Example Use

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```
devtools::document()
```

```
## Warning: [/home/thgaertner/Documents/Masterarbeit/Package/nofone/R/
## adjtreat.R:25] @example spans multiple lines. Do you want @examples?
```

```
## Warning: [/home/thgaertner/Documents/Masterarbeit/Package/nofone/R/
## basic_functions.R:64] @example spans multiple lines. Do you want @examples?
```

```
## Writing NAMESPACE
## Writing NAMESPACE
## Writing find_optimum_rec.Rd
## Writing find_optimum_iterate.Rd
```

```
knitr::opts_chunk$set(echo = TRUE)
```

Introduction

This R Markdown document shows the usage of the package `cino1`.

```
# Install local package
devtools::document()
```

```
## Warning: [/home/thgaertner/Documents/Masterarbeit/Package/nofone/R/
## adjtreat.R:25] @example spans multiple lines. Do you want @examples?
```

```
## Warning: [/home/thgaertner/Documents/Masterarbeit/Package/nofone/R/
## basic_functions.R:64] @example spans multiple lines. Do you want @examples?
```

```
## Writing NAMESPACE
## Writing NAMESPACE
```

```
install.packages("~/Documents/Masterarbeit/Package/nofone/", repos = NULL, type="source")
# load package
library(cinof1)
library(doParallel)
```

Data

In this package, a sample data frame is included. It contains data for 300 patients within an n of 1 study. The data has the following structure:

- *patient_id*: Unique patient identifier
- *date*: Date of data points
- *day*: Day in study
- *Block*: identifies treatment block
- *Activity*: Dummy variable for steps per day

- *treatment*: Dummy variable for 2 treatments as factors
- *Uncertain_Low_Back_Pain*: Dummy variable for Uncertain loq back pain on scale 1-15

```
load("data/simpatdat.rda")
# Summarize Data
summary(simpatdat)
```

```
##    patient_id            date           day               treatment
##  Min.   : 0.00   2018-01-01:  20   Min.   :  1.00   Treatment_1:1120
##  1st Qu.: 4.75   2018-01-02:  20   1st Qu.: 28.75   Treatment_2:1120
##  Median : 9.50   2018-01-03:  20   Median : 56.50
##  Mean   : 9.50   2018-01-04:  20   Mean   : 56.50
##  3rd Qu.:14.25   2018-01-05:  20   3rd Qu.: 84.25
##  Max.   :19.00   2018-01-06:  20   Max.   :112.00
##                  (Other)   :2120
##  Uncertain_Low_Back_Pain     block         Activity
##  Min.   : 6.000          Min.   :1.00   Min.   :   45.19
##  1st Qu.: 9.000          1st Qu.:1.75   1st Qu.: 5563.32
##  Median : 9.000          Median :2.50   Median : 6910.56
##  Mean   : 9.231          Mean   :2.50   Mean   : 6943.34
##  3rd Qu.:10.000          3rd Qu.:3.25   3rd Qu.: 8290.16
##  Max.   :12.000          Max.   :4.00   Max.   :14084.38
##
```

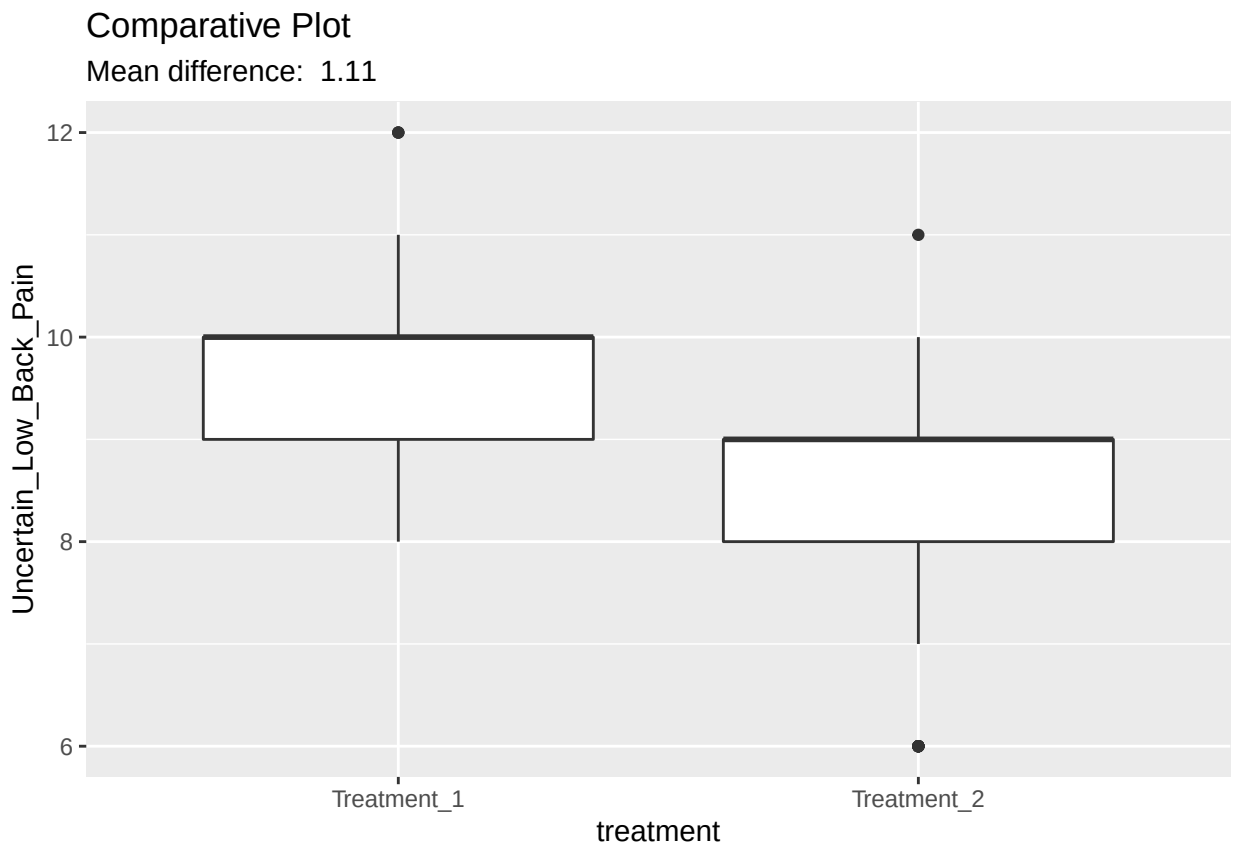
Basic Functions

Basic functions for analyse N-of-1 studys are for example wilcox test or comparative plots. These two functions are provided in this package.

Comparative Plot

To get a first idea about the data and the difference between treatment 1 and treatment 2, a comparative plot could be used. It shows the outcome on the y-Axis against the different treatments on the x-Axis,

```
# Define outcome and exposure column
outcome <- "Uncertain_Low_Back_Pain"
exposure <- "treatment"
# Plot outcome among different exposures
comparative.plot(simpatdat, exposure = exposure, outcome = outcome)
```



Wilcox Test

To validate, that there is a difference in both treatments, the Wilcox test could be used. It calculates the p-value for the null hypothesis, that there location shift is equal to zero.

```
# Define outcome and exposure column
outcome <- "Uncertain_Low_Back_Pain"
exposure <- "treatment"
# Perform Wilcox test among different exposures
wilcox.nofone(simpatdat, exposure = exposure, outcome = outcome)
```

```
##
##  Wilcoxon rank sum test
##
## data:  Uncertain_Low_Back_Pain by treatment
## W = 1048691, p-value < 2.2e-16
## alternative hypothesis: true location shift is not equal to 0
```

Adjust Wash In and Wash Out

```
outcome <- "Uncertain_Low_Back_Pain"
exposure <- "treatment"
variables <- c("Activity")
id <- "patient_id"
time_col <- "day"
```

```
result <- estimate.gamma.tau(data = simpatdat, outcome = outcome, exposure = exposure, variables = varia

result
```

```
## $data
##   treatment.Treatment_1.gamma treatment.Treatment_2.gamma
## 1                           1                           1
## 2                           2                           1
## 3                           1                           2
## 4                           2                           2
##   treatment.Treatment_1.tau treatment.Treatment_2.tau        r2
## 1                         1                         1 0.3925277
## 2                         2                         1 0.3922651
## 3                         1                         2 0.4098408
## 4                         2                         2 0.4429989
##   treatment.Treatment_1.Estimate treatment.Treatment_1.Std..Error
## 1                     1.11654798                       0.03050288
## 2                    -0.03097696                       0.16987892
## 3                    -0.48246803                       0.19819322
## 4                    -3.24965646                       0.27524924
##   treatment.Treatment_2.Estimate treatment.Treatment_2.Std..Error
## 1                             NA                              NA
## 2                      -1.145895                       0.1638043
## 3                      -1.656651                       0.2029606
## 4                      -4.357631                       0.2717909
##
## $best
##   treatment.Treatment_1.gamma treatment.Treatment_2.gamma
## 4                           2                           2
##   treatment.Treatment_1.tau treatment.Treatment_2.tau
## 4                         2                         2
```

```
fit.adj.lm(data = simpatdat, outcome = outcome, exposure = exposure, variables = variables, effects = re
```

```
## Warning in if (is.na(effects)) {: the condition has length > 1 and only the
## first element will be used
```

```
##
## Call:
## lm(formula = formula(str_formula), data = data, na.action = na.omit)
##
## Coefficients:
##                          (Intercept)  treatment.Treatment_1.gamma.2.tau.2
##                            1.360e+01                           -3.250e+00
##                             Activity  treatment.Treatment_2.gamma.2.tau.2
##                           -8.569e-05                           -4.358e+00
```

Bayesian

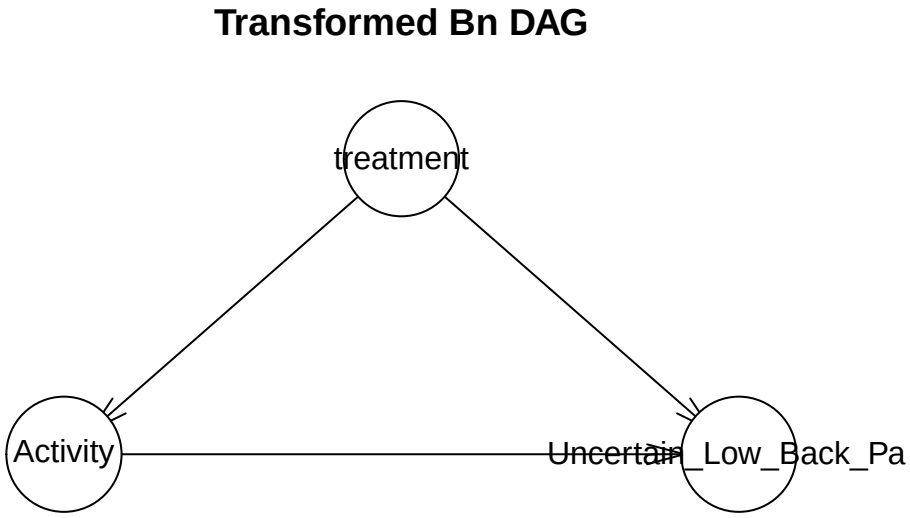
Bayesian Networks are used to calculated the probability of outcome variables adjusted for confounders. For that, a dag is required, which identifies the relations between the variables. In this implementation, also lags are included and could be specified in the dag by adding `.lag=` to the variable name.

Preprocess Data

```
# specify column names
id <- "patient_id"
time_col <- "day"

# Load data
load("data/simpatdag.rda")
load("data/simpatdat.rda")

# Dag preprocessing
bn.dag <- bn.prep.dag(simpatdag)
```

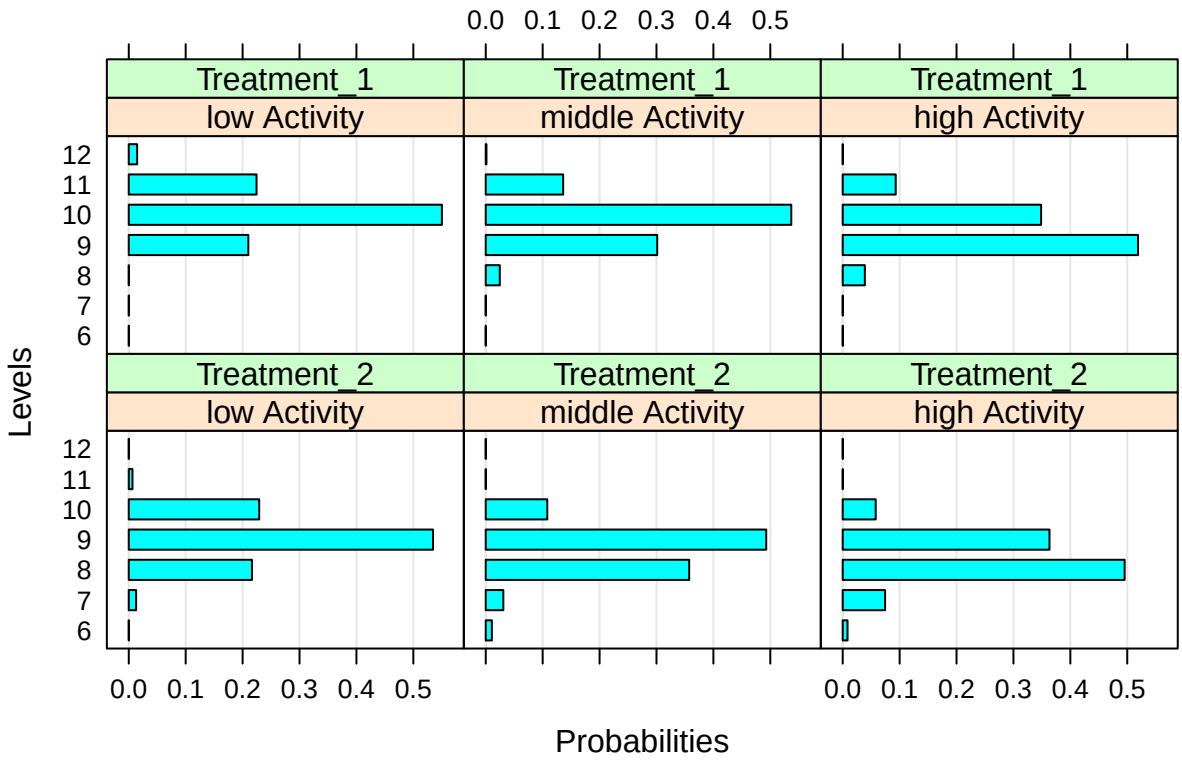



```
# Data Preprocessing (Factorization)
simpatdat$Uncertain_Low_Back_Pain <- as.factor(simpatdat$Uncertain_Low_Back_Pain)
simpatdat$Activity <- cut(simpatdat$Activity, 3, labels=c("low Activity", "middle Activity", "high Acti
bn.data <- bn.prep.data(bn.dag, simpatdat, id, time_col)
bn.data <- na.omit(bn.data)
```

Fit and Plot Results

```
fitted.bn <- bn.fit.dag(bn.data, bn.dag, method="bayes")

library(bnlearn)
bn.fit.barchart(fitted.bn$Uncertain_Low_Back_Pain)
```



G-Estimation

G-Estimation is used to adjust the analysis for causal inferences. For that, three different methods are implemented

Load Data

```
load("data/simpatdat.rda")
```

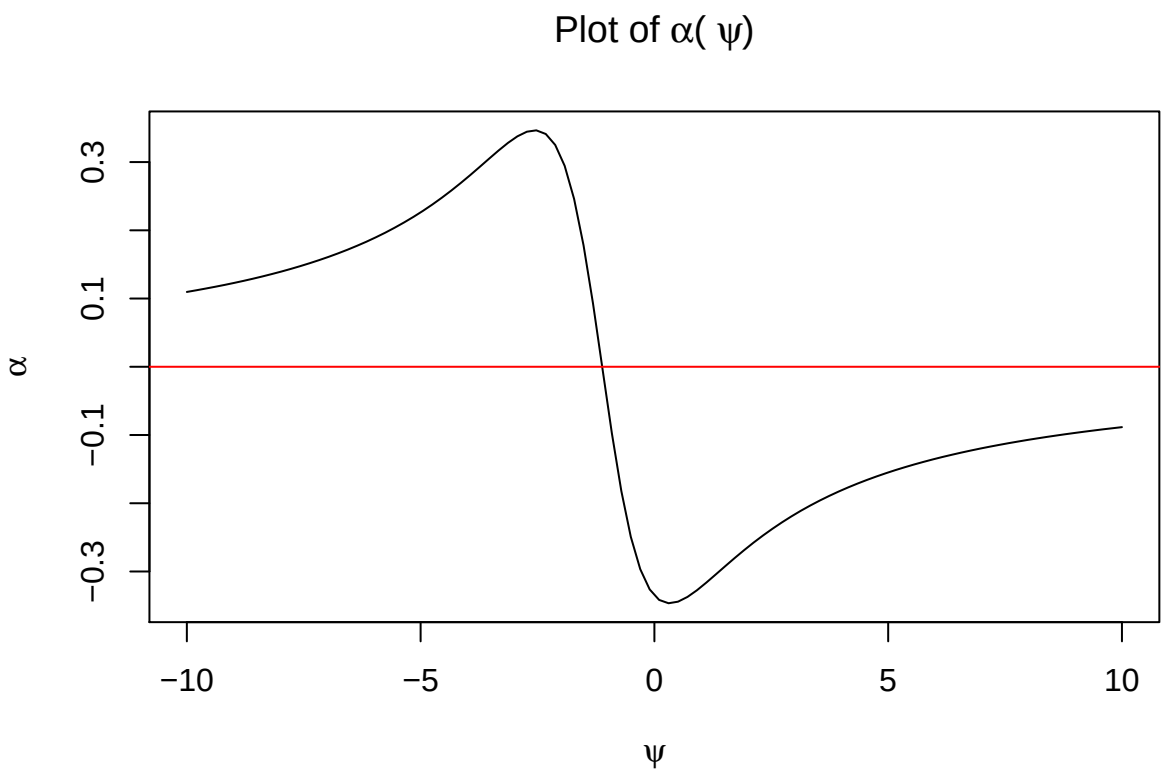
Fit G-Estimation by Iteration

It iterates over several values for ψ and returns a data frame with ψ and corresponding α

```
outcome <- "Uncertain_Low_Back_Pain"
exposure <- "treatment"
confounder <- c("Activity")
id <- "patient_id"
df <- nofgest(simpatdat, outcome, exposure, confounder, id, method="iterate", steps=100, upper_bound_psi
```

This function is useful to plot a curve for α and ψ.

```
plot( df$PSI ,df$Beta, type="l", main=expression(paste("Plot of ", alpha, "( ", psi,")")),
        xlab=expression(psi),
        ylab=expression(alpha))
# Add a second line
lines( c(-100,100),c(0,0), type = "l", col = "red")
```



Fit G-Estimation by Recursive Mean

This function approximate ψ by an interval search.

```
outcome <- "Uncertain_Low_Back_Pain"
exposure <- "treatment"
confounder <- c("Activity")
id <- "patient_id"
nofgest(simpatdat, outcome, exposure, confounder, id, method="rec_mean", max_number_it = 10, verbose=FA
```

```
## [1] "Max Iterations:"
```

```
##    upper_psi   upper_beta    upper_se lower_psi   lower_beta   lower_se
## 1  -1.109375 -0.003446206 0.040946897 -1.117188 0.0003072594 0.03584373
## 2  -1.109375 -0.003446206 0.040946897 -1.117188 0.0003072594 0.03584373
## 3  -1.109375 -0.003446206 0.040946897 -1.125000 0.0040606711 0.03584373
## 4  -1.093750 -0.010950659 0.040608006 -1.125000 0.0040606711 0.03584373
## 5  -1.062500 -0.025931203 0.039908527 -1.125000 0.0040606711 0.03584373
## 6  -1.000000 -0.055632933 0.038450862 -1.125000 0.0040606711 0.03584373
## 7  -1.000000 -0.055632933 0.038450862 -1.250000 0.0635736508 0.03584373
## 8  -1.000000 -0.055632933 0.038450862 -1.500000 0.1720752047 0.03584373
## 9  -1.000000 -0.055632933 0.038450862 -2.000000 0.3086996366 0.03584373
## 10  0.000000 -0.335496982 0.025465297 -2.000000 0.3086996366 0.03584373
## 11  2.000000 -0.264243363 0.008784946 -2.000000 0.3086996366 0.03584373
##    iteration
## 1         10
## 2          9
```

```
## 3          8
## 4          7
## 5          6
## 6          5
## 7          4
## 8          3
## 9          2
## 10         1
## 11         0
```

Fit G-Estimation by Recursive Improved

This function approximate ψ by an optimized interval search.

```
outcome <- "Uncertain_Low_Back_Pain"
exposure <- "treatment"
confounder <- c("Activity")
id <- "patient_id"
nofgest(simpatdat, outcome, exposure, confounder, id, method="rec", max_number_it = 10, verbose=FALSE)
```

```
## [1] "Converged! Optimal Psi:  -1.1165479816877"
```

```
##    upper_psi    upper_beta    upper_se lower_psi   lower_beta   lower_se
## 1 -1.1165480 -1.179378e-17 0.041099672 -1.116548 9.698380e-08 0.03584373
## 2 -1.1165480 -1.179378e-17 0.041099672 -1.116548 9.698380e-08 0.03584373
## 3 -1.1165480 -1.915311e-15 0.041099672 -1.116548 9.698380e-08 0.03584373
## 4 -1.1162943 -1.219032e-04 0.041094300 -1.116548 9.698380e-08 0.03584373
## 5 -1.1162943 -1.219032e-04 0.041094300 -1.157368 1.959637e-02 0.03584373
## 6 -0.9804303 -6.482132e-02 0.037986401 -1.157368 1.959637e-02 0.03584373
## 7 -0.9804303 -6.482132e-02 0.037986401 -2.000000 3.086996e-01 0.03584373
## 8  0.1551857 -3.438355e-01 0.024008679 -2.000000 3.086996e-01 0.03584373
## 9  2.0000000 -2.642434e-01 0.008784946 -2.000000 3.086996e-01 0.03584373
##   iteration
## 1         8
## 2         7
## 3         6
## 4         5
## 5         4
## 6         3
## 7         2
## 8         1
## 9         0
```