Package 'QualInt'

February 19, 2015

Title Test for Qualitative Interactions

Version 1.0.0

Author Lixi Yu, Eun-Young Suh, Guohua (James) Pan

Maintainer Lixi Yu <lixi-yu@uiowa.edu>

Description Used for testing for qualitative interactions between treatment effects and patient subgroups. Here the term treatment effect means a comparison result of two treatments within each patient subgroup. Models included in this package are Gaussian, binomial and Cox models. Methods included here are interval based graphical approach and Gail Simon LRT.

Depends survival, ggplot2

License GPL-2

LazyLoad yes

NeedsCompilation no

Repository CRAN

Date/Publication 2014-10-13 09:58:21

R topics documented:

QualInt-package *R-package for qualitative interaction test*

Description

Test for qualitative interactions between treatment effects and patient subgroups for continuous, binary and suvival responses. The term treatment effect means a comparison result between two treatments within each patient subgroup.

Details

Package:	QualInt
Type:	Package
Version:	1.0.0
Date:	2014-10-13
License:	GPL-2

This package could be used to calculate the pvalue and power for qualitative interaction testing. Two testing methods are included in the package, which are Interval Based Graphical Approach and Gail Simon Likelihood Ratio Test.

For a complete list of all the functions available in this package with individual help pages, use library(help = "QualInt")

Author(s)

Lixi Yu, Eun-Young Suh, Guohua (James) Pan
Maintainer: Lixi Yu <lixi-yu@uiowa.edu>

References

Gail and Simon (1985), Testing for qualitative interactions between treatment effects and patient subsets, Biometrics, 41, 361-372.

Pan and Wolfe (1993), Tests for generalized problems of detecting qualitative interaction, Technical Report No. 526, Department of Statistics, The Ohio State University.

Pan and Wolfe (1997), Test for qualitative interaction of clinical significance, Statistics in Medicine, 16, 1645-1652.

Examples

```
test9 <- qualval(effect = c(1.0, 0.5, -2.0), se = c(0.86, 0.64, 0.32))
print(test9)
plot(test9)

#### Continuous ####
ynorm <- rnorm(300)
trtment <- sample(c(0, 1), 300, prob = c(0.4, 0.6),
```

```
                  replace = TRUE)
subgrp <- sample(c(0, 1, 2), 300, prob = c(1/3, 1/3, 1/3),
                 replace = TRUE)
test1 <- qualint(ynorm, trtment, subgrp)
test2 <- qualint(ynorm, trtment, subgrp, test = "LRT")
plot(test1)
print(test1)
coef(test1)
ibga(test1)

#### Binary ####
ybin <- sample(c(0, 1), 300, prob = c(0.3, 0.7),
               replace = TRUE)
test4 <- qualint(ybin, trtment, subgrp, type = "binary")

#### Survival ####
time <- rpois(300, 200)
censor <- sample(c(0, 1), 300, prob = c(0.7, 0.3),
                 replace = TRUE)
test6 <- qualint(Surv(time, censor), trtment, subgrp)
```

`coef.qualint` *Extract estimation results from a "qualint" object*

Description

Similar to other coef methods, this function extracts the estimation results from an "qualint" object.

Usage

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

Arguments

`object`	a qualint object
`...`	not used. Additional print arguments

Details

This function extracts the results related with estimating results of the interaction test from a "qualint" object. It returns a matrix which contains the estimating results of the treatment effects which will used directly in the testing process later. FOr continuous responses, it is the mean difference. For binary responses, it is the risk difference, log relative risk or log odds ratio. For survival responses, it it the log hazard ratio.

Value

A numeric matrix (see above). For `type = "continuous"`, it is the estimation results for mean difference. For `type = "binary"`, it is for risk difference, log relative risk or log odds ration. For `type = "survival"`, it is for log hazard ratio.

Author(s)

Lixi Yu, Eun-Young Suh, Guohua (James) Pan
Maintainer: Lixi Yu <lixi-yu@uiowa.edu>

References

Gail and Simon (1985), Testing for qualitative interactions between treatment effects and patient subsets, Biometrics, 41, 361-372.

Pan and Wolfe (1993), Tests for generalized problems of detecting qualitative interaction, Technical Report No. 526, Department of Statistics, The Ohio State University.

Pan and Wolfe (1997), Test for qualitative interaction of clinical significance, Statistics in Medicine, 16, 1645-1652.

See Also

`print.qualint`, `plot.qualint`

Examples

```
ynorm <- rnorm(300)
trtment <- sample(c(0, 1), 300, prob = c(0.4, 0.6),
                  replace = TRUE)
subgrp <- sample(c(0, 1, 2), 300, prob = c(1/3, 1/3, 1/3),
                 replace = TRUE)
test1 <- qualint(ynorm, trtment, subgrp)
coef(test1)
```

---

ibga *Extract IBGA results from a "qualint" object*

Description

Extract the testing results of IBGA from a "qualint" object. Only available when `test = "IBGA"`. Produce an error signal if `test = "LRT"`.

Usage

```
ibga(x)
```

Arguments

x	a qualint object

Details

This function extracts the results related with the IBGA graph from a "qualint" object, which is a matrix which contains the estimating and testing information of the treatment effects (see examples). FOr continuous responses, it is the mean difference. For binary responses, it is the risk difference, relative risk or odds ratio. For survival responses, it it hazard ratio.

Value

A numeric matrix depending on `scale` (see above).

Author(s)

Lixi Yu, Eun-Young Suh, Guohua (James) Pan
Maintainer: Lixi Yu <lixi-yu@uiowa.edu>

References

Gail and Simon (1985), Testing for qualitative interactions between treatment effects and patient subsets, Biometrics, 41, 361-372.

Pan and Wolfe (1993), Tests for generalized problems of detecting qualitative interaction, Technical Report No. 526, Department of Statistics, The Ohio State University.

Pan and Wolfe (1997), Test for qualitative interaction of clinical significance, Statistics in Medicine, 16, 1645-1652.

See Also

`coef.qualint`

Examples

```
ynorm <- rnorm(300)
trtment <- sample(c(0, 1), 300, prob = c(0.4, 0.6),
                  replace = TRUE)
subgrp <- sample(c(0, 1, 2), 300, prob = c(1/3, 1/3, 1/3),
                 replace = TRUE)
test1 <- qualint(ynorm, trtment, subgrp)
ibga(test1)
```

---

plot.qualint *Plot the interval based graph from a "qualint" object*

Description

Produce an interval based graph from an "qualint" object. Only available when `test = "IBGA"`. Produce an error signal if `test = "LRT"`.

Usage

```
## S3 method for class 'qualint'
plot(x, ...)
```

Arguments

x	a qualint object
...	additional coef arguments

Details

Differect scales are used here for different types of responses. For continous one, the mean differece is plotted. For binary one, one from the risk difference, relative risk or odds ratio will be plotted, depending on user's choice. For survival responses, the hazard ratio is plotted.

Author(s)

Lixi Yu, Eun-Young Suh, Guohua (James) Pan
Maintainer: Lixi Yu <lixi-yu@uiowa.edu>

References

Gail and Simon (1985), Testing for qualitative interactions between treatment effects and patient subsets, Biometrics, 41, 361-372.

Pan and Wolfe (1993), Tests for generalized problems of detecting qualitative interaction, Technical Report No. 526, Department of Statistics, The Ohio State University.

Pan and Wolfe (1997), Test for qualitative interaction of clinical significance, Statistics in Medicine, 16, 1645-1652.

See Also

print.qualint, coef.qualint

Examples

```
ynorm <- rnorm(300)
trtment <- sample(c(0, 1), 300, prob = c(0.4, 0.6),
                  replace = TRUE)
subgrp <- sample(c(0, 1, 2), 300, prob = c(1/3, 1/3, 1/3),
                 replace = TRUE)
test1 <- qualint(ynorm, trtment, subgrp)
plot(test1)
```

`print.qualint` *Print a summary of a "qualint" object*

Description

Similar to other print methods, this function prints a summary from an "qualint" object.

Usage

```
## S3 method for class 'qualint'
print(x, digits = max(3, getOption("digits") - 3), ...)
```

Arguments

`x`	a qualint object
`digits`	significant digits in printout
`...`	not used. Additional print arguments

Details

This function prints the important information in a format that's easier for people to understand from a "qualint" object (see examples).

Value

A summary of the testing results (see above).

Author(s)

Lixi Yu, Eun-Young Suh, Guohua (James) Pan
Maintainer: Lixi Yu <lixi-yu@uiowa.edu>

References

Gail and Simon (1985), Testing for qualitative interactions between treatment effects and patient subsets, Biometrics, 41, 361-372.

Pan and Wolfe (1993), Tests for generalized problems of detecting qualitative interaction, Technical Report No. 526, Department of Statistics, The Ohio State University.

Pan and Wolfe (1997), Test for qualitative interaction of clinical significance, Statistics in Medicine, 16, 1645-1652.

See Also

`coef.qualint`, `plot.qualint`

Examples

```
ynorm <- rnorm(300)
trtment <- sample(c(0, 1), 300, prob = c(0.4, 0.6),
                  replace = TRUE)
subgrp <- sample(c(0, 1, 2), 300, prob = c(1/3, 1/3, 1/3),
                 replace = TRUE)
test1 <- qualint(ynorm, trtment, subgrp)
print(test1)
```

---

qualint *Test for qualitative interactions from complete data*

Description

Test for qualitative interactions between treatment effects and patient subgroups. Perform the testing based on the estimated treatment effects and their standard errors. Output all the results related with qualitative interaction tests as a "qualint" object, which includes all the results related with the testing. Two common tests for qualitative interactions are included: IBGA and LRT, among which IBGA is the default. Useful for three types of responses: continuous, binary and survival data. Complete data is needed as input.

Usage

```
qualint(y, trtment, subgrp, type = c("continuous", "binary", "survival"),
  scale = c("MD", "RD", "RR", "OR", "HR"), test = c("IBGA", "LRT"),
  alpha = 0.05, plotout = FALSE)
```

Arguments

y	response variable. A numeric vector for `type = "continuous"`. A numeric vector with values equal to either 1 or 0 for `type = "binary"`. A "Surv" object for `type = "survival"` (The function `Surv()` in package **survival** produces such a matrix).
trtment	treatment variable. A vector with different values representing different treatment groups. Each element corresponds to the treatment the patient received. Should have the same length as `y`.
subgrp	patient subgroup variable. A vector with the same length as `y` and `trtment`, with different values representing different patient subgroups. Each element corresponds to the patient subgroup the patient belongs to.
type	response type (see above). Three types of responses are included right now: `continuous, binary, survival`. By default, it assumes the response variable is continuous.
scale	the scale type for treatment effects. When `type = "continuous"`, `scale = "MD"` by default (mean difference). When `type = "binary"`, three types of scales are available, which are `scale = "RD"` (risk difference), `"RR"` (relative risk) or `"OR"` (odds ratio). When `type = "survival"`, `scale = "HR"` (hazard ratio).

test	testing method. Choose either "IBGA" (interval based graphical approach) or "LRT" (Gail Simon likelihood ratio test).
alpha	significance level. The type I error for qualitative interaction tesing. The default is 0.05.
plotout	whether output the plot or not for test = "IBGA". There is no plot output for test = "LRT".

Details

In order to test for qualitative interactions between treatment effects and patient subgoups, estimated treatment effects and their standard errors are necessary. For continuous responses, mean difference is derived as the meansure of treatment effects with with its standard error equal to $\sqrt{sd_1^2/n_1 + sd_2^2/n_2}$. For binary responses, three different scales are available to measure the treatment effects: risk difference, log relative risk and log odds ratio. Their standard errors could easily obtained according to formulas. For survival responses, the log hazard ratio is used to evaluate the treatment effects. The cox regression model is used in this function to estimate the log hazard ratio and also its standard error.

For the IBGA graph, however, we plot it according to common measures of treatment effects instead of the one used in the calculation. For continuous responses, mean difference is used since it is the common treament effect scale. For binary responses, the function plots risk difference, relative risk, and odds ratio directly. For survival responses, hazard ratios are plotted instead of log hazard ratios.

In the power calculation, this function assumes the estimated treatment effect scale and its standard errors are equal to the true values. For IBGA method, an explicit formula is available, so it is very easy to calculate the power. For LRT, a simulation is used to assess the power since no explicit formula is available.

Value

An object with S3 class "qualint".

call	the call that produces this object.
n	the sample size for each treatment in each subgroup.
type	response type.
alpha	significance level for the test.
treatment	treatment factors.
reference	reference treatment used for the comparison.
nsbp	the number of patient subgroups.
subgroup	subgroup factors.
scale	the scale type for treatment effects (see above).
effect	estimated treatment effects.
se	standard error of treatment effects estimators.
LowerCI	the lower limit of the confidence interval.
UpperCI	the upper limit of the confidence interval.
test	testing method used here, either "IBGA" or "LRT".

index	the testing index used only for test = "IBGA".
cvalue	the critical value used only for test = "LRT".
LowerTI	the lower limit of the testing interval used when test = "IBGA".
UpperTI	the upper limit of the testing interval used when test = "IBGA".
pvalue	the pvalue for qualitative interactions.
power	the power based on the observed data.
nobs	the number of subjects.
missing	the indexes of subjects with missing values.

Author(s)

Lixi Yu, Eun-Young Suh, Guohua (James) Pan
Maintainer: Lixi Yu <lixi-yu@uiowa.edu>

References

Gail and Simon (1985), Testing for qualitative interactions between treatment effects and patient subsets, Biometrics, 41, 361-372.

Pan and Wolfe (1993), Tests for generalized problems of detecting qualitative interaction, Technical Report No. 526, Department of Statistics, The Ohio State University.

Pan and Wolfe (1997), Test for qualitative interaction of clinical significance, Statistics in Medicine, 16, 1645-1652.

See Also

print.qualint, coef.qualint, plot.qualint, qualval

Examples

```
#### Continuous ####
ynorm <- rnorm(300)
trtment <- sample(c(0, 1), 300, prob = c(0.4, 0.6),
                  replace = TRUE)
subgrp <- sample(c(0, 1, 2), 300, prob = c(1/3, 1/3, 1/3),
                  replace = TRUE)
test1 <- qualint(ynorm, trtment, subgrp)
plot(test1)
print(test1)
coef(test1)
test2 <- qualint(ynorm, trtment, subgrp, plotout = TRUE)
test3 <- qualint(ynorm, trtment, subgrp, test = "LRT")

#### Binary ####
ybin <- sample(c(0, 1), 300, prob = c(0.3, 0.7),
               replace = TRUE)
test4 <- qualint(ybin, trtment, subgrp, type = "binary")
test5 <- qualint(ybin, trtment, subgrp, type = "binary",
                  scale = "RR", test = "LRT")
```

```
#### Survival ####
time <- rpois(300, 200)
censor <- sample(c(0, 1), 300, prob = c(0.7, 0.3),
                 replace = TRUE)
test6 <- qualint(Surv(time, censor), trtment, subgrp)
test7 <- qualint(Surv(time, censor), trtment, subgrp,
                 type = "survival", test = "LRT")
test8 <- qualint(Surv(time, censor), trtment, subgrp,
                 test = "IBGA", plotout = TRUE)
```

---

qualval *Test for qualitative interactions from estimation*

Description

Test for qualitative interactions between treatment effects and patient subgroups from the estimated treatment effect and its standard error directly. Output all the results related with qualitative interaction tests as a "qualint" object, just like the "qualint" function. Two common tests for qualitative interactions are included: IBGA and LRT, among which IBGA is the default. Users need to input the estiamted treatment effect and its standard erro themselves, therefore could accommodate any types of responses.

Usage

```
qualval(effect, se, test = c("IBGA", "LRT"), alpha = 0.05,
  plotout = FALSE)
```

Arguments

effect	treatment effects. A numeric vector as the estimated (for pvalue) or designed (for power) treatment effects for different patient subgroups.
se	standard error of estimated treatmen effects. A numeric vector as the standard error for the estimated treatment effects.
test	testing method. Choose either "IBGA" (interval based graphical approach) or "LRT" (Gail Simon likelihood ratio test).
alpha	significance level. The type I error for qualitative interaction tesing. The default is 0.05.
plotout	whether output the plot or not for test = "IBGA". There is no plot output for test = "LRT".

Details

This function is a more generalized version of qualint in the sense that it could be used for any types of responses. However, comepared to qualint, the user needs to input the estimated (for pvalue) or designed (for power) treatment effects and its standard error by themselves to use this function. It gives more freedom and allows users to choose the method they prefer before testing for qualitative interactions.

Value

An object with S3 class "qualint".

`call`	the call that produces this object.
`n`	the sample size for each treatment in each subgroup.
`type`	response type.
`alpha`	significance level for the test.
`treatment`	treatment factors.
`reference`	reference treatment used for the comparison.
`nsbp`	the number of patient subgroups.
`subgroup`	subgroup factors.
`scale`	the scale type for treatment effects (see above).
`effect`	estimated treatment effects.
`se`	standard error of treatment effects estimators.
`LowerCI`	the lower limit of the confidence interval.
`UpperCI`	the upper limit of the confidence interval.
`test`	testing method used here, either "IBGA" or "LRT".
`index`	the testing index used only for `test = "IBGA"`.
`cvalue`	the critical value used only for `test = "LRT"`.
`LowerTI`	the lower limit of the testing interval used when `test = "IBGA"`.
`UpperTI`	the upper limit of the testing interval used when `test = "IBGA"`.
`pvalue`	the pvalue for qualitative interactions.
`power`	the power based on the observed data.
`nobs`	the number of subjects.
`missing`	the indexes of subjects with missing values.

Author(s)

Lixi Yu, Eun-Young Suh, Guohua (James) Pan
Maintainer: Lixi Yu <lixi-yu@uiowa.edu>

References

Gail and Simon (1985), Testing for qualitative interactions between treatment effects and patient subsets, Biometrics, 41, 361-372.

Pan and Wolfe (1993), Tests for generalized problems of detecting qualitative interaction, Technical Report No. 526, Department of Statistics, The Ohio State University.

Pan and Wolfe (1997), Test for qualitative interaction of clinical significance, Statistics in Medicine, 16, 1645-1652.

See Also

`print.qualint`, `coef.qualint`, `plot.qualint`, `qualint`

Examples

```
test9 <- qualval(effect = c(1.0, 0.5, -2.0), se = c(0.86, 0.64, 0.32))
print(test9)
plot(test9)
```

Index