# Package 'ed50'

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**Type** Package

**Title** Estimate ED50 and Its Confidence Interval

**Version** 0.1.1

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**Description** Functions of five estimation method for ED50 (50 percent effective dose) are provided, and they are respectively
Dixon-Mood method (1948) <doi:10.2307/2280071>, Choi's original turning point method (1990) <doi:10.2307/2531453> and it's modified version given by us, as well as logistic regression and isotonic regression. Besides, the package also supports comparison between two estimation results.

**Imports** stats, boot, utils

**License** GPL-3

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**NeedsCompilation** no

**Repository** CRAN

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## Contents

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`bootBC.ci` *Estimate Confidence Interval of ED50 Using Isotonic Regression*

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## Description

Estimate confidence interval of ED50 using isotonic regression based on bootstrap method.

## Usage

```
bootBC.ci(tObserved, tBoot, conf = 0.95)
```

## Arguments

| | |
|---|---|
| `tObserved` | the vector of observed statistics. |
| `tBoot` | The matrix with R rows each of which is a bootstrap replicate of the statistics. |
| `conf` | Confidence level. |

## Examples

```
library(ed50)
library(boot)
pavaData <- preparePava(groupS)
bootResult <- boot(data = groupS,
              statistic = bootIsotonicRegression,
                      R = 10,
                    sim = 'parametric',
                ran.gen = bootIsotonicResample,
                    mle = list(baselinePava = pavaData,
                               firstDose = 2.5,
                          PROBABILITY.GAMMA = 0.5),
           baselinePava = pavaData,
      PROBABILITY.GAMMA = 0.5)
bootBC.ci(tObserved = bootResult$t0[3],
              tBoot = bootResult$t[, 3],
               conf = 0.95)
```

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`bootIsotonicRegression`
*Isotonic Regression Function*

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## Description

Function of isotonic regression.

### Usage

```
bootIsotonicRegression(data, PROBABILITY.GAMMA = 0.5, baselinePava)
```

### Arguments

| | |
|---|---|
| data | the same dataframe called by the boot function. |
| PROBABILITY.GAMMA | the target effect probability in the BCD experiment; default = 0.5 and need not be specified. |
| baselinePava | the dataframe prepared by the function preparePava. |

### Examples

```
library(ed50)
pavaData <- preparePava(groupS)
bootIsotonicRegression(data = groupS, PROBABILITY.GAMMA = 0.5, baselinePava = pavaData)
```

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## bootIsotonicResample *The resample function of isotonic regression*

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### Description

The function is designed as an argument for the boot function of the Canty Bootstrap package.

### Usage

```
bootIsotonicResample(data, mle)
```

### Arguments

| | |
|---|---|
| data | Original experiment data. |
| mle | A list of additional arguments to be used by bootIsotonicResample. |

### Examples

```
library(ed50)
pavaData <- preparePava(groupS)
bootIsotonicResample(data = groupS,
                     mle = list(baselinePava = pavaData,
                                firstDose = 2.5,
                           PROBABILITY.GAMMA = 0.5))
```

## compare *Compare ED50 Estimation of Independent Two-sample Case*

### Description

Test the statistical difference of two independent estimation results of ED50.

### Usage

```
compare(group1, group2, alpha = 0.05)
```

### Arguments

| | |
|---|---|
| group1 | A list object of ED50 estimation. |
| group2 | Another list object of ED50 estimation to be compared with. |
| alpha | The significant level of test. 0.05 is the defaut value. |

### Value

The difference between two groups of ED50 estimation in terms of statistical significance.

### References

Noguchi, K., & Marmolejo-Ramos, F. (2016). Assessing equality of means using the overlap of range-preserving confidence intervals. American Statistician, 70(4), 325-334.

### Examples

```
library(ed50)
ans1 <- estimate(groupS$doseSequence, groupS$responseSequence, method = 'ModTurPoint')
ans2 <- estimate(groupSN$doseSequence, groupSN$responseSequence, method = 'Dixon-Mood')
compare(ans1, ans2)
```

## estimate *Estimate ED50*

### Description

Estimate 50 percent effective dose using different methods.

### Usage

```
estimate(doseSequence, doseResponse, confidence = 0.95,
  method = c("Dixon-Mood", "Choi", "ModTurPoint", "Logistic",
  "Isotonic"), tpCiScale = 2.4/qnorm(0.975), boot.n = 10000)
```

### Arguments

| | |
|---|---|
| doseSequence | A sequence of doses given in order |
| doseResponse | A sequence of response results shown in order |
| confidence | The confidence level of interval estimate |
| method | The method used to estimate ED50, there are five methods here, respectively Dixon-Mood, Choi (Choi's Original Turning Point), ModTurPoint (Modified Turning Point), Logistic (Logistic Regression) and Isotonic (Isotonic Regression). The defaut is Dixon-Mood. |
| tpCiScale | The scale level to enlarge the confidence interval estimated by Modified Turning Point Method. The default value is `2.4/qnorm(0.975)`. |
| boot.n | The number of boot process if Logistic method is chosen to estimate ED50. |

### Value

A list of estimation result consisting of method of estimation, ED50 estimate, standard error of ED50 estimate, confidence level and estimate of confidence interval.

### References

Dixon, W. J., & Mood, A. M. (1948). A method for obtaining and analyzing sensitivity data. Publications of the American Statistical Association, 43(241), 109-126. Choi, S. C. (1990). Interval estimation of the ld50based on an up-and-down experiment. Biometrics, 46(2), 485-492. Pace, N. L., & Stylianou, M. P. (2007). Advances in and limitations of up-and-down methodology: a precis of clinical use, study design, and dose estimation in anesthesia research. Anesthesiology, 107(1), 144-52.

### Examples

```
library(ed50)
estimate(groupS$doseSequence, groupS$responseSequence, method = 'Dixon-Mood')
estimate(groupS$doseSequence, groupS$responseSequence, method = 'Logistic', boot.n = 1000)
```

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## generateData *Generate Simulation Data of Up-and-Down Experiment*

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### Description

The function is used to generate simulation data of up-and-down experiment, and provide three cases that tolerance distribution obeys normal, triangle or chi-square distribution.

### Usage

```
generateData(number, useTurPoint = FALSE, start, doseStep = 1,
  distribution = c("Normal", "Triangle", "Chi-square"), normalMean = 0,
  normalStd = 1, triMean = 0, triWidth = 2, chiDegree = 1)
```

### Arguments

| | |
|---|---|
| number | The number of experiments in a trail. |
| useTurPoint | A logical value indicating whether the parameter number refers to the amount of turning points. The default value is FALSE. |
| start | The first dose level given in this trail. |
| doseStep | A fix value that represents the difference between two adjacent dose levels. |
| distribution | The tolerance distribution, including normal, triangle and chi-square distribution, and the default distribution is N(0, 1). |
| normalMean | Parameter mean of normal distribution, the default value is 0. |
| normalStd | Parameter std of normal distribution, the default value is 1. |
| triMean | Parameter mean of triangle distribution, the default value is 0. |
| triWidth | Parameter width of triangle distribution, the default value is 2. |
| chiDegree | Parameter degree of freedom of chi-square distribution, the default value is 1. |

### Value

A data frame.

### Examples

```
library(ed50)
generateData(number = 20, start = 2, doseStep = 0.2, distribution = 'Normal')
generateData(number = 40, start = 2, doseStep = 0.2, distribution = 'Chi-square')
```

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## groupS *A Real Experiment Dose Data*

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### Description

A group of real experiment data based on up-and-down method.

### Usage

```
groupS
```

### Format

A data of 36 samples and 2 variables:

**responseSequence** A value of 0 or 1 indicating the experiment outcome. 0 refers to a failure outcome while 1 refers to a success.

**doseSequence** The dose given in each experiment.

## Source

The data is from the article in the references below.

## References

Niu B, Xiao JY, Fang Y, et al. Sevoflurane-induced isoelectric EEG and burst suppression: differential and antagonistic effect of added nitrous oxide. Anaesthesia 2017; 72: 570-9.

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`groupSN` *A Real Experiment Dose Data*

---

## Description

A group of real experiment data based on up-and-down method.

## Usage

```
groupSN
```

## Format

A data of 38 samples and 2 variables:

**responseSequence** A value of 0 or 1 indicating the experiment outcome. 0 refers to a failure outcome while 1 refers to a success.

**doseSequence** The dose given in each experiment.

## Source

The data is from the article in the references below.

## References

Niu B, Xiao JY, Fang Y, et al. Sevoflurane-induced isoelectric EEG and burst suppression: differential and antagonistic effect of added nitrous oxide. Anaesthesia 2017; 72: 570-9.

## gTableOrigin *G Table*

### Description

A table containing parameter G used in Dixon-Mood method.

### Usage

```
gTableOrigin
```

### Format

A data table containing 3 columns:

**Ratio** The ratio of dose step and estimate standard error

**G1** The value of parameter G when the estimate of ED50 falls on a dose level

**G2** The value of parameter G when the estimate of ED50 falls between two dose levels

### Source

The table is obtained from Figure 2 in the reference below

### References

Dixon, W. J., & Mood, A. M. (1948). A method for obtaining and analyzing sensitivity data. Publications of the American Statistical Association, 43(241), 109-126.

## preparePava *Covert Data Using PAVA Algorithm*

### Description

Covert data using PAVA algorithm, the result is uesd for isotonic regression estimation.

### Usage

```
preparePava(data)
```

### Arguments

| | |
|---|---|
| data | A data frame of dose experiments. |

### Examples

```
library(ed50)
preparePava(groupS)
preparePava(groupSN)
```

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