

Package ‘clinicalsignificance’

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Type Package

Title Determine the Clinical Significance in Clinical Trials

Version 1.2.0

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](https://doi.org/10.1016/S0005-7894(84)80002-7)>.

License GPL (>= 3)

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<https://github.com/pedscience/clinicalsignificance>

BugReports <https://github.com/pedscience/clinicalsignificance/issues>

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

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

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anxiety	<i>Anxiety Data</i>
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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	<i>Anxiety Data (Complete)</i>
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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	<i>Check the Clinical Significance Cutoff Based on Population Descriptives</i>
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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 <code>clinisig</code> . 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 <ul style="list-style-type: none"> • "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 also 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 (optional)

pre	Pre measurement (only needed if the time variable contains more than two measurements)
post	Post measurement (only needed if the time variable contains more than two measurements)
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 (only needed for the NK method)
better_is	Which direction means a better outcome for the employed outcome? Available are <ul style="list-style-type: none"> • "lower" (lower outcome scores are desirable, the default) and • "higher" (higher outcome scores are desirable)
method	Clinical significance method. Available are <ul style="list-style-type: none"> • "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 Jacobson & Truax (1991) method to determine both criteria is used, but there are other methods implemented (see description of arguments).

To calculate the cutoff between populations, it is generally recommended to use cutoff "c", thus, incorporating information of the clinical and functional population into the cutoff calculation (regardless of the employed method).

During this analysis, a patient can be classified in one of five categories:

- Recovered (demonstrated a reliable change in the desired direction and belonged to the clinical population before and to the functional population after intervention)
- Improved (demonstrated a reliable change in the desired direction but is still in the same population after intervention as compared to before)
- Unchanged (did not demonstrate a reliable change)
- Deteriorated (demonstrated a reliable change in the undesired direction but is still in the same population after intervention as compared to before)
- Harmed (demonstrated a reliable change in the undesired direction and belonged to the functional population before and to the clinical population after intervention)

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](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

To obtain patient-wise results, use `get_augmented_data()`.

Usage

```
get_augmented_data(x)
```

Arguments

x A clinisig object.

Details

This function returns the patient-wise results, containing the considered pre and post intervention value, its raw change as well as the RCI and the individual category a patient belongs to.

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 <ul style="list-style-type: none">• "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

<code>x</code>	A clinisig object
<code>which</code>	Which n should be returned? Available options are <ul style="list-style-type: none">• "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	<i>Get A Summary Table From A clinisig Object</i>
-------------------	---

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 <ul style="list-style-type: none">• 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](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., Schmalings, K. B., Holtzworth-Munroe, A., Katt, J. L., Wood, L. F., & Follette, 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](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,
  which = c("point", "trajectory"),
  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	Category name. You have several options to color different features. Available are <ul style="list-style-type: none">• 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)

	<ul style="list-style-type: none"> • 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 each participants trajectory (with "trajectory")
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

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