Package ‘QualInt’

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Title Test for Qualitative Interactions
Version 1.0.0
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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.
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**QualInt-package**

R-package for qualitative interaction test

### Description

Test for qualitative interactions between treatment effects and patient subgroups for continuous, binary and survival 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 p-value 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)

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### References


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

### Examples

```r
test9 <- qualval(effect = c(1.0, 0.5, -2.0), se = c(0.06, 0.64, 0.32))
print(test9)
plot(test9)

### Continuous ###
ynorm <- rnorm(300)
ttment <- sample(c(0, 1), 300, prob = c(0.4, 0.6),
```
coef.qualint

```
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 is 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.

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References
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
plot.qualint

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 is hazard ratio.

Value

A numeric matrix depending on scale (see above).

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References

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

See Also

cdf.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".
plot.qualint

Usage

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

Arguments

- `x`: a qualint object
- `...`: additional coef arguments

Details

Different scales are used here for different types of responses. For continuous one, the mean difference 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.

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References


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

See Also

`print.qualint`, `coef.qualint`

Examples

```r
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

```r
## 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).

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References


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)
treatment <- 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, treatment, 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, treatment, 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).

treatment 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 treatment, 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).
**Details**

In order to test for qualitative interactions between treatment effects and patient subgroups, estimated treatment effects and their standard errors are necessary. For continuous responses, mean difference is derived as the measure of treatment effects 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 treatment 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.

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References
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)

### Continuous ###

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")
## qualval

**Test for qualitative interactions from estimation**

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 estimated treatment effect and its standard error themselves, therefore could accommodate any types of responses.

### Usage

```r
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 treatment 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 testing. 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, compared 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 p-value for qualitative interactions.
power
the power based on the observed data.
nobs
the number of subjects.
missing
the indexes of subjects with missing values.

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References


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)
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