict.quint` function is newly included in this package. The final new feature is a `validate.quint` function for estimating the bias (i.e., optimism) of a grown QUINT tree.

The core function of the package is `quint`.

Author(s)

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References

Dusseldorp E., Doove L. and Van Mechelen, I. Quint: An R package for the identification of subgroups of clients who differ in which treatment alternative is best for them. *Behavior research*

methods (ahead-of-print), 1-14. DOI: 10.3758/s13428-015-0594-z.

Dusseldorp E. and Van Mechelen I. (2014). Qualitative interaction trees: a tool to identify qualitative treatment-subgroup interactions. *Statistics in Medicine*, 33(2), 219-237. DOI: 10.1002/sim.5933.

Scheier M.F., Helgeson V.S., Schulz R., et al.(2007). Moderators of interventions designed to enhance physical and psychological functioning among younger women with early-stage breast cancer. *Journal of Clinical Oncology*, 25, 5710-5714. DOI: 10.1200/JCO.2007.11.7093.

See Also

[quint.summary.quint](#), [quint.control](#), [prune.quint](#), [predict.quint](#), [quint.validate](#)

bcrp

Breast Cancer Recovery Project

Description

Data from a three-arm randomized controlled trial. Women with early-stage breast cancer were randomly assigned to a nutrition intervention ($n = 85$), an education intervention ($n = 83$) or standard care ($n = 84$). They were measured before and after treatment. These data contain the baseline measurement and the 9-month follow-up.

Usage

bcrp

Format

A data frame with 252 observations on the following 14 variables:

physt1 physical functioning (from SF-36) at baseline.

cesdt1 depression score (CESD) at baseline.

physt3 physical functioning (from SF-36) at 9 months follow-up.

cesdt3 depression score (CESD) at 9 months follow-up.

negsoct1 negative social interaction at baseline.

uncomt1 unmitigated communion at baseline.

disopt1 dispositional optimism at baseline.

comorbid number of comorbidities (e.g. diabetes, migraines, arthritis, or angina).

age age at baseline.

wcht1 weight change since diagnosis: yes [1] or no [0].

nationality Caucasian [1] or not [0].

marital married [1] or not [0].

trext treatment extensiveness index: lumpectomy without or with one form of adjuvant therapy (radiation or chemo) [-1.77], lumpectomy with radiation and chemotherapy [0.26], mastectomy without or with lumpectomy, and without or with one form of adjuvant therapy [0.56], mastectomy without or with lumpectomy, and radiation and chemotherapy [2.59].

cond experimental condition: nutrition [1], education [2] or standard care [3].

Details

IMPORTANT: for questions about these data contact Elise Dusseldorp: elise.dusseldorp@fsw.leidenuniv.nl.

Source

The authors thank M.F. Scheier for making his data available.

References

If you use these data, please refer to: Scheier M.F., Helgeson V.S., Schulz R., et al. (2007). Moderators of interventions designed to enhance physical and psychological functioning among younger women with early-stage breast cancer. *Journal of Clinical Oncology*, 25, 5710-5714.

An example of a complete analysis on these data using the quint package is given in: Dusseldorp E., Doove L. and Van Mechelen I. (2015). Quint: An R package for the identification of subgroups of clients who differ in which treatment alternative is best for them. *Behavior research methods (ahead-of-print)*, 1-14. DOI: 10.3758/s13428-015-0594-z.

An application of quint to these data is given in: Dusseldorp E. and Van Mechelen I. (2014). Qualitative interaction trees: a tool to identify qualitative treatment-subgroup interactions. *Statistics in Medicine*, 33(2), 219-237. DOI: 10.1002/sim.5933.

plot.quint

Visualisation of a Qualitative Interaction Tree

Description

Plot function for a quint object. The plot shows the result of quint: a binary tree with (a) splitting variable(s) and split point(s). The colors of the leaves of the tree correspond to the final subgroups: Subgroup 1 (P1), those patients for whom the mean treatment outcome (Y) is higher for Treatment A than B, is GREEN; Subgroup 2 (P2), those patients for whom the mean treatment outcome (Y) is higher for Treatment B than A, is RED, and Subgroup 3 (P3), those for whom the mean treatment outcome (Y) is about the same for both treatments, is GREY. Within the leaves the effect size d is displayed, with its 95 percent confidence interval. This effect size is the standardized mean difference between Treatment A and B. The plot function uses the plot method from the package **partykit** of Hothorn & Zeileis (2013).

Usage

```
## S3 method for class 'quint'
plot(x, digits = 2, ...)
```

Arguments

x	fitted tree of class quint.
digits	specified number of decimal places of the splitpoints in the graph (default is 2).
...	additional arguments to be passed.

Details

For categorical variables we recommend to use short names for levels to avoid overlapping labels at split points.

Author(s)

Cor Ninaber and Elise Dusseldorp

References

Torsten Hothorn and Achim Zeileis (2013). partykit: A Toolkit for Recursive Partytioning. R package version 0.1-5.

See Also

[quint,quint.control,bcrp](#)

predict.quint

Predictions for new data with a QUINT object

Description

Predicts for (new) subjects the treatment subgroups (P1, P2 or P3) based on a fitted quint object. The meaning of the subgroups are based on the two treatment categories used to fit the quint object.

Usage

```
## S3 method for class 'quint'
predict(object, newdata, type = "class", ...)
```

Arguments

object	an object of the class “quint”.
newdata	a data frame with data on new subjects for whom predictions should be made. The data frame should contain at least the variables used in the splits of the fitted tree. It is not necessary to include the treatment variable.
type	character string denoting the type of predicted object to be returned. The default is set to type="class": a vector with predicted treatment subgroup classes per subject is returned. If set to "matrix", a matrix is returned with the leaf and corresponding node of the tree to which a subject is assigned.
...	optional additional arguments.

Value

One of the following objects is returned depending on output type specified in the function:

If `type="class"`: vector of predicted treatment classes for every individual in the data set. Returns NA for subjects with missing values on one or more of the splitting variables.

If `type="matrix"`: a matrix with predicted locations of subjects within the fitted tree. The leaf numbers are in the first column and the corresponding node numbers in the second column. Returns NA for subjects with missing values on one or more of the splitting variables.

See Also

[quint](#), [prune.quint](#)

Examples

```
data(bcrp)
formula1<- I(cesdt1-cesdt3)~cond | nationality+marital+wcht1+age+
  trext+comorbid+disopt1+uncomt1+negsoct1

set.seed(10)
control1<-quint.control(maxl=5,B=2)
quint1<-quint(formula1, data= subset(bcrp,cond<3),control=control1) #Grow a QUINT tree

prquint1<-prune(quint1) #Prune QUINT tree to optimal size

#Predict for the same data set the treatment classes for patients individually:
predquint1<-predict(prquint1, newdata=subset(bcrp,cond<3), type='class')
predquint1
```

prune.quint

Pruning of a Qualitative Interaction Tree

Description

Determines the optimally pruned size of the tree by applying the one standard error rule to the results from the bias-corrected bootstrap procedure.

Usage

```
## S3 method for class 'quint'
prune(tree, pp = 1, ...)
```

Arguments

<code>tree</code>	fitted tree of the class <code>quint</code> .
<code>pp</code>	pruning parameter, the constant (c) to be used in the c *standard error rule. The default value is 1.
<code>...</code>	optional additional arguments.

Details

The pruning algorithm of `quint` is explained in Dusseldorp & Van Mechelen (2014), Appendix B of the online supplementary material. It is based on the bias-corrected bootstrap pruning procedure (Le Blanc & Crowley, 1993) and the one standard error rule (Breiman, Friedman, Olshen, & Stone, 1984). The one standard error rule for `quint` uses the estimates of the bias-corrected criterion value (C) and its standard error for each value of L (= maximum number of leaves). The optimally pruned tree corresponds to the smallest tree with a bias-corrected C higher or equal to the maximum bias-corrected C minus its standard error.

Value

Returns an object of class `quint`. The number of leaves of this object is equal to the optimally pruned size of the tree.

References

- Breiman L., Friedman J.H., Olshen R.A. and Stone C.J. (1984). *Classification and Regression Trees*. Chapman & Hall/CRC: Boca Raton.
- Dusseldorp E. and Van Mechelen I. (2014). Qualitative interaction trees: a tool to identify qualitative treatment-subgroup interactions. *Statistics in Medicine*, 33(2), 219-237. DOI: 10.1002/sim.5933.
- LeBlanc M. and Crowley J. (1993). Survival trees by goodness of split. *Journal of the American Statistical Association*, 88, 457-467.

See Also

[quint.control](#), [quint](#)

Examples

```
data(bcrp)
formula2<- I(cesdt1-cesdt3)~cond |age+trext++uncomt1+ disopt1+negsoct1
#Adjust the control parameters only to save computation time in the example;
#The default control parameters are preferred
control2<-quint.control(maxl=6,B=2)
set.seed(2) #this enables you to repeat the results of the bootstrap procedure
quint2<-quint(formula2, data= subset(bcrp,cond<3),control=control2)
quint2pr<-prune(quint2)
summary(quint2pr)
```

Description

This is the core function of the package. It performs a subgroup analysis by QUalitative INteraction Trees (QUINT; Dusseldorp & Van Mechelen, 2014) and is suitable for data from a two-arm randomized controlled trial. Ingredients of the analysis are: one continuous outcome variable Y (the effect variable), one dichotomous treatment variable T (indicating two treatment conditions, e.g., A and B), and several background characteristics X_1, \dots, X_J . These background characteristics are measured at baseline and may have a numeric or ordinal measurement level (i.e., in R a numeric or integer variable) or a nominal measurement level (i.e., in R a factor). They are used to identify the following subgroups (i.e., partition classes): Subgroup 1: Those patients for whom Treatment A is better than Treatment B (P1); Subgroup 2: Those for whom Treatment B is better than Treatment A (P2), and Subgroup 3: Those for whom it does not make any difference (P3).

Usage

```
quint(formula, data, control = NULL)
```

Arguments

formula	a description of the model to be fit. The format is $Y \sim T \mid X_1 + \dots + X_J$, where the variable before the $ $ represents the dichotomous treatment variable T and the variables after the $ $ are the baseline characteristics used for partitioning. If the data are in the order Y, T, X_1, \dots, X_J , no formula is needed. The lay-out of this formula is based on Zeileis & Croissant (2010).
data	a dataframe containing the variables in the model. The treatment variable can be a numeric or a factor variable with two values (or levels).
control	a list with control parameters as returned by quint.control .

Details

The method QUINT uses a sequential partitioning algorithm. The algorithm starts with a tree consisting of a single node, that is, the root node containing all patients. Next, it follows a stepwise binary splitting procedure. This procedure implies that in each step a node, a baseline characteristic, a split of that characteristic, and an assignment of the leaves of the current tree to partition classes 1, 2, and 3 (P1 to P3) are chosen that maximize the partitioning criterion. Note that this means that after each split, all leaves of the tree are re-assigned afresh to the partition classes P1, P2, and P3.

Value

Returns an object of class `quint` with components:

call	the call that created the object.
crit	the partitioning criterion used to grow the tree. The default is the Effect size criterion. Use <code>crit="dm"</code> for the Difference in means criterion.
control	the control parameters used in the analysis.
fi	the fit information of the final tree.
si	the split information of the final tree.

li	the leaf information of the final tree. Treatment A is denoted with T=1, and treatment B is denoted with T=2. Can display either the output for Difference in Means (crit='dm') or Cohen's <i>d</i> effect size (crit='es').
data	the data used to grow the tree.
nind	an $N \times L$ matrix indicating leaf membership.
siboot	an $L \times 9 \times B$ array with split information for each bootstrap sample: C_boot = value of <i>C</i> ; C_compdif = value of Difference in treatment outcome component; checkdif = indicates if pooled Difference in treatment outcome component in test set (i.e., original sample) is positive, with values: 0 = yes, 1 = negative in P1, 2 = negative in P2, 3 = negative in P1 and P2; C_compcard = value of Cardinality component; checkcard = indicates if value of pooled cardinality in test set is zero, with values: 0 = no, 1 = zero in P1, 2 = zero in P2, 3 = zero in P1 and P2; opt = value of optimism (C_boot - C_orig).
indexboot	an $N \times B$ matrix indicating bootstrap sample membership.

References

- Dusseldorp E., Doove L. and Van Mechelen I. Quint: An R package for the identification of subgroups of clients who differ in which treatment alternative is best for them. *Behavior research methods (ahead-of-print)*, 1-14. DOI: 10.3758/s13428-015-0594-z.
- Dusseldorp E. and Van Mechelen I. (2014). Qualitative interaction trees: a tool to identify qualitative treatment-subgroup interactions. *Statistics in Medicine*, 33(2), 219-237. DOI: 10.1002/sim.5933.
- Zeileis A. and Croissant Y. (2010). Extended model formulas in R: Multiple parts and multiple responses. *Journal of Statistical Software*, 34(1), 1-13.

See Also

[summary.quint](#), [quint.control](#), [prune.quint](#), [bcrp](#)

Examples

```
#EXAMPLE with data from the Breast Cancer Recovery Project
data(bcrp)
#Start with expliciting the model for quint
#The outcome Y is a change score between timepoint 3 and timepoint 1
#A positive Y value indicates an improvement in depression (i.e., a decrease)

formula1<- I(cesdt1-cesdt3)~cond | nationality+marital+wcht1+age+
  trext+comorbid+disopt1+uncomt1+negsoct1

#Perform a quint analysis
#The BCRP data contain 3 conditions. Quint only works now for 2 conditions.
#For the example, we disregard the control condition
#To save computation time, we also adjust the control parameters

set.seed(2)
control1<-quint.control(maxl=5,B=2)
quint1<-quint(formula1, data= subset(bcrp,cond<3),control=control1)
```

```
#Inspect the main results of the analysis:
summary(quint1)

#Inspect the assignments of the patients to the leaves of the tree
quint1$kind

#plot the tree
plot(quint1)
```

quint.control *Control Parameters for QUINT Algorithm*

Description

Various parameters that control aspects of the “quint” algorithm. Appendix A of Dusseldorp & Van Mechelen (2013) gives a detailed overview of the choices that can be made.

Usage

```
quint.control(crit = "es", maxl = 10, a1 = NULL, a2 = NULL, w = NULL,
  Bootstrap = TRUE, B = 25, dmin = 0.3)
```

Arguments

crit	the type of difference in treatment outcome used in the partitioning criterion: "es" (Treatment effect sizes) or "dm" (Difference in treatment means).
maxl	maximum number of leaves (L) of the tree. Default value is 10.
a1	the minimal sample size of Treatment A ($T = 1$) in a leaf.
a2	the minimal sample size of Treatment B ($T = 2$) in a leaf.
w	a vector with w_1 and w_2 representing the weights of, respectively, the Difference in treatment outcome component and the Cardinality component of the partitioning criterion. If $\text{crit} = \text{"dm"}$, the default value of w_1 is $1/\log(1 + IQR(Y))$. If $\text{crit} = \text{"es"}$, the default value of w_1 is $1/\log(1 + 3)$. The default of w_2 is $1/\log(0.50N)$.
Bootstrap	whether the bias-corrected bootstrap procedure should be performed. The default is TRUE.
B	the number of bootstrap samples to be drawn. The default is 25.
dmin	the minimum absolute standardized mean difference in treatment outcome in each of the two leaves after the first split of the tree. This value is used to check whether a qualitative interaction is present in the data (the qualitative interaction condition); dmin controls the balance between Type I error and Type II error. The default value of dmin is 0.30.

Value

A list containing the options.

References

- Dusseldorp E., Doove L. and Van Mechelen I. (2015). Quint: An R package for the identification of subgroups of clients who differ in which treatment alternative is best for them. *Behavior research methods (ahead-of-print)*, 1-14. DOI: 10.3758/s13428-015-0594-z.
- Dusseldorp E. and Van Mechelen I. (2014). Qualitative interaction trees: a tool to identify qualitative treatment-subgroup interactions. *Statistics in Medicine*, 33(2), 219-237. DOI: 10.1002/sim.5933.

See Also

[quint](#)

Examples

```
data(bcrp)
formula1<- I(cesdt1-cesdt3)~cond | nationality+marital+wcht1+age+
  trext+comorbid+disopt1+uncomt1+negoct1
#Specify the Difference in treatment outcome as Difference in means
#and skip the bias-corrected bootstrap procedure
#and change the maximum number of leaves
control3<-quint.control(crit="dm",Bootstrap=FALSE,maxl=3)
quint3<-quint(formula1, data= subset(bcrp,cond<3),control=control3)
summary(quint3)

#Set number of bootstrap samples at 10
control4<-quint.control(B=10)

#Set minimal sample size in each treatment group at 5
control5<-quint.control(a1=5,a2=5)
```

quint.validate

Validation of a Qualitative Interaction Tree

Description

A bootstrap-based validation procedure to estimate the optimism in the effect sizes of a QUINT tree which gives insight in the generalizability of the results.

Usage

```
quint.validate(object, B = 10, allresults = FALSE)
```

Arguments

object	a (pruned) QUINT tree object of class quint.
B	number of bootstrap samples. Default number is 10; for better accuracy B=1000 is recommended.
allresults	option to return an extended list of output. Default is set to FALSE. See <i>Value</i> section for details.

Details

In this procedure bootstrap trees are grown of the same leaf size as the (pruned) QUINT tree. The bootstrap samples are drawn from the data used to grow the original tree. For every bootstrap tree the largest and smallest (i.e., largest negative) treatment mean differences (or treatment effect sizes) of two leaves are saved. Treatment mean differences in the leaves are then predicted using the original data set as input for each bootstrapped tree. From these predictions, the largest and smallest treatment mean differences are saved. For each bootstrap tree, the largest predicted treatment effect is subtracted from the largest treatment effect in the bootstrap sample. The average of these values is the bias (i.e., the optimism) for the largest treatment effects. This is done likewise for the smallest treatment effects. Subsequently, the bias is computed as the difference between the bias for the largest effects minus the bias for the smallest effects.

The details of this validation procedure are described in Appendix C of Dusseldorp & Van Mechelen (2014).

Value

Returns a list with the following components:

estopt	the estimated optimism for either the treatment effect size (biasd) or the raw treatment mean difference (biasdif).
li	a data frame with leaf information output similar to the leaf information output of the (pruned) QUINT tree object. An extra column is added for the bias-corrected differences in treatment outcomes (d or diff). The bias-corrected values are only computed for the leaves with the most extreme values, i.e. the largest and smallest treatment effects. Hence, the other leaves get the value NA in this column.
optd	a matrix with computed estimated optimism of the treatment effect size per bootstrapped tree. The first column contains the difference between the largest and smallest effect size of the bootstrapped tree. The second column contains the difference between the largest and smallest predicted effect size. Returned when <code>allresults</code> is set to TRUE and <code>crit='es'</code> is specified in the QUINT object.
optdif	a matrix with computed estimated optimism of the raw mean difference bootstrapped tree. The first column contains the difference between the largest and smallest raw mean difference of the bootstrapped tree. The second column contains the difference between the largest and smallest predicted raw mean difference. Returned when <code>allresults</code> is set to TRUE and <code>crit='es'</code> is specified in the QUINT object.
resultd	a vector with the estimated overall mean optimism, the mean bias for the smallest and for the largest effect size. Returned when <code>allresults</code> is set to TRUE and <code>crit="es"</code> .
resultdif	a vector with the estimated overall mean optimism, the mean bias for the smallest and largest raw mean difference. Returned when <code>allresults</code> is set to TRUE and <code>crit="dm"</code> .

References

Dusseldorp E. and Van Mechelen I. (2014). Qualitative interaction trees: a tool to identify qualitative treatment-subgroup interactions. *Statistics in Medicine*, 33(2), 219-237. DOI: 10.1002/sim.5933.

See Also

[quint](#), [prune.quint](#), [quint.control](#)

Examples

```
data(bcrp)
formula1<- I(cesdt1-cesdt3)~cond | nationality+marital+wcht1+age+
  trext+comorbid+disopt1+uncomt1+negsoct1

set.seed(10)
control1<-quint.control(maxl=5,B=2)
quint1<-quint(formula1, data= subset(bcrp,cond<3),control=control1) #Grow a QUINT tree

prquint1<-prune(quint1) #Prune tree to optimal size

set.seed(3)
valquint1<-quint.validate(prquint1, B=10) #estimate the optimism by bootstrapping 10 times
valquint1
```

summary.quint

Summarizing Qualitative Interaction Tree Information

Description

Summary method for an object of class `quint`.

Usage

```
## S3 method for class 'quint'
summary(object, digits = 2, ...)
```

Arguments

<code>object</code>	a <code>quint</code> object. This can be the output of quint .
<code>digits</code>	specified number of decimal places (default is 2).
<code>...</code>	optional additional arguments.

Details

This function is a method for the generic function `summary` for class `quint`. It extracts the following essential components from a `quint` object: 1) Specification of the partitioning criterion; 2) Fit information; 3) Split information, and 4) Leaf information.

Value

prints a summarized version of the quint output.

Examples

```
data(bcrp)
formula1<- I(cesdt1-cesdt3)~cond | nationality+marital+wcht1+
  age+trext+comorbid+disopt1+uncomt1+negsoct1
control1<-quint.control(max1=5,Bootstrap=FALSE)
quint1<-quint(formula1, data= subset(bcrp,cond<3),control=control1 )
summary(quint1)
```

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