Package 'clinicalsignificance'

June 3, 2022

Type Package

Title Determine the Clinical Significance in Clinical Trials

Version 1.0.0

Description A clinical significance analysis can be used to determine if an
intervention has a meaningful or practical effect for patients. You provide
a tidy data set plus a few more metrics and this package will take care of
it to make your results publication ready as proposed by Jacobson et al.,
(1984) <doi:10.1016/S0005-7894(84)80002-7>.

License GPL (>= 3)

Encoding UTF-8

LazyData true

Depends R (>= 2.10)

RoxygenNote 7.2.0

Imports checkmate, crayon, dplyr, ggplot2, insight, lme4, magrittr,
purrr, rlang, tibble, tidyr

Suggests knitr, rmarkdown, testthat (>= 3.0.0), tidyverse, vdiffr

Config/testthat/edition 3

VignetteBuilder knitr

NeedsCompilation no

Author Benedikt Claus [aut, cre] (<https://orcid.org/0000-0001-9501-0954>)

Maintainer Benedikt Claus <b.claus@pedscience.de>

Repository CRAN

Date/Publication 2022-06-03 07:30:05 UTC

R topics documented:

---

anxiety   *Anxiety Data*

Description

A fictional dataset with missings to exemplify the use of HLM method for clinical significance.

Usage

```
anxiety
```

Format

A data frame with 580 rows and 4 variables:

subject Participant

treatment Treatment. Either Placebo or Intervention.

measurement Number of measurement

anxiety Anxiety score, lower is better.

Details

In a fictional clinical trial, participants were split up to belong to either a medical placebo ("Placebo") or psychotherapeutic intervention ("Intervention") group.

They underwent outpatient treatment during which they were followed for 5 measurements at which a fictional anxiety score was measured. This anxiety score may range from 0 - 60.

The functional population (i.e., non-anxious individuals) can be expected to have a mean score of $M = 8$ points with a standard deviation of $SD = 4$.

| anxiety_complete | *Anxiety Data (Complete)* |

Description

A fictional complete dataset to exemplify the use of HLM method for clinical significance.

Usage

```
anxiety_complete
```

Format

A data frame with 580 rows and 4 variables:

subject Participant

treatment Treatment. Either Placebo or Intervention.

measurement Number of measurement

anxiety Anxiety score, lower is better.

Details

In a fictional clinical trial, participants were split up to belong to either a medical placebo ("Placebo") or psychotherapeutic intervention ("Intervention") group.

They underwent outpatient treatment during which they were followed for 5 measurements at which a fictional anxiety score was measured. This anxiety score may range from 0 - 60.

The functional population (i.e., non-anxious individuals) can be expected to have a mean score of M = 8 points with a standard deviation of SD = 4.

| check_cutoff | *Check the Clinical Significance Cutoff Based on Population Descriptives* |

Description

Check the Clinical Significance Cutoff Based on Population Descriptives

Usage

```
check_cutoff(
  object = NULL,
  m_clinical,
  sd_clinical,
  m_functional = NA,
  sd_functional = NA,
  type = c("a", "b", "c"),
  better_is = c("lower", "higher"),
  resolution = 300
)
```

Arguments

object	An object of class clinisig. This is optional and can be used to visualize cutoffs after conducting a clinical significance analysis.
m_clinical	Mean of clinical population
sd_clinical	SD of clinical population
m_functional	M of functional population
sd_functional	SD of functional population
type	Cutoff type. Available are "a", "b", and "c". Defaults to "a" (see details for further information in which cutoff to choose)
better_is	Which direction means a better outcome for the employed outcome? Available are
	• "lower" (lower outcome scores are desirable, the default) and
	• "higher" (higher outcome scores are desirable)
resolution	Curve resolution (number of points to be drawn). This may improve smoothness of highly peaked curves.

Value

A ggplot2

Examples

```
# Check cutoff with manually specified values
check_cutoff(m_clinical = 40, sd_clinical = 12, m_functional = 10, sd_functional = 12)


# Or check the cutoff after you conducted a clinical significance analysis
results <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
```

```
    m_functional = 30,
    sd_functional = 7,
    type = "c"
  )

check_cutoff(results)
```

---

claus_2020   *Placebo Amplification Data*

Description

A dataset containing the data from Claus et al. (2020). In a routine inpatient setting for unipolar depressive disorders they implemented an intervention that sought to amplify the placebo response of antidepressants. In the study, two groups were compared: treatment as usual (TAU) and placebo amplification (PA). Participants were examined four times during their treatment.

Usage

```
claus_2020
```

Format

An object of class tbl_df with 172 rows and 9 columns.

id Participant ID

age Age

sex Sex

treatment Treatment (TAU for treatment as usual and PA for placebo amplification)

time Measurement

bdi Beck Depression Inventory (2nd Edition) score

shaps Snaith-Hamilton Pleasure Scale score

who WHO-Five Well-Being Index score

hamd Hamilton Rating Scale for Depression score

Source

https://osf.io/rc754/

References

- Claus, B. B., Scherbaum, N., & Bonnet, U. (2020). Effectiveness of an Adjunctive Psychotherapeutic Intervention Developed for Enhancing the Placebo Effect of Antidepressants Used within an Inpatient-Treatment Program of Major Depression: A Pragmatic Parallel-Group, Randomized Controlled Trial. Psychotherapy and Psychosomatics, 89(4), 258-260. https://doi.org/10.1159/000505855

---

clinical_significance   *Clinical Significance*

Description

This function conducts a clinical significance analysis by determining which patients changed reliably and moved from the clinical to the functional population during a study.

Usage

```
clinical_significance(
  data,
  id,
  time,
  outcome,
  group = NULL,
  pre = NULL,
  post = NULL,
  m_functional = NA,
  sd_functional = NA,
  type = "a",
  reliability,
  reliability_post,
  better_is = c("lower", "higher"),
  method = c("JT", "GLN", "HLL", "EN", "NK", "HA", "HLM")
)
```

Arguments

data	A tidy data frame
id	Participant ID
time	Time variable
outcome	Outcome variable
group	Grouping variable
pre	Pre measurement
post	Post measurement
m_functional	Mean of the functional population
sd_functional	Standard deviation of the functional population
type	Cutoff type. Available are "a", "b", and "c". Defaults to "a" (see details for further information in which cutoff to choose)
reliability	The instrument's reliability estimate. If you selected the NK method, the here specified reliability will be the instrument's pre measurement reliability

reliability_post

>The instrument's reliability at post measurement. This is only relevant for the NK method

better_is

>Which direction means a better outcome for the employed outcome? Available are
>
>- "lower" (lower outcome scores are desirable, the default) and
>- "higher" (higher outcome scores are desirable)

method

>Clinical significance method. Available are
>
>- "JT" (Jacobson & Truax, 1991, the default)
>- "GLN" (Gulliksen, Lord, and Novick; Hsu, 1989, Hsu, 1995)
>- "HLL" (Hsu, Linn & Nord; Hsu, 1989)
>- "EN" (Edwards & Nunnally; Speer, 1992)
>- "NK" (Nunnally & Kotsch, 1983), requires a reliability estimate at post measurement. If this is not supplied, reliability and reliability_post are assumed to be equal
>- "HA" (Hageman & Arrindell, 1999)
>- "HLM" (Hierarchical Linear Modeling; Raudenbush & Bryk, 2002), requires at least three measurements per patient

Details

By default, the JT method is used, but there are other methods implemented (see description of arguments).

It is generally recommended to use cutoff "c", thus, incorporating information of the clinical and functional population into the cutoff calculation.

Value

An S3 object of class clinisig

References

- Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. Journal of Consulting and Clinical Psychology, 59(1), 12–19. https://doi.org/10.1037//0022-006X.59.1.12

- Hsu, L. M. (1989). Reliable changes in psychotherapy: Taking into account regression toward the mean. Behavioral Assessment, 11(4), 459–467.

- Hsu, L. M. (1995). Regression toward the mean associated with measurement error and the identification of improvement and deterioration in psychotherapy. Journal of Consulting and Clinical Psychology, 63(1), 141–144. https://doi.org/10.1037//0022-006x.63.1.141

- Speer, D. C. (1992). Clinically significant change: Jacobson and Truax (1991) revisited. Journal of Consulting and Clinical Psychology, 60(3), 402–408. https://doi.org/10.1037/0022-006X.60.3.402

- Nunnally, J. C., & Kotsch, W. E. (1983). Studies of individual subjects: Logic and methods of analysis. British Journal of Clinical Psychology, 22(2), 83–93. https://doi.org/10.1111/j.2044-8260.1983.tb00582.x

- Hageman, W. J., & Arrindell, W. A. (1999). Establishing clinically significant change: increment of precision and the distinction between individual and group level analysis. Behaviour Research and Therapy, 37(12), 1169–1193. https://doi.org/10.1016/S0005-7967(99)00032-7
- Raudenbush, S. W., & Bryk, A. S. (2002). Hierarchical Linear Models - Applications and Data Analysis Methods (2nd ed.). Sage Publications.

Examples

```
# Clinical significane for "negative" outcomes (lower values are desirable)
jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80
  )


# Clinical significane for "positive" outcomes (higher values are desirable)
jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = das,
    pre = "pre",
    reliability = 0.80,
    better_is = "higher"
  )


# Clinical significance incorporating descriptives of a functional population.
# Make sure to select type = "c" to incorporate the specified functional
# descriptives.
jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 7,
    type = "c"
  )


# Change the clinical significance method
jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
```

```
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 7,
    type = "c",
    method = "EN"
  )

jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 7,
    type = "c",
    method = "HA"
  )


# And plot your results
results <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 7,
    type = "c"
  )

plot(results)
```

---

get_augmented_data   *Get Data Augmented With Clinical Significance Categories*

Description

Get Data Augmented With Clinical Significance Categories

Usage

```
get_augmented_data(x)
```

Arguments

x	A clinisig object.

Value

A tibble with used data and clinical significance categories

Examples

```
results <- jacobson_1989 %>%
clinical_significance(
  id = subject,
  time = time,
  outcome = gds,
  pre = "pre",
  reliability = 0.80,
  m_functional = 30,
  sd_functional = 7,
  type = "c"
)

get_augmented_data(results)
```

---

get_beneficial_direction
                    Get the Specified Beneficial Direction of a Clinical Significance Analysis

---

Description

Get the Specified Beneficial Direction of a Clinical Significance Analysis

Usage

```
get_beneficial_direction(x, ...)
```

Arguments

x	A clinisig object
...	Additional arguments

Value

A string

Examples

```
results <- jacobson_1989 %>%
clinical_significance(
  id = subject,
  time = time,
  outcome = gds,
  pre = "pre",
  reliability = 0.80
)

get_beneficial_direction(results)
```

---

get_cutoff   *Get Used Cutoff And Type From A clinisig Object*

Description

Get Used Cutoff And Type From A clinisig Object

Usage

```
get_cutoff(x, with_descriptives = FALSE)
```

Arguments

x   A clinisig object

with_descriptives

                     Logical indicating whether you want to retrieve only the cutoff type and value
                     or the summary statistics on which it is based on. The default is FALSE.

Value

A tibble with cutoff information

Examples

```
results <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 10,
    type = "c"
  )

get_cutoff(results)
```

get_cutoff_descriptives
Get Descriptives Used In The Cutoff Calculation

Description

Get Descriptives Used In The Cutoff Calculation

Usage

```
get_cutoff_descriptives(x)
```

Arguments

x   A clinisig object

Value

A tibble with means and standard deviations of the clinical and functional population

Examples

```
results <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 10,
    type = "c"
  )

get_cutoff_descriptives(results)
```

get_data   *Get Data From A clinisig Object*

Description

Get Data From A clinisig Object

Usage

```
get_data(x, dataset = "data")
```

Arguments

x	A clinisig object.
dataset	The dataset you wish to retrieve. Available options are

- "original" (the raw original dataset)
- "wide" (the original dataset in wide format)
- "data" (the dataset which is used in the calculations). The default is "data"

Value

A tibble

Examples

```
results <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 10,
    type = "c"
  )

get_data(results)
get_data(results, "wide")
get_data(results, "original")
```

---

get_method	*Get the employed clinical significance method*

Description

You may choose between several methods to conduct clinical significance analyses. This function can retrieve the employed method of a clinisig object.

Usage

```
get_method(x)
```

Arguments

x	A clinisig object

Value

A string

Examples

```
results <- jacobson_1989 %>%
clinical_significance(
  id = subject,
  time = time,
  outcome = gds,
  pre = "pre",
  reliability = 0.80
)

get_method(results)
```

---

get_n   *Get Number Of Participants From A clinisig Object*

Description

Get Number Of Participants From A clinisig Object

Usage

```
get_n(x, which = "all")
```

Arguments

x   A clinisig object

which   Which n should be returned? Available options are

- "all", n in the original and used data set (the default)
- "original", n in the original dataset
- "used", n in the used data set, so after conversion to wide format and omitting cases with missing values

Value

A tibble with number of participants

Examples

```
results <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 10,
    type = "c"
```

```
  )

  get_n(results)
  get_n(results, which = "original")
  get_n(results, which = "used")
```

---

get_reliability   *Get Reliability Of A clinisig Object*

Description

Get Reliability Of A clinisig Object

Usage

```
get_reliability(x)
```

Arguments

x   A clinisig object

Value

A tibble showing the reliability

Examples

```
results <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 10,
    type = "c"
  )

results_nk <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    reliability_post = 0.85,
    m_functional = 30,
    sd_functional = 10,
    type = "c",
```

```
    method = "NK"
  )

get_reliability(results)
get_reliability(results_nk)
```

---

get_summary_table   *Get A Summary Table From A clinisig Object*

Description

Retrieve the summary table in a tidy tibble format. This is especially useful to plot the results or conduct sensitivity analyses.

Usage

```
get_summary_table(x, which = c("individual", "group"))
```

Arguments

x   A clinisig object.

which   Which level of summary table to return. This is only necessary for method "HA" since two summary tables are reported. Available are

- individual, the default
- group, group level results according to Hageman & Arrindell (1999)

Value

A tibble with clinical significance categories

References

- Hageman, W. J., & Arrindell, W. A. (1999). Establishing clinically significant change: increment of precision and the distinction between individual and group level analysis. Behaviour Research and Therapy, 37(12), 1169–1193. https://doi.org/10.1016/S0005-7967(99)00032-7

Examples

```
results <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 10,
    type = "c"
```

```
  )

results_ha <- jacobson_1989 %>%
  clinical_significance(
    id = subject,
    time = time,
    outcome = gds,
    pre = "pre",
    reliability = 0.80,
    m_functional = 30,
    sd_functional = 10,
    type = "c",
    method = "HA"
  )

get_summary_table(results)
get_summary_table(results_ha)
get_summary_table(results_ha, which = "group")
```

jacobson_1989   *Marital Therapy Data*

Description

A dataset containing the data from Jacobson et al. (1989). The purpose of the study was to examine
two forms of behavioral marital therapy,

Usage

```
jacobson_1989
```

Format

An object of class `tbl_df` with 60 rows and 4 columns.

subject Subject ID

time Measurement

das Dyadic Adjustment Scale score

gds Global Distress Scale score

References

- Jacobson, N. S., Schmaling, K. B., Holtzworth-Munroe, A., Katt, J. L., Wood, L. F., & Fol-
  lette, V. M. (1989). Research-structured vs clinically flexible versions of social learning-based
  marital therapy. Behaviour Research and Therapy, 27(2), 173-180. https://doi.org/10.1016/0005-
  7967(89)90076-4
- Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining
  meaningful change in psychotherapy research. Journal of Consulting and Clinical Psychology,
  59(1), 12-19. https://doi.org/10.1037//0022-006X.59.1.12

| plot.clinisig | *Plot Clinical Significance Results* |

Description

Plot the results of a clinical significance analysis.

Usage

```
## S3 method for class 'clinisig'
plot(
  x,
  lower_limit = 0,
  upper_limit = 100,
  rci_fill = "grey10",
  rci_alpha = 0.1,
  diagonal_color = "black",
  show = NULL,
  which = c("point", "trajectory", "slope"),
  include_cutoff = TRUE,
  include_cutoff_band = FALSE,
  x_lab = NULL,
  y_lab = NULL,
  color_lab = "Group",
  overplotting = 0.02,
  ...
)
```

Arguments

x	A clinisig object
lower_limit	Numeric, lower plotting limit. Defaults to 0
upper_limit	Numeric, upper plotting limit. Defaults to 100
rci_fill	String, a color (name or HEX code) for RCI filling
rci_alpha	Numeric, controls the transparency of the RCI. This can be any value between 0 and 1.
diagonal_color	String, a color (name or HEX code) for the line indicating no change.
show	String. You have several options to color different features. Available are

- "category" (shows all categories at once) which is the default
- "recovered" (shows recovered participants)
- "improved" (shows improved participants)
- "unchanged" (shows unchanged participants)
- "deteriorated" (shows deteriorated participants, if available)
- "harmed" (shows harmed participants, if available)

which	String. Which plot type should be shown? Defaults to `"point"` which yields the default clinical significance plot. The HLM method incorporates multiple measurements per participant, so a reduction to pre and post values may remove important information. Therefore, you can additionally choose to plot either

  - each participants trajectory (with `"trajectory"`), or
  - each participants fitted Empirical Bayes slope (with `"slope"`)

include_cutoff	Logical. Should the clinical cutoff be plotted as well? Defaults to TRUE.
include_cutoff_band	
	Logical. If method was HA, a region of uncertainty around the cutoff can be plotted
x_lab	String, x axis label. Default is `"Pre"` for point and `"Measurement"` for trajectory and slope plot.
y_lab	String, y axis label. Default is `"Post"` for point, `"Outcome Score"` for trajectory, and `"Fitted Score"` for slope plot.
color_lab	String, color guide label. Default is `"Group"`.
overplotting	Numeric, control amount of overplotting. Defaults to 0.02 (i.e., 2% of range between lower and upper limit).
...	Additional arguments

Details

The resulting plot is a generic clinical significance plot with pre-intervention assessment scores on the x-axis and post-intervention assessment scores on the y-axis. By default, the cutoff between the clinical and functional population is plotted as well as the RCI band.

Value

A ggplot2 plot

---

print.clinisig	*Print Clinical Significance Results*

Description

Print Clinical Significance Results

Usage

```
## S3 method for class 'clinisig'
print(x, ...)
```

Arguments

x	A clinisig object
...	Additional arguments passed to `export_table()`

Value

No return value, called for side effects

---

summary.clinisig   *Summary Method for a clinisig object*

Description

Summary Method for a clinisig object

Usage

```
## S3 method for class 'clinisig'
summary(object, ...)
```

Arguments

object   A clinisig object

...   Additional arguments

Value

No return value, called for side effects

Index