

Package ‘hce’

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Type Package

Title Design and Analysis of Hierarchical Composite Endpoints

Version 0.6.0

Description Simulate and analyze hierarchical composite endpoints. Win odds is the main analysis method, but other win statistics (win ratio, net benefit) are implemented as well in case of no censoring. See Gasparyan SB et al (2023) "Hierarchical Composite Endpoints in COVID-19: The DARE-19 Trial." Case Studies in Innovative Clinical Trials, 95-148. Chapman; Hall/CRC. <doi:10.1201/9781003288640-7>.

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 ADET

Event-Time dataset for kidney outcomes.

Description

A dataset with multiple kidney outcomes over time scale outcomes of 1500 patients in the ADSL dataset.

Usage

ADET

Format

a data frame with 604 rows (events) and 6 variables:

ID patient identifiers, numeric

AVAL occurrence time of the event, numeric

PARAM name of the event, character

PARAMCD coded name of the event, character

PARAMN type of the event, outcomes 1-7, where a higher value means a better outcome, numeric

TRTPN treatment values, 1 Active or 2 Placebo, numeric

Source

Heerspink HL et al "Development and validation of a new hierarchical composite endpoint for clinical trials of kidney disease progression." Journal of the American Society of Nephrology (2023): [doi:10.1681/ASN.000000000000243](https://doi.org/10.1681/ASN.000000000000243).

Examples

```
head(ADET)
# Number of unique patients
length(unique(ADET$ID))
# Number of events per event type
barplot(table(ADET$PARAM))
```

ADLB	<i>Laboratory dataset for Glomerular Filtration Rate (GFR) measurements.</i>
------	--

Description

A dataset of laboratory measurements of kidney function over time for the 1500 patients in the ADSL dataset.

Usage

ADLB

Format

a data frame with 13980 rows and 8 variables:

ID patient identifiers, numeric

TRTPN treatment values, 1 Active or 2 Placebo, numeric

AVAL measurement value, numeric

ADAY measurement day in the study, numeric

AVISITN hospital visit number, numeric

PARAM name of the event, GFR measurements, character

PARAMCD coded name of the event, GFR, character

PARAMN type of the event is set to 7 for all measurements, numeric

Source

Heerspink HL et al "Development and validation of a new hierarchical composite endpoint for clinical trials of kidney disease progression." Journal of the American Society of Nephrology (2023): [doi:10.1681/ASN.000000000000243](https://doi.org/10.1681/ASN.000000000000243).

Examples

```
head(ADLB)
```

ADSL	<i>Baseline characteristics dataset of patients with kidney function assessments.</i>
------	---

Description

A data frame with baseline characteristics for 1500 patients used to derive KHCE dataset.

Usage

```
ADSL
```

Format

a data frame with 1500 rows and 4 variables:

ID patient identifiers, numeric

TRTPN treatment values, 1 Active or 2 Placebo, numeric

EGFRBL Baseline GFR values of patients, numeric

STRATAN strata 1-4, higher value means a higher risk for kidney disease progression, numeric

Source

Heerspink HL et al "Development and validation of a new hierarchical composite endpoint for clinical trials of kidney disease progression." Journal of the American Society of Nephrology (2023): [doi:10.1681/ASN.000000000000243](https://doi.org/10.1681/ASN.000000000000243).

Examples

```
head(ADSL)
```

as_hce	<i>A generic function for coercing data structures to hce objects</i>
--------	---

Description

A generic function for coercing data structures to hce objects

Usage

```
as_hce(x, ...)
```

Arguments

x	an object used to select a method.
...	additional parameters.

Value

an hce object.

See Also

[as_hce.data.frame\(\)](#).

Examples

```
### data frames
data(HCE1)
HCE <- as_hce(HCE1)
calcWINS(HCE)
```

as_hce.data.frame	<i>Coerce a data frame to an hce object</i>
-------------------	---

Description

Coerce a data frame to an hce object

Usage

```
## S3 method for class 'data.frame'
as_hce(x, ...)
```

Arguments

x	a data frame.
...	additional parameters.

Value

an hce object.

Examples

```
KHCE <- as_hce(KHCE)
calcWO(KHCE)
```

calcWINS	<i>A generic function for calculating win statistics</i>
----------	--

Description

A generic function for calculating win statistics

Usage

```
calcWINS(x, ...)
```

Arguments

`x` an object used to select a method.
`...` further arguments passed to or from other methods.

Value

a data frame containing calculated values.

See Also

[calcWINS.hce\(\)](#), [calcWINS.formula\(\)](#), [calcWINS.data.frame\(\)](#) methods.

calcWINS.data.frame	<i>Win statistics calculation using a data frame</i>
---------------------	--

Description

Win statistics calculation using a data frame

Usage

```
## S3 method for class 'data.frame'
calcWINS(x, AVAL, TRTP, ref, alpha = 0.05, WOnull = 1, ...)
```

Arguments

x	a data frame containing subject-level data.
AVAL	variable in the data with ordinal analysis values.
TRTP	the treatment variable in the data.
ref	the reference treatment group.
alpha	2-sided significance level. The default is 0.05.
WOnull	the null hypothesis. The default is 1.
...	additional parameters.

Value

a list containing win statistics and their confidence intervals. It contains the following named data frames:

- summary a data frame containing number of wins, losses, and ties of the active treatment group and the overall number of comparisons.
- WP a data frame containing the win probability and its confidence interval.
- NetBenefit a data frame containing the net benefit and its confidence interval. This is just a $2x-1$ transformation of WP and its CI.
- WO a data frame containing the win odds and its confidence interval.
- WR1 a data frame containing the win ratio and its confidence interval, using the transformed standard error of the gamma statistic.
- WR2 a data frame containing the win ratio and its confidence interval, using the standard error calculated using P_{ties} .
- gamma a data frame containing Goodman Kruskal's gamma and its confidence interval.
- SE a data frame containing standard errors used to calculate the Confidence intervals for win statistics.

References

The theory of win statistics is covered in the following papers.

- For the win proportion CI calculation see
 Gasparian SB et al. (2021) "Adjusted win ratio with stratification: calculation methods and interpretation." *Statistical Methods in Medical Research* 30.2: 580-611. doi:10.1177/0962280220942558.
- The win odds CI is calculated using the formula in
 Gasparian SB et al. (2021) "Power and sample size calculation for the win odds test: application to an ordinal endpoint in COVID-19 trials." *Journal of Biopharmaceutical Statistics* 31.6: 765-787. doi:10.1080/10543406.2021.1968893.

- The win ratio the first CI uses the standard error derived from the standard error of the gamma statistic presented in

Gasparyan SB, Kowalewski EK, Buenconsejo J, Koch GG. (2023) "Hierarchical Composite Endpoints in COVID-19: The DARE-19 Trial." In Case Studies in Innovative Clinical Trials, Chapter 7, 95–148. Chapman; Hall/CRC. doi:10.1201/9781003288640-7.

- The win ratio the second CI uses the standard error presented in

Yu RX, Ganju J. (2022) "Sample size formula for a win ratio endpoint." Statistics in Medicine 41.6: 950-63. doi:10.1002/sim.9297.

- The Goodman Kruskal's gamma and its CI match those in DescTools::GoodmanKruskalGamma() and are based on

Agresti A. (2002) Categorical Data Analysis. John Wiley & Sons, pp. 57-59. doi:10.1002/0471249688.

Brown MB, Benedetti JK. (1977) "Sampling Behavior of Tests for Correlation in Two-Way Contingency Tables." Journal of the American Statistical Association 72, 309-315. doi:10.1080/01621459.1977.10480995.

Goodman LA, Kruskal WH. (1954) "Measures of association for cross classifications." Journal of the American Statistical Association 49, 732-764. doi:10.1080/01621459.1954.10501231.

Goodman LA, Kruskal WH. (1963) "Measures of association for cross classifications III: Approximate sampling theory." Journal of the American Statistical Association 58, 310-364. doi:10.1080/01621459.1963.10500850.

See Also

calcWINS(), calcWINS.hce(), calcWINS.formula().

Examples

```
calcWINS(x = COVID19b, AVAL = "GROUP", TRTP = "TRTP", ref = "Placebo")
```

calcWINS.formula	<i>Win statistics calculation using formula syntax</i>
------------------	--

Description

Win statistics calculation using formula syntax

Usage

```
## S3 method for class 'formula'
calcWINS(x, data, ...)
```


Arguments

x	an object of class formula.
data	a data frame.
...	additional parameters.

Value

a list containing win statistics and their confidence intervals. It contains the following named data frames:

- summary a data frame containing number of wins, losses, and ties of the active treatment group and the overall number of comparisons.
- WP a data frame containing the win probability and its confidence interval.
- NetBenefit a data frame containing the net benefit and its confidence interval. This is just a $2x-1$ transformation of WP and its CI.
- WO a data frame containing the win odds and its confidence interval.
- WR1 a data frame containing the win ratio and its confidence interval, using the transformed standard error of the gamma statistic.
- WR2 a data frame containing the win ratio and its confidence interval, using the standard error calculated using P_{ties} .
- gamma a data frame containing Goodman Kruskal's gamma and its confidence interval.
- SE a data frame containing standard errors used to calculate the Confidence intervals for win statistics.

References

The theory of win statistics is covered in the following papers.

- For the win proportion CI calculation see
 Gasparyan SB et al. (2021) "Adjusted win ratio with stratification: calculation methods and interpretation." *Statistical Methods in Medical Research* 30.2: 580-611. doi:10.1177/0962280220942558.
- The win odds CI is calculated using the formula in
 Gasparyan SB et al. (2021) "Power and sample size calculation for the win odds test: application to an ordinal endpoint in COVID-19 trials." *Journal of Biopharmaceutical Statistics* 31.6: 765-787. doi:10.1080/10543406.2021.1968893.
- The win ratio the first CI uses the standard error derived from the standard error of the gamma statistic presented in
 Gasparyan SB, Kowalewski EK, Buenconsejo J, Koch GG. (2023) "Hierarchical Composite Endpoints in COVID-19: The DARE-19 Trial." In *Case Studies in Innovative Clinical Trials*, Chapter 7, 95–148. Chapman; Hall/CRC. doi:10.1201/9781003288640-7.

- The win ratio the second CI uses the standard error presented in
 Yu RX, Ganju J. (2022) "Sample size formula for a win ratio endpoint." *Statistics in Medicine* 41.6: 950-63. doi:10.1002/sim.9297.
- The Goodman Kruskal's gamma and its CI match those in DescTools::GoodmanKruskalGamma() and are based on

Agresti A. (2002) *Categorical Data Analysis*. John Wiley & Sons, pp. 57-59. doi:10.1002/0471249688.

Brown MB, Benedetti JK. (1977) "Sampling Behavior of Tests for Correlation in Two-Way Contingency Tables." *Journal of the American Statistical Association* 72, 309-315. doi:10.1080/01621459.1977.10480995.

Goodman LA, Kruskal WH. (1954) "Measures of association for cross classifications." *Journal of the American Statistical Association* 49, 732-764. doi:10.1080/01621459.1954.10501231.

Goodman LA, Kruskal WH. (1963) "Measures of association for cross classifications III: Approximate sampling theory." *Journal of the American Statistical Association* 58, 310-364. doi:10.1080/01621459.1963.10500850.

See Also

`calcWINS()`, `calcWINS.hce()`, `calcWINS.data.frame()`.

Examples

```
# Example 1
calcWINS(x = GROUP ~ TRTP, data = COVID19b)
# Example 2
calcWINS(x = GROUP ~ TRTP, data = COVID19, ref = "Placebo", alpha = 0.01, WOnull = 1.2)
```

calcWINS.hce

Win statistics calculation for hce objects

Description

Win statistics calculation for hce objects

Usage

```
## S3 method for class 'hce'
calcWINS(x, ...)
```

Arguments

x an hce object.
 ... additional parameters.

Value

a list containing win statistics and their confidence intervals. It contains the following named data frames:

- summary a data frame containing number of wins, losses, and ties of the active treatment group and the overall number of comparisons.
- WP a data frame containing the win probability and its confidence interval.
- NetBenefit a data frame containing the net benefit and its confidence interval. This is just a $2x-1$ transformation of WP and its CI.
- WO a data frame containing the win odds and its confidence interval.
- WR1 a data frame containing the win ratio and its confidence interval, using the transformed standard error of the gamma statistic.
- WR2 a data frame containing the win ratio and its confidence interval, using the standard error calculated using Pties.
- gamma a data frame containing Goodman Kruskal's gamma and its confidence interval.
- SE a data frame containing standard errors used to calculate the Confidence intervals for win statistics.

References

The theory of win statistics is covered in the following papers.

- For the win proportion CI calculation see
 Gasparian SB et al. (2021) "Adjusted win ratio with stratification: calculation methods and interpretation." *Statistical Methods in Medical Research* 30.2: 580-611. doi:10.1177/0962280220942558.
- The win odds CI is calculated using the formula in
 Gasparian SB et al. (2021) "Power and sample size calculation for the win odds test: application to an ordinal endpoint in COVID-19 trials." *Journal of Biopharmaceutical Statistics* 31.6: 765-787. doi:10.1080/10543406.2021.1968893.
- The win ratio the first CI uses the standard error derived from the standard error of the gamma statistic presented in
 Gasparian SB, Kowalewski EK, Buenconsejo J, Koch GG. (2023) "Hierarchical Composite Endpoints in COVID-19: The DARE-19 Trial." In *Case Studies in Innovative Clinical Trials*, Chapter 7, 95–148. Chapman; Hall/CRC. doi:10.1201/9781003288640-7.
- The win ratio the second CI uses the standard error presented in
 Yu RX, Ganju J. (2022) "Sample size formula for a win ratio endpoint." *Statistics in Medicine* 41.6: 950-63. doi:10.1002/sim.9297.
- The Goodman Kruskal's gamma and its CI match those in DescTools: :GoodmanKruskalGamma() and are based on

Agresti A. (2002) Categorical Data Analysis. John Wiley & Sons, pp. 57-59. doi:10.1002/0471249688.

Brown MB, Benedetti JK. (1977) "Sampling Behavior of Tests for Correlation in Two-Way Contingency Tables." Journal of the American Statistical Association 72, 309-315. doi:10.1080/01621459.1977.10480995.

Goodman LA, Kruskal WH. (1954) "Measures of association for cross classifications." Journal of the American Statistical Association 49, 732-764. doi:10.1080/01621459.1954.10501231.

Goodman LA, Kruskal WH. (1963) "Measures of association for cross classifications III: Approximate sampling theory." Journal of the American Statistical Association 58, 310-364. doi:10.1080/01621459.1963.10500850.

See Also

`calcWINS()`, `calcWINS.formula()`, `calcWINS.data.frame()`.

Examples

```
# Example 1
COVID19HCE <- hce(GROUP = COVID19$GROUP, TRTP = COVID19$TRTP)
calcWINS(COVID19HCE)
# Example 2
COVID19bHCE <- hce(GROUP = COVID19b$GROUP, TRTP = COVID19b$TRTP)
calcWINS(COVID19bHCE, ref = "Placebo", WOnull = 1.1, alpha = 0.01)
```

calcWO

A generic function for calculating win odds

Description

A generic function for calculating win odds

Usage

```
calcWO(x, ...)
```

Arguments

`x` an object used to select a method.
`...` further arguments passed to or from other methods.

Value

a data frame containing calculated values.

See Also

[calcWO.hce\(\)](#), [calcWO.formula\(\)](#), [calcWO.data.frame\(\)](#) methods.

calcWO.data.frame	<i>Win odds calculation using a data frame</i>
-------------------	--

Description

Win odds calculation using a data frame

Usage

```
## S3 method for class 'data.frame'
calcWO(x, AVAL, TRTP, ref, alpha = 0.05, WOnull = 1, ...)
```

Arguments

x	a data frame containing subject-level data.
AVAL	variable in the data with ordinal analysis values.
TRTP	the treatment variable in the data.
ref	the reference treatment group.
alpha	significance level. The default is 0.05.
WOnull	the null hypothesis. The default is 1.
...	additional parameters.

Value

a data frame containing the win odds and its confidence interval. It contains the following columns:

- WO calculated win odds.
- LCL lower confidence limit.
- UCL upper confidence limit.
- SE standard error of the win odds.
- WOnull win odds of the null hypothesis (specified in the WOnull argument).
- alpha two-sided significance level for calculating the confidence interval (specified in the alpha argument).
- Pvalue p-value associated with testing the null hypothesis.
- WP calculated win probability.
- WP_SE standard error of the win probability.
- WP_SD standard deviation of the win probability, calculated as WP_SE multiplied by \sqrt{N} .
- N total number of patients in the analysis.

References

Gasparyan SB et al. "Adjusted win ratio with stratification: calculation methods and interpretation." *Statistical Methods in Medical Research* 30.2 (2021): 580-611. doi:10.1177/0962280220942558

See Also

`calcWO()`, `calcWO.hce()`, `calcWO.formula()`.

Examples

```
data(HCE4)
calcWO(x = HCE4, AVAL = "AVAL", TRTP = "TRTP", ref = "P")
```

calcWO.formula	<i>Win odds calculation using formula syntax</i>
----------------	--

Description

Win odds calculation using formula syntax

Usage

```
## S3 method for class 'formula'
calcWO(x, data, ...)
```

Arguments

x	an object of class formula.
data	a data frame.
...	additional parameters.

Value

a data frame containing the win odds and its confidence interval. It contains the following columns:

- WO calculated win odds.
- LCL lower confidence limit.
- UCL upper confidence limit.
- SE standard error of the win odds.
- WOnull win odds of the null hypothesis (specified in the WOnull argument).
- alpha two-sided significance level for calculating the confidence interval (specified in the alpha argument).
- Pvalue p-value associated with testing the null hypothesis.
- WP calculated win probability.
- WP_SE standard error of the win probability.

- WP_SD standard deviation of the win probability, calculated as WP_SE multiplied by sqrt(N).
- N total number of patients in the analysis.
- formula returning the specified formula in the x argument.
- ref showing how the reference group was selected. Can be modifying by specifying the ref argument.

References

Gasparyan SB et al. "Adjusted win ratio with stratification: calculation methods and interpretation." *Statistical Methods in Medical Research* 30.2 (2021): 580-611. doi:[10.1177/0962280220942558](https://doi.org/10.1177/0962280220942558)

See Also

[calcWO\(\)](#), [calcWO.hce\(\)](#), [calcWO.data.frame\(\)](#).

Examples

```
#Example 1
data(HCE1)
calcWO(AVAL ~ TRTP, data = HCE1)

#Example 2
calcWO(data = COVID19, GROUP ~ TRTP, ref = "Placebo")
```

calcWO.hce

Win odds calculation for hce objects

Description

Win odds calculation for hce objects

Usage

```
## S3 method for class 'hce'
calcWO(x, ...)
```

Arguments

x an hce object.
... additional parameters.

Value

a data frame containing the win odds and its confidence interval. It contains the following columns:

- WO calculated win odds.
- LCL lower confidence limit.
- UCL upper confidence limit.
- SE standard error of the win odds.
- WOnull win odds of the null hypothesis (specified in the WOnull argument).
- alpha two-sided significance level for calculating the confidence interval (specified in the alpha argument).
- Pvalue p-value associated with testing the null hypothesis.
- WP calculated win probability.
- WP_SE standard error of the win probability.
- WP_SD standard deviation of the win probability, calculated as WP_SE multiplied by sqrt(N).
- N total number of patients in the analysis.

References

Gasparyan SB et al. "Adjusted win ratio with stratification: calculation methods and interpretation." *Statistical Methods in Medical Research* 30.2 (2021): 580-611. doi:[10.1177/0962280220942558](https://doi.org/10.1177/0962280220942558)

See Also

`calcWO()`, `calcWO.formula()`, `calcWO.data.frame()`.

Examples

```
Rates_A <- c(1, 1.5)
Rates_P <- c(2, 2)
dat <- simHCE(n = 500, TTE_A = Rates_A, TTE_P = Rates_P, CM_A = 1.25, CM_P = 1)
calcWO(dat)
calcWO(dat, ref = "A", WOnull = 1, alpha = 0.01)
```

COVID19

COVID-19 ordinal scale dataset (full report).

Description

A dataset with COVID-19 ordinal scale outcomes for 1062 patients.

Usage

COVID19

Format

a data frame with 1062 rows and 2 variables:

GROUP type of the event, ordinal outcomes 1-8, where a higher value means a better outcome

TRTP treatment values, A Active or P Placebo, character

Source

Beigel JH et al. "Remdesivir for the treatment of Covid-19-final report." New England Journal of Medicine 383.19 (2020): 1813-1836. doi:[10.1056/NEJMoa2007764](https://doi.org/10.1056/NEJMoa2007764).

Examples

```
#Frequencies
table(COVID19)
mosaicplot(table(COVID19), col = c(1, 8, 6, 2, 4, 5, 3, 7),
xlab = "Treatment", ylab = "Ordinal Scale", main = "COVID-19 ordinal scale")
# Convert to an hce object
COVID19HCE <- hce(GROUP = COVID19$GROUP, TRTP = COVID19$TRTP)
# Summary wins, losses, and ties with win odds
summaryWO(COVID19HCE, ref = "Placebo")
```

COVID19b

COVID-19 ordinal scale dataset (preliminary report).

Description

A dataset with COVID-19 ordinal scale outcomes for 844 patients.

Usage

COVID19b

Format

a data frame with 844 rows and 2 variables:

GROUP type of the event, ordinal outcomes 1-8, where a higher value means a better outcome

TRTP treatment values, Active or Placebo, character

Source

Beigel JH et al. "Remdesivir for the treatment of Covid-19-final report." New England Journal of Medicine 383.19 (2020): 1813-1836. doi:[10.1056/NEJMoa2007764](https://doi.org/10.1056/NEJMoa2007764).

Examples

```
#Frequencies
table(COVID19b)
mosaicplot(table(COVID19b), col = c(1, 8, 6, 2, 4, 5, 3, 7),
xlab = "Treatment", ylab = "Ordinal Scale", main = "COVID-19 ordinal scale")
# Calculate win statistics
calcWINS(x = COVID19b, AVAL = "GROUP", TRTP = "TRTP", ref = "Placebo")
```

hce

*Helper function for hce objects***Description**

Helper function for hce objects

Usage

```
hce(
  GROUP = character(),
  TRTP = character(),
  AVAL0 = 0,
  ORD = sort(unique(GROUP))
)
```

Arguments

GROUP	a character vector of the same length as AVAL containing events.
TRTP	a character vector of the same length as AVAL containing assigned treatment groups.
AVAL0	a numeric vector of analysis values within each category. The default is 0.
ORD	a character vector containing ordered unique values of the GROUP variable for determining the hierarchy of events.

Value

an object of class hce. Its is a subject-level data frame (each row corresponds to one subject), containing the following columns:

- SUBJID subject ID.
- GROUP a character vector specifying the type of the outcome the patient experienced - either a TTE (time-to-event) or C (continuous).
- GROUPN a numeric vector version of the GROUP column.
- AVAL0 original analysis values - time of the time-to-event outcomes or the continuous outcome.
- AVAL derived analysis value $AVAL = AVAL0 + GROUPN$.
- TRTP assigned treatment groups.

See Also

[as_hce\(\)](#) for coercing to hce objects.

Examples

```
# Example 1
set.seed(2022)
d <- hce(GROUP = sample(x = c("A", "B", "C"), size = 10, replace = TRUE),
TRTP = rep(c("Active", "Control"), each = 5),
AVAL0 = c(rnorm(5, mean = 1), rnorm(5)), ORD = c("A", "B", "C"))
calcW0(d, ref = "Control")
```

HCE1	HCE1, HCE2, HCE3, HCE4 <i>datasets for 1000 patients with different treatment effects.</i>
------	--

Description

A simulated dataset containing the ordinal values and other attributes for 1000 patients. HCE1

Usage

HCE1

Format

a data frame with 1000 rows and 6 variables:

SUBJID subject ID, numbers from 1 to 1000

GROUP type of the event, either Time-To-Event (TTE) or Continuous (C), character

GROUPN type of the event, for the ordering of outcomes in the GROUP variable, numeric

AVAL $AVAL = AVAL0 + GROUPN$, ordinal analysis values for the HCE analysis, numeric, but caution NOT to apply numeric operations; will give meaningless results

AVAL0 original values for each type of the event, time for TTE outcomes, numeric values for Continuous outcomes, numeric

TRTP treatment values, A Active or P Placebo, character

HCE2	HCE1, HCE2, HCE3, HCE4 <i>datasets for 1000 patients with different treatment effects.</i>
------	--

Description

A simulated dataset containing the ordinal values and other attributes for 1000 patients. HCE2

Usage

HCE2

Format

a data frame with 1000 rows and 6 variables:

SUBJID subject ID, numbers from 1 to 1000

GROUP type of the event, either Time-To-Event (TTE) or Continuous (C), character

GROUPN type of the event, for the ordering of outcomes in the GROUP variable, numeric

AVAL $AVAL = AVAL_0 + GROUPN$, ordinal analysis values for the HCE analysis, numeric, but caution NOT to apply numeric operations; will give meaningless results

AVAL0 original values for each type of the event, time for TTE outcomes, numeric values for Continuous outcomes, numeric

TRTP treatment values, A Active or P Placebo, character

HCE3	HCE1, HCE2, HCE3, HCE4 <i>datasets for 1000 patients with different treatment effects.</i>
------	--

Description

A simulated dataset containing the ordinal values and other attributes for 1000 patients. HCE3

Usage

HCE3

Format

a data frame with 1000 rows and 6 variables:

SUBJID subject ID, numbers from 1 to 1000

GROUP type of the event, either Time-To-Event (TTE) or Continuous (C), character

GROUPN type of the event, for the ordering of outcomes in the GROUP variable, numeric

AVAL $AVAL = AVAL_0 + GROUPN$, ordinal analysis values for the HCE analysis, numeric, but caution NOT to apply numeric operations; will give meaningless results

AVAL0 original values for each type of the event, time for TTE outcomes, numeric values for Continuous outcomes, numeric

TRTP treatment values, A Active or P Placebo, character

HCE4	HCE1, HCE2, HCE3, HCE4 <i>datasets for 1000 patients with different treatment effects.</i>
------	--

Description

A simulated dataset containing the ordinal values and other attributes for 1000 patients. HCE4

Usage

HCE4

Format

a data frame with 1000 rows and 6 variables:

SUBJID subject ID, numbers from 1 to 1000

GROUP type of the event, either Time-To-Event (TTE) or Continuous (C), character

GROUPN type of the event, for the ordering of outcomes in the GROUP variable, numeric

AVAL $AVAL = AVAL_0 + GROUPN$, ordinal analysis values for the HCE analysis, numeric, but caution NOT to apply numeric operations; will give meaningless results

AVAL0 original values for each type of the event, time for TTE outcomes, numeric values for Continuous outcomes, numeric

TRTP treatment values, A Active or P Placebo, character

KHCE

*Kidney Hierarchical Composite Endpoint dataset.***Description**

A dataset with kidney ordinal scale outcomes of 1500 patients in the ADSL dataset.

Usage

KHCE

Format

a data frame with 1500 rows and 11 variables:

ID patient identifiers, numeric

TRTPN treatment values, 1 Active or 2 Placebo, numeric

AVAL0 original values for each type of the event, time for TTE outcomes 1-6, numeric values for Continuous outcome 7, numeric

AVAL $AVAL = AVAL0 + GROUPN$, ordinal analysis values for the HCE analysis, numeric, but caution NOT to apply numeric operations; will give meaningless results

GROUP name of the event, character

GROUPN ordinal outcomes corresponding to PARAMN values, numeric

PARAMCD coded name of the event, character

PARAMN severity of the event, outcomes 1-7, where a higher value means a better outcome, character

STRATAN strata 1-4, higher value means more severe kidney disease, numeric

EGFRBL Baseline GFR values of patients, numeric

TRTP treatment values, A Active or P Placebo, character

PADY primary analysis day (in years), length of the fixed follow-up, numeric

Source

Heerspink HL et al "Development and validation of a new hierarchical composite endpoint for clinical trials of kidney disease progression." Journal of the American Society of Nephrology (2023): [doi:10.1681/ASN.000000000000243](https://doi.org/10.1681/ASN.000000000000243).

Examples

```
# Adjusted win odds
res <- regWO(x = KHCE, AVAL = "AVAL", TRTP = "TRTP", COVAR = "STRATAN", ref = "P")
res
```

minWO	<i>Minimum detectable or WO for alternative hypothesis for given power (no ties)</i>
-------	--

Description

Minimum detectable or WO for alternative hypothesis for given power (no ties)

Usage

```
minWO(N, power = 0.5, SD = NULL, k = 0.5, alpha = 0.05, WOnull = 1, digits = 2)
```

Arguments

N	a numeric vector of sample size values (two arms combined).
power	the given power. The default is 0.5 corresponding to the minimum detectable win odds. A numeric vector of length 1.
SD	assumed standard deviation of the win proportion. By default uses the conservative SD. A numeric vector of length 1.
k	proportion of active group in the overall sample size. Default is 0.5 (balanced randomization). A numeric vector of length 1.
alpha	the significance level for the 2-sided test. Default is 0.05. A numeric vector of length 1.
WOnull	the win odds value of the null hypothesis (default is 1). A numeric vector of length 1.
digits	precision to use for reporting calculated win odds.

Value

a data frame containing the calculated WO with input values.

References

Gasparyan SB et al. (2021) "Power and sample size calculation for the win odds test: application to an ordinal endpoint in COVID-19 trials." *Journal of Biopharmaceutical Statistics* 31.6: 765-787. [doi:10.1080/10543406.2021.1968893](https://doi.org/10.1080/10543406.2021.1968893)

See Also

[powerWO\(\)](#), [sizeWO\(\)](#) for WO power and sample size calculation.

Examples

```
minWO(N = 100, digits = 5)
minWO(N = 1200, power = 0.9)
minWO(N = 1200, power = 0.9, k = 0.75)
```

plot.hce_results *A print method for hce_results objects*

Description

A print method for hce_results objects

Usage

```
## S3 method for class 'hce_results'  
plot(x, ...)
```

Arguments

x an object of class hce_results.
... additional arguments to be passed to `base::plot()` function.

Value

no return value, called for plotting.

Examples

```
WO <- minWO(N = 100:1000)  
plot(WO)  
POW <- powerWO(N = 100:1000, WO = 1.2)  
plot(POW, ylim = c(0, 1))
```

powerWO *Power calculation for the win odds test (no ties)*

Description

Power calculation for the win odds test (no ties)

Usage

```
powerWO(N, WO, SD = NULL, k = 0.5, alpha = 0.05, WOnull = 1)
```


Arguments

N	a numeric vector of sample size values.
WO	the given win odds for the alternative hypothesis. A numeric vector of length 1.
SD	assumed standard deviation of the win proportion. By default uses the conservative SD. A numeric vector of length 1.
k	proportion of active group in the overall sample size. Default is 0.5 (balanced randomization). A numeric vector of length 1.
alpha	the significance level for the 2-sided test. Default is 0.05. A numeric vector of length 1.
WOnull	the win odds value of the null hypothesis (default is 1). A numeric vector of length 1.

Value

a data frame containing the calculated power with input values.

References

Gasparian SB et al. (2021) "Power and sample size calculation for the win odds test: application to an ordinal endpoint in COVID-19 trials." *Journal of Biopharmaceutical Statistics* 31.6 : 765-787. doi:[10.1080/10543406.2021.1968893](https://doi.org/10.1080/10543406.2021.1968893)

See Also

[sizeWO\(\)](#), [minWO\(\)](#) for WO sample size or minimum detectable WO calculation.

Examples

```
# Example 1- Use the default standard deviation
powerWO(N = 1000, WO = 1.2)
powerWO(N = seq(500, 1500, 100), WO = 1.2)
# Example 2 - Use data-driven win odds and standard deviation from the COVID19 dataset
res <- calcWO(x = COVID19, AVAL = "GROUP", TRTP = "TRTP", ref = "Placebo")
print(res)
powerWO(N = 500, WO = res$WO, SD = res$SD_WP)
powerWO(N = 500, WO = res$WO) # power with the default standard deviation for the win proportion.
# Example 3 - Non-balanced 3:1 randomization
powerWO(N = 1000, WO = 1.2, k = 0.75)
```

print.hce_results *A print method for hce_results objects*

Description

A print method for hce_results objects

Usage

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

Arguments

x an object of class hce_results.
 ... additional arguments to be passed to `base::print()` function.

Value

no return value, called for printing.

Examples

```
print(powerWO(N = 1000, WO = 1.2))
```

 propWINS

Proportion of wins/losses/ties given the win odds and the win ratio

Description

Proportion of wins/losses/ties given the win odds and the win ratio

Usage

```
propWINS(WO, WR, Overall = 1, alpha = NULL, N = NULL)
```

Arguments

WO win odds.
 WR win ratio.
 Overall number of comparisons, the sample size of the active treatment multiplied by the sample size of the placebo. The default is 1, hence gives the proportion.
 alpha significance level for the win ratio confidence interval. The default is NULL hence the confidence interval is not produced.
 N the combined sample size of two treatment groups. The default is NULL. If alpha is specified then either N should be specified or `Overall > 1`. For given `Overall`, the pooled sample size is calculated as $N = 2 \cdot \sqrt{\text{Overall}}$.

Details

- **Win ratio** defined as $WR = \frac{W}{L}$.
- **Win odds** defined as $WO = \frac{W+0.5T}{L+0.5T} = \frac{WP}{1-WP}$.
- **Net Benefit** defined as $NB = \frac{W-L}{O}$.

Given the overall number of comparisons O , the win proportion WP and the win ratio WR , it is possible to find the total number of wins and losses. Indeed, first the win odds can be found $WO = \frac{WP}{1-WP}$ and

$$L = O * \frac{2WP - 1}{WR - 1},$$

$$W = WR * O * \frac{2WP - 1}{WR - 1},$$

$$T = O - W - L.$$

Value

a data frame with a number (or proportion if Overall = 1) of wins/losses/ties. If alpha is specified returns also WR confidence interval.

References

- For the relationship between win odds and win ratio see
 Gasparian SB et al. "Hierarchical Composite Endpoints in COVID-19: The DARE-19 Trial". Case Studies in Innovative Clinical Trials, Chapter 7 (2023): 95-148. Chapman and Hall/CRC. doi:10.1201/9781003288640-7.
- The win ratio CI uses the standard error presented in
 Yu RX, Ganju J. (2022) "Sample size formula for a win ratio endpoint." Statistics in Medicine 41.6: 950-63. doi:10.1002/sim.9297.

Examples

```
# Example 1
propWINS(WR = 2, WO = 1.5)
# Example 2 - Back-calculation
COVID19HCE <- hce(GROUP = COVID19$GROUP, TRTP = COVID19$TRTP)
res <- calcWINS(COVID19HCE)
WR <- res$WR1$WR
WO <- res$WO$WO
Overall <- res$summary$TOTAL
propWINS(WR = WR, WO = WO, Overall = Overall)
## Verify
res$summary
# Example 3 - Confidence interval
propWINS(WR = 1.4, WO = 1.3, alpha = 0.05, Overall = 2500)
propWINS(WR = 2, WO = 1.5, alpha = 0.01, N = 500)
```

regWO	<i>A generic function for win odds regression</i>
-------	---

Description

A generic function for win odds regression

Usage

```
regWO(x, ...)
```

Arguments

x	an object used to select a method.
...	further arguments passed to or from other methods.

Value

a data frame containing calculated values.

See Also

[regWO.data.frame\(\)](#) methods.

regWO.data.frame	<i>Win odds regression using a data frame</i>
------------------	---

Description

Win odds regression using a data frame

Usage

```
## S3 method for class 'data.frame'
regWO(x, AVAL, TRTP, COVAR, ref, alpha = 0.05, WOnull = 1, ...)
```

Arguments

x	a data frame containing subject-level data.
AVAL	variable in the data with ordinal analysis values.
TRTP	the treatment variable in the data.
COVAR	a numeric covariate.
ref	the reference treatment group.
alpha	significance level. The default is 0.05.
WOnull	the null hypothesis. The default is 1.
...	additional parameters.

Value

a data frame containing the win odds and its confidence interval.

- WO_beta adjusted win odds.
- LCL lower confidence limit for adjusted WO.
- UCL upper confidence limit for adjusted WO.
- SE standard error of the adjusted win odds.
- WOnull win odds of the null hypothesis (specified in the WOnull argument).
- alpha two-sided significance level for calculating the confidence interval (specified in the alpha argument).
- Pvalue p-value associated with testing the null hypothesis.
- N total number of patients in the analysis.
- beta adjusted win probability.
- SE_beta standard error for the adjusted win probability.
- SD_beta standard deviation for the adjusted win probability.
- WP (non-adjusted) win probability.
- SE_WP standard error of the non-adjusted win probability.
- SD_WP standard deviation of the non-adjusted win probability.
- WO non-adjusted win odds.
- COVAR_MEAN_DIFF mean difference between two treatment groups of the numeric covariate.
- COVAR_VAR sum of variances of two treatment groups of the numeric covariate.
- COVAR_COV covariance between the response and the numeric covariate.

References

Gasparyan SB et al. (2021) "Adjusted win ratio with stratification: calculation methods and interpretation." *Statistical Methods in Medical Research* 30.2: 580-611. doi:[10.1177/0962280220942558](https://doi.org/10.1177/0962280220942558).

See Also

[regWO\(\)](#).

Examples

```
# A baseline covariate that is highly correlated with the outcome
set.seed(2023)
dat <- COVID19
n <- nrow(dat)
dat$Severity <- ifelse(dat$GROUP > 4, rnorm(n, 0), rnorm(n, 100))
tapply(dat$Severity, dat$TRTP, mean)
regWO(x = dat, AVAL = "GROUP", TRTP = "TRTP", COVAR = "Severity", ref = "Placebo")
# Without adjustment
calcWO(x = dat, AVAL = "GROUP", TRTP = "TRTP", ref = "Placebo")
```

simHCE	<i>Simulate hce object with given event rates of time-to-event outcomes (Weibull), mean and SD of the continuous outcome (normal or log-normal) by treatment group</i>
--------	--

Description

Simulate hce object with given event rates of time-to-event outcomes (Weibull), mean and SD of the continuous outcome (normal or log-normal) by treatment group

Usage

```
simHCE(
  n,
  n0 = n,
  TTE_A,
  TTE_P,
  CM_A,
  CM_P,
  CSD_A = 1,
  CSD_P = 1,
  fixedfy = 1,
  yeardays = 360,
  pat = 100,
  shape = 1,
  logC = FALSE,
  seed = NULL
)
```

Arguments

n	sample size in the active treatment group.
n0	sample size in the placebo group.
TTE_A	event rates per year in the active group for the time-to-event outcomes.
TTE_P	event rates per year in the placebo group for the time-to-event outcomes. Should have the same length as TTE_A.
CM_A	mean value for the continuous outcome of the active group.
CM_P	mean value for the continuous outcome of the placebo group.
CSD_A	standard deviation for the continuous outcome of the active group.
CSD_P	standard deviation for the continuous outcome of the placebo group.
fixedfy	length of follow-up in years.
yeardays	number of days in a year.
pat	scale of provided event rates (per pat-years).

shape	shape of the Weibull distribution for time-to-event outcomes. Default is exponential distribution with shape = 1.
logC	logical, whether to use log-normal distribution for the continuous outcome.
seed	the seed for generating random numbers.

Value

an object of class `hce` containing the following columns:

- ID subject identifier.
- TRTP planned treatment group - "A" for active, "P" for Placebo.
- GROUP type of the outcome, either "TTE" for time-to-event outcomes or "C" for continuous. Only one continuous outcome is possible, but no restriction on the number of "TTE" outcomes.
- GROUPN order of outcomes in GROUP, with a higher value signifying a better outcome.
- AVALT the timing of the time-to-event outcomes.
- AVAL0 numeric values of the continuous outcome and the timing of "TTE" outcomes.
- AVAL analysis values derived as $AVAL0 + GROUPN$. For the continuous outcome the values of $AVAL0$ are shifted to start always from 0.
- seed the seed of the random sample. If not specified in seed argument will be selected based on system time.
- PADY primary analysis day, the length of fixed follow-up in days calculated as `yeardays` multiplied by `fixedfy`.

See Also

[hce\(\)](#), [as_hce\(\)](#) for the helper a coerce function to `hce` objects.

Examples

```
# Example 1
Rates_A <- c(1.72, 1.74, 0.58, 1.5, 1)
Rates_P <- c(2.47, 2.24, 2.9, 4, 6)
dat <- simHCE(n = 2500, TTE_A = Rates_A, TTE_P = Rates_P,
             CM_A = -3, CM_P = -6, CSD_A = 16, CSD_P = 15, fixedfy = 3)
head(dat)

# Example 2
Rates_A <- 10
Rates_P <- 15
dat <- simHCE(n = 1000, n0 = 500, TTE_A = Rates_A, TTE_P = Rates_P,
             CM_A = 0.1, CM_P = 0, seed = 5, shape = 0.2, logC = TRUE)
summaryWO(dat)
```

sizeWO

*Sample size calculation for the win odds test (no ties)***Description**

Sample size calculation for the win odds test (no ties)

Usage

```
sizeWO(WO, power, SD = NULL, k = 0.5, alpha = 0.05, WOnull = 1)
```

Arguments

WO	a numeric vector of win odds values.
power	the given power. A numeric vector of length 1.
SD	assumed standard deviation of the win proportion. By default uses the conservative SD. A numeric vector of length 1.
k	proportion of active group in the overall sample size. Default is 0.5 (balanced randomization). A numeric vector of length 1.
alpha	the significance level for the 2-sided test. Default is 0.05. A numeric vector of length 1.
WOnull	the win odds value of the null hypothesis (default is 1). A numeric vector of length 1.

Value

a data frame containing the sample size with input values.

References

Gasparyan SB et al. (2021) "Power and sample size calculation for the win odds test: application to an ordinal endpoint in COVID-19 trials." *Journal of Biopharmaceutical Statistics* 31.6: 765-787. [doi:10.1080/10543406.2021.1968893](https://doi.org/10.1080/10543406.2021.1968893).

See Also

[powerWO\(\)](#), [minWO\(\)](#) for WO power or minimum detectable WO calculation.

Examples

```
sizeWO(WO = 1.25, power = 0.9)
sizeWO(WO = 1.25, power = 0.9, k = 0.75)
sizeWO(WO = seq(1.05, 1.5, 0.05), power = 0.9)
```

sizeWR	<i>Sample size calculation for the win ratio test (with WR = 1 null hypothesis)</i>
--------	---

Description

Sample size calculation for the win ratio test (with WR = 1 null hypothesis)

Usage

```
sizeWR(WR, power, WO = NULL, Pties = NULL, k = 0.5, alpha = 0.05)
```

Arguments

WR	a numeric vector of win odds values.
power	the given power. A numeric vector of length 1.
WO	win odds. Should be specified only if Pties is not specified. A numeric vector of length 1.
Pties	probability of ties. A numeric vector of length 1.
k	proportion of active group in the overall sample size. Default is 0.5 (balanced randomization). A numeric vector of length 1.
alpha	the significance level for the 2-sided test. Default is 0.05. A numeric vector of length 1.

Value

a data frame containing the sample size with input values.

References

Yu RX, Ganju J. (2022) "Sample size formula for a win ratio endpoint." *Statistics in Medicine*, 41.6: 950-63. doi:[10.1002/sim.9297](https://doi.org/10.1002/sim.9297).

See Also

[sizeWO\(\)](#) for WO sample size calculation.

Examples

```
sizeWR(WR = 1.35, Pties = 0.125, power = 0.8)
sizeWR(WR = 1.35, WO = 1.3, power = seq(0.5, 0.9, 0.05))
```

stratWO	<i>A generic function for stratified win odds with adjustment</i>
---------	---

Description

A generic function for stratified win odds with adjustment

Usage

```
stratWO(x, ...)
```

Arguments

x an object used to select a method.
... further arguments passed to or from other methods.

Value

a list containing the stratified results and results by strata.

See Also

[stratWO.data.frame\(\)](#) methods.

stratWO.data.frame	<i>Stratified win odds with adjustment</i>
--------------------	--

Description

Stratified win odds with adjustment

Usage

```
## S3 method for class 'data.frame'  
stratWO(  
  x,  
  AVAL,  
  TRTP,  
  STRATA,  
  ref,  
  COVAR = NULL,  
  alpha = 0.05,  
  WOnull = 1,  
  ...  
)
```

Arguments

x	a data frame containing subject-level data.
AVAL	variable in the data with ordinal analysis values.
TRTP	the treatment variable in the data.
STRATA	a character variable for stratification.
ref	the reference treatment group.
COVAR	a numeric covariate.
alpha	the reference treatment group.
WOnull	the null hypothesis. The default is 1.
...	additional parameters.

Value

a data frame containing the following columns:

- WO stratified (or adjusted/stratified) win odds.
- LCL lower confidence limit for adjusted (or adjusted/stratified) WO.
- UCL upper confidence limit for adjusted (or adjusted/stratified) WO.
- SE standard error of the adjusted (or adjusted/stratified) win odds.
- WOnull win odds of the null hypothesis (specified in the WOnull argument).
- alpha two-sided significance level for calculating the confidence interval (specified in the alpha argument).
- Pvalue p-value associated with testing the null hypothesis.
- WP adjusted (or adjusted/stratified) win probability.
- SE_WP standard error for the adjusted (or adjusted/stratified) win probability.
- SD_WP standard deviation of the adjusted (or adjusted/stratified) win probability.
- N total number of patients in the analysis.
- Type "STRATIFIED" or "STRATIFIED/ADJUSTED" depending on whether COVAR is specified.

References

Gasparian SB et al. (2021) "Adjusted win ratio with stratification: calculation methods and interpretation." *Statistical Methods in Medical Research* 30.2: 580-611. doi:[10.1177/0962280220942558](https://doi.org/10.1177/0962280220942558).

See Also

[stratWO\(\)](#).

Examples

```
# Stratified win odds
res <- stratWO(x = KHCE, AVAL = "AVAL", TRTP = "TRTP",
STRATA = "STRATAN", ref = "P")
res
## Compare with the win odds in each stratum separately
lapply(split(KHCE, KHCE$STRATAN), calcWO, AVAL = "AVAL", TRTP = "TRTP", ref = "P")
# Stratified and adjusted win odds
res <- stratWO(x = KHCE, AVAL = "AVAL", COVAR = "EGFRBL",
TRTP = "TRTP", STRATA = "STRATAN", ref = "P")
res
```

summaryWO

A generic function for summarizing win odds

Description

A generic function for summarizing win odds

Usage

```
summaryWO(x, ...)
```

Arguments

x an object used to select a method.
... further arguments passed to or from other methods.

Value

a data frame containing calculated values.

See Also

[summaryWO.hce\(\)](#), [summaryWO.formula\(\)](#), [summaryWO.data.frame\(\)](#) methods.

summaryWO.data.frame *Win odds summary for a data frame*

Description

Win odds summary for a data frame

Usage

```
## S3 method for class 'data.frame'  
summaryWO(x, AVAL, TRTP, ref, GROUP = NULL, ...)
```

Arguments

x	a data frame containing subject-level data.
AVAL	variable in the data with ordinal analysis values.
TRTP	the treatment variable in the data.
ref	the reference treatment group.
GROUP	an optional variable for grouping.
...	additional parameters.

Value

a list containing the summary of wins, losses, and ties. It contains the following named objects:

- summary a data frame containing number of wins, losses, and ties by treatment group and the overall number of comparisons.
- summary_by_GROUP (if GROUP variable is specified) a summary data frame by GROUP.
- WO calculated WO (win odds) and WP (win probability) and their standard errors.

See Also

[calcwO\(\)](#), [summaryWO\(\)](#), [summaryWO.data.frame\(\)](#) methods.

Examples

```
summaryWO(x = HCE3, AVAL = "AVAL", TRTP = "TRTP", ref = "P", GROUP = "GROUP")
```

summaryWO.formula	<i>Win odds summary using formula syntax</i>
-------------------	--

Description

Win odds summary using formula syntax

Usage

```
## S3 method for class 'formula'  
summaryWO(x, data, ...)
```

Arguments

x	an object of class formula.
data	a data frame.
...	additional parameters.

Value

a list containing the summary of wins, losses, and ties. It contains the following named objects:

- summary a data frame containing number of wins, losses, and ties by treatment group and the overall number of comparisons.
- WO calculated WO (win odds) and WP (win probability) and their standard errors.
- formula returning the specified formula in the x argument.
- ref showing how the reference group was selected. Can be modifying by specifying the ref argument.

Examples

```
summaryWO(data = COVID19, GROUP ~ TRTP)  
summaryWO(data = COVID19, GROUP ~ TRTP, GROUP = "GROUP", ref = "Placebo")
```

summaryWO.hce	<i>Win odds summary for hce objects</i>
---------------	---

Description

Win odds summary for hce objects

Usage

```
## S3 method for class 'hce'  
summaryWO(x, ...)
```

Arguments

`x` an hce object.
`...` additional parameters.

Value

a list containing the summary of wins, losses, and ties. It contains the following named objects:

- `summary` a data frame containing number of wins, losses, and ties by treatment group and the overall number of comparisons.
- `summary_by_GROUP` (if `GROUP` variable is specified) a summary data frame by `GROUP`.
- `WO` calculated `WO` (win odds) and `WP` (win probability) and their standard errors.

See Also

[calcWO\(\)](#), [summaryWO\(\)](#), [summaryWO.data.frame\(\)](#) methods.

Examples

```
dat <- as_hce(HCE4)
summaryWO(dat, ref = "P")
```

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