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>.

License GPL (>= 3)

Encoding UTF-8

LazyData true

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

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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,  # Mean of clinical population
  sd_clinical,  # SD of clinical population
  m_functional = NA,  # M of functional population
  sd_functional = NA,  # SD of functional population
  type = c("a", "b", "c"),  # Cutoff type. Available are "a", "b", and "c". Defaults to "a" (see details for further information in which cutoff to choose)
  better_is = c("lower", "higher"),  # 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 = 300  # Curve resolution (number of points to be drawn). This may improve smoothness of highly peaked curves.
)

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


**clinical_significance**  

**Clinical Significance**

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

```r
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)

### Source

https://osf.io/rc754/

### References

**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 on 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

- "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 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


Examples

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

# Clinical significance 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",
    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"
  )
get_augmented_data

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)

c tactic41

get_cutoff_descriptives(x)

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

```r
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**

```r
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**

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

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,
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**


### plot.clinisig

#### Plot Clinical Significance Results

**Description**

Plot the results of a clinical significance analysis.

**Usage**

```r
## 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
  - 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 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

Description

Print Clinical Significance Results

Usage

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

Arguments

x A clinisig object

... Additional arguments passed to export_table()
**summary.clinisig**

**Value**

No return value, called for side effects

---

**summary.clinisig**  
*Summary Method for a clinisig object*

---

**Description**

Summary Method for a clinisig object

**Usage**

```r
## 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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