

Package ‘CTLDA’

September 3, 2024

Title CTLDA: A Combined Test for Longitudinal Data Analysis in Randomized Clinical Trials

Version 0.1.0

Description Longitudinal data analysis methods for treatment effect estimates and signal detections in progressive disease with repeated measures.

License GPL (>= 2)

Encoding UTF-8

LazyData false

Roxygen list(markdown = TRUE)

RoxygenNote 7.2.3

Suggests knitr,
rmarkdown

Config/testthat/edition 3

Depends R (>= 4.3.0)

Imports splines (>= 4.3.1), lme4 (>= 1.1.34), nlme (>= 3.1.162), clubSandwich (>= 0.5.10), stats (>= 4.3.1), utils (>= 4.3.1), contrast (>= 0.24.2), ACAT (>= 0.91), dplyr (>= 1.1.2), robustbase (>= 0.99.0), pracma (>= 2.4.2)

VignetteBuilder knitr

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const.decline.m12	<i>const.decline.m12</i>
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Description

PMRM (constant decline)

Usage

const.decline.m12(dat)

Arguments

dat a data frame of standard longitudinal data

Value

a list of fitted progression model for repeated measures and p-value

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

const.delay.m12	<i>const.delay.m12</i>
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Description

PMRM (constant delay)

Usage

const.delay.m12(dat)

Arguments

dat a data frame of standard longitudinal data

Value

a list of fitted progression model for repeated measures and p-value

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

CTLDA	<i>CTLDA</i>
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Description

CTLDA: A Combined Test for Longitudinal Data Analysis in Randomized Clinical Trials using Cauchy Combination Test

Usage

CTLDA(pvec)

Arguments

pvec a vector a p-values to be combined

Value

a numerical value of p-value from Cauchy Combination Test

Author(s)

Song Zhai

References

Zhai, S., Shen, J. and Mehrotra, D.V. (2016). CTLDA: A Combined Test for Longitudinal Data Analysis in Randomized Clinical Trials.

f.const.decline.m12 *f.const.decline.m12*

Description

PMRM (constant decline) core function

Usage

```
f.const.decline.m12(t, v0, v1, v2, v3, v4, b)
```

Arguments

t	time
v0	mean response at visit 0 in the placebo arm
v1	mean response at visit 1 in the placebo arm
v2	mean response at visit 2 in the placebo arm
v3	mean response at visit 3 in the placebo arm
v4	mean response at visit 4 in the placebo arm
b	parameter of interest

Value

mean response in the active arm

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

f.const.delay.m12 *f.const.delay.m12*

Description

PMRM (constant delay) core function

Usage

```
f.const.delay.m12(t, v0, v1, v2, v3, v4, b)
```

Arguments

t	time
v0	mean response at visit 0 in the placebo arm
v1	mean response at visit 1 in the placebo arm
v2	mean response at visit 2 in the placebo arm
v3	mean response at visit 3 in the placebo arm
v4	mean response at visit 4 in the placebo arm
b	parameter of interest

Value

mean response in the active arm

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

f.prop.decline.m12	<i>f.prop.decline.m12</i>
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Description

PMRM (proportional decline) core function

Usage

```
f.prop.decline.m12(t, v0, v1, v2, v3, v4, b)
```

Arguments

t	time
v0	mean response at visit 0 in the placebo arm
v1	mean response at visit 1 in the placebo arm
v2	mean response at visit 2 in the placebo arm
v3	mean response at visit 3 in the placebo arm
v4	mean response at visit 4 in the placebo arm
b	parameter of interest

Value

mean response in the active arm

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

f.prop.delay.m12	<i>f.prop.delay.m12</i>
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Description

PMRM (proportional delay) core function

Usage

f.prop.delay.m12(t, v0, v1, v2, v3, v4, b)

Arguments

t	time
v0	mean response at visit 0 in the placebo arm
v1	mean response at visit 1 in the placebo arm
v2	mean response at visit 2 in the placebo arm
v3	mean response at visit 3 in the placebo arm
v4	mean response at visit 4 in the placebo arm
b	parameter of interest

Value

mean response in the active arm

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

`f.unstruct.decline.m12`*f.unstruct.decline.m12*

Description

PMRM (unstructured decline) core function

Usage

```
f.unstruct.decline.m12(t, v0, v1, v2, v3, v4, b1, b2, b3, b4)
```

Arguments

t	time
v0	mean response at visit 0 in the placebo arm
v1	mean response at visit 1 in the placebo arm
v2	mean response at visit 2 in the placebo arm
v3	mean response at visit 3 in the placebo arm
v4	mean response at visit 4 in the placebo arm
b1	parameter of interest
b2	parameter of interest
b3	parameter of interest
b4	parameter of interest

Value

mean response in the active arm

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

`f.unstruct.delay.m12` *f.unstruct.delay.m12*

Description

PMRM (unstructured delay) core function

Usage

```
f.unstruct.delay.m12(t, v0, v1, v2, v3, v4, b1, b2, b3, b4)
```

Arguments

<code>t</code>	time
<code>v0</code>	mean response at visit 0 in the placebo arm
<code>v1</code>	mean response at visit 1 in the placebo arm
<code>v2</code>	mean response at visit 2 in the placebo arm
<code>v3</code>	mean response at visit 3 in the placebo arm
<code>v4</code>	mean response at visit 4 in the placebo arm
<code>b1</code>	parameter of interest
<code>b2</code>	parameter of interest
<code>b3</code>	parameter of interest
<code>b4</code>	parameter of interest

Value

mean response in the active arm

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

MMRM	<i>MMRM</i>
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Description

MMRM (last-visit)

Usage

```
MMRM(dat, duration)
```

Arguments

<code>dat</code>	a data frame of standard longitudinal data
<code>duration</code>	a numerical value of study duration

Value

a numeric list including fitted linear mixed effects model and contrast test results

Author(s)

Song Zhai

References

Detry, M.A. and Ma, Y. (2016). Analyzing repeated measurements using mixed models. *Jama*, 315(4), 407-408.

<code>ncs_ranslp_df2</code>	<i>ncs_ranslp_df2</i>
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Description

Natural Cubic Spline

Usage

```
ncs_ranslp_df2(dat, intercept = TRUE)
```

Arguments

<code>dat</code>	a data frame of standard longitudinal data
<code>intercept</code>	an indicator whether or not to include intercept

Value

a numeric list including fitted natural cubic spline model and Wald test results

Author(s)

Song Zhai

References

Donohue, M.C., Langford, O., Insel, P.S., et al. (2023). Natural cubic splines for the analysis of Alzheimer’s clinical trials. *Pharmaceutical statistics*, 22(3), 508-519

<i>pAUC</i>	<i>pAUC</i>
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Description

pAUC (partial AUC): *pAUC* measures the treatment effect as the area between active and placebo time-to-response curves over the post-baseline visits

Usage

```
pAUC(dat, start, nboot = 1000)
```

Arguments

<i>dat</i>	a data frame of standard longitudinal data
<i>start</i>	a numerical value of starting visit point to calculate the area
<i>nboot</i>	number of bootstraps

Value

a list of the observed area, null distribution of the area, and the p-value

Author(s)

Song Zhai

References

Atri, A., Hendrix, S.B., Pejovic, V., et al. (2015). Cumulative, additive benefits of memantine-donepezil combination over component monotherapies in moderate to severe Alzheimer’s dementia: a pooled area under the curve analysis. *Alzheimer’s Research & Therapy*, 7, 1-12.

prop.decline.m12	<i>prop.decline.m12</i>
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Description

PMRM (proportional decline)

Usage

```
prop.decline.m12(dat)
```

Arguments

dat	a data frame of standard longitudinal data
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Value

a list of fitted progression model for repeated measures and p-value

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

prop.delay.m12	<i>prop.delay.m12</i>
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Description

PMRM (proportional delay)

Usage

```
prop.delay.m12(dat)
```

Arguments

dat	a data frame of standard longitudinal data
-----	--

Value

a list of fitted progression model for repeated measures and p-value

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

simulate_corr	<i>simulate_corr</i>
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Description

Simulate variance-covariance matrix and correlation matrix

Usage

```
simulate_corr(pattern, M)
```

Arguments

pattern	a character of desired variance-covariance pattern name
M	a vector of visit points

Value

a list of variance-covariance matrix and correlation matrix

Author(s)

Song Zhai

References

Zhai, S., Shen, J. and Mehrotra, D.V. (2016). CTLDA: A Combined Test for Longitudinal Data Analysis in Randomized Clinical Trials.

simulate_TE	<i>simulate_TE</i>
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Description

Simulate treatment effect pattern

Usage

```
simulate_TE(f, M, pattern)
```

Arguments

f	time-to-response function in the placebo arm
M	a numerical vector of visit points
pattern	a character of desired treatment effect pattern

Value

a numerical vector of mean responses at visit points in the active arm

Author(s)

Song Zhai

References

Zhai, S., Shen, J. and Mehrotra, D.V. (2016). CTLDA: A Combined Test for Longitudinal Data Analysis in Randomized Clinical Trials.

simulate_trial	<i>simulate_trial</i>
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Description

Simulate trial

Usage

```
simulate_trial(
  n_arm = 200,
  M = c(0, 3, 6, 9, 12),
  mean_pbo,
  mean_act,
  cov,
  sd,
  adjust = TRUE
)
```

Arguments

n_arm	a numerical value of sample size per arm
M	a numerical vector of visit points
mean_pbo	a numerical vector of mean responses at visit points in placebo arm
mean_act	a numerical vector of mean responses at visit points in active arm
cov	a matrix of variance-covariance matrix
sd	a numerical value of standard deviation
adjust	an indicator of whether or not to adjust mean responses

Value

a data frame of simulated longitudinal data

Author(s)

Song Zhai

References

Zhai, S., Shen, J. and Mehrotra, D.V. (2016). CTLDA: A Combined Test for Longitudinal Data Analysis in Randomized Clinical Trials.

spline_nonpara	<i>spline_nonpara</i>
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Description

Spline function

Usage

```
spline_nonpara(ys.train, xs.train, xs.test)
```

Arguments

- ys.train mean responses in the training set
- xs.train visit points in the trauning set
- xs.test visit points in the testing set

Value

mean responses in the testing set

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

unstruct.decline.m12	<i>unstruct.decline.m12</i>
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Description

PMRM (unstructured decline)

Usage

```
unstruct.decline.m12(dat)
```

Arguments

- dat a data frame of standard longitudinal data

Value

a list of fitted progression model for repeated measures and p-value

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

unstruct.delay.m12	<i>unstruct.delay.m12</i>
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Description

PMRM (unstructured delay)

Usage

```
unstruct.delay.m12(dat)
```

Arguments

dat a data frame of standard longitudinal data

Value

a list of fitted progression model for repeated measures and p-value

Author(s)

Song Zhai

References

Raket, L.L. (2022). Progression models for repeated measures: Estimating novel treatment effects in progressive diseases. *Statistics in Medicine*, 41(28), 5537-5557.

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