Package 'mecor'

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Type Package

Title Measurement Error Correction in Linear Models with a Continuous

Outcome

Version 1.0.0

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Description Covariate measurement error correction is implemented by means of regression calibration by Carroll RJ, Ruppert D, Stefanski LA & Crainiceanu CM (2006, ISBN:1584886331), efficient regression calibration by Spiegelman D, Carroll RJ & Kipnis V (2001) doi:10.1002/sim.3713. Outcome measuretion by Bartlett JW, Stavola DBL & Frost C (2009) doi:10.1002/sim.3713. Outcome measurement error correction is implemented by means of the method of moments by Buonaccorsi JP (2010, ISBN:1420066560) and efficient method of moments by Keogh RH, Carroll RJ, Tooze JA, Kirkpatrick SI & Freedman LS (2014) doi:10.1002/sim.7011. Standard error estimation of the corrected estimators is implemented by means of the Delta method by Rosner B, Spiegelman D & Willett WC (1990) doi:10.1093/oxfordjournals.aje.a115715> and Rosner B, Spiegelman D & Wil-

lett WC (1992) <doi:10.1093/oxfordjournals.aje.a116453>, the Fieller method described by Buonaccorsi JP (2010, ISBN:1420066560), and the Bootstrap by Carroll RJ, Ruppert D, Stefanski LA & Crainiceanu CM (2006, ISBN:1584886331).

Depends R (>= 2.10)

License GPL-3

Encoding UTF-8

LazyData true

URL https://github.com/LindaNab/mecor

Imports lme4, lmerTest, numDeriv

Suggests knitr, rmarkdown

VignetteBuilder knitr

RoxygenNote 7.1.2

NeedsCompilation no

Repository CRAN

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R topics documented:

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bloodpressure

PDAC blood pressure data [replicates study]

Description

Index

Blood pressure, age and creatinine levels of 450 pregnant women from the Pregnancy Day Assessment Clinic.

Usage

bloodpressure

Format

A data frame with 450 rows and 6 variables:

```
creatinine Serum creatinine (umol/L)
age Age (years)
sbp30 Systolic blood pressure at 30 minutes (mm Hg)
sbp60 Systolic blood pressure at 60 minutes (mm Hg)
sbp90 Systolic blood pressure at 90 minutes (mm Hg)
sbp120 Systolic blood pressure at 120 minutes (mm Hg)
```

Details

This is a simulated dataset inspired by data that was originally published at the Dryad Digital Repository: <doi:10.5061/dryad.0bq15>

haemoglobin 3

References

Elizabeth Anne McCarthy, Thomas A Carins, Yolanda Hannigan, Nadia Bardien, Alexis Shub, and Susan P Walker. Data from: Effectiveness and safety of 1 vs 4h blood pressure profile with clinical and laboratory assessment for the exclusion of gestational hypertension and pre-eclampsia: a retrospective study in a university affiliated maternity hospital. Dryad (2015). <doi:10.5061/dryad.0bq15>.

Examples

```
data("bloodpressure", package = "mecor")

haemoglobin

Low-dose iron supplements haemoglobin data [internal outcome-validation study]
```

Description

Capillary haemoglobin and venous haemoglobin levels of 400 subjects of a trial investigating the efficacy of low-dose iron supplements during pregnancy. Venous haemoglobin levels were observed of approximately 25% of the subjects included in the trial.

Usage

haemoglobin

Format

A data frame with 400 rows and 3 variables:

```
capillary Haemoglobin levels measured in capillary blood (g/L) supplement Low-dose iron supplement (20 mg/d) (0 = no, 1 = yes) venous Haemoglobin levels measured in venous blood (g/L)
```

Details

This is a simulated data set inspired by a trial investigating low-dose iron supplements <doi:10.1093/ajcn/78.1.145>. A motivating example using the example data can be found here: <doi:10.1002/sim.8359>

References

Maria Makrides, Caroline A Crowther, Robert A Gibson, Rosalind S Gibson, and C Murray Skeaff. Efficacy and tolerability of low-dose iron supplements during pregnancy: a randomized controlled trial. The American Journal of Clinical Nutrition (2003). <doi:10.1093/ajcn/78.1.145>

Linda Nab, Rolf HH Groenwold, Paco MJ Welsing, and Maarten van Smeden. Measurement error in continuous endpoints in randomised trials: Problems and solutions. Statistics in Medicine (2019). <doi:10.1002/sim.8359>

```
data("haemoglobin", package = "mecor")
```

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haemoglobin_ext

Haemoglobin external data [external outcome-validation study]

Description

Capillary haemoglobin and venous haemoglobin levels of 100 individuals.

Usage

```
haemoglobin_ext
```

Format

A data frame with 100 rows and 2 variables:

capillary Haemoglobin levels measured in capillary blood (g/L)

venous Haemoglobin levels measured in venous blood (g/L)

Details

This is a simulated data set accompanying the dataset "haemoglobin", that is inspired by a trial investigating low-dose iron supplements <doi:10.1093/ajcn/78.1.145>. A motivating example using the example data can be found here: <doi:10.1002/sim.8359>

References

Maria Makrides, Caroline A Crowther, Robert A Gibson, Rosalind S Gibson, and C Murray Skeaff. Efficacy and tolerability of low-dose iron supplements during pregnancy: a randomized controlled trial. The American Journal of Clinical Nutrition (2003). <doi:10.1093/ajcn/78.1.145>

Linda Nab, Rolf HH Groenwold, Paco MJ Welsing, and Maarten van Smeden. Measurement error in continuous endpoints in randomised trials: Problems and solutions. Statistics in Medicine (2019). <doi:10.1002/sim.8359>

```
data("haemoglobin_ext", package = "mecor")
```

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ipwm	Weighting for	Confounding	and Joint	Misclassification of	Exposure
	and Outcome				

Description

ipwm implements a method for estimating the marginal causal odds ratio by constructing weights (modified inverse probability weights) that address both confounding and joint misclassification of exposure and outcome.

Usage

```
ipwm(
  formulas,
  data,
 outcome_true,
 outcome_mis = NULL,
 exposure_true,
  exposure_mis = NULL,
 nboot = 1000,
  conf_level = 0.95,
  fix_nNAs = FALSE,
  semiparametric = FALSE,
 optim_args = list(method = "BFGS"),
  force_optim = FALSE,
  sp = Inf,
  print = TRUE
)
```

Arguments

formulas	a list of objects of class formula specifying the probability models for the stats::terms of some factorisation of the joint conditional probability function of exposure_true, exposure_mis, outcome_true and outcome_mis, given covariates
data	data.frame containing exposure.true, exposure.mis, outcome.true, outcome.mis and covariates. Missings (NAs) are allowed on variables exposure_true and outcome_true.
outcome_true	a character string specifying the name of the true outcome variable that is free of misclassification but possibly unknown (NA) for some (but not all) subjects
outcome_mis	a character string specifying the name of the counterpart of outcome_true that is available on all subjects but potentially misclassifies subjects' outcomes. The default (outcome_mis = NULL) indicates absence of outcome misclassification
exposure_true	a character string specifying the name of the true exposure variable that is free of misclassification but possibly unknown (NA) for some (but not all) subjects

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exposure_mis a character string specifying the name of the counterpart of exposure_true

that is available on all subjects but potentially misclassifies subjects as exposed or as non-exposed. The default (exposure_mis = NULL) indicates absence of

exposure misclassification

nboot number of bootstrap samples. Setting nboot == 0 results in point estimation

only.

conf_level the desired confidence level of the confidence interval

fix_nNAs logical indicator specifying whether or not to fix the joint distribution of is.na(exposure_true)

and is.na(outcome_true). If TRUE, stratified bootstrap sampling is done ac-

cording to the missing data pattern.

semiparametric logical indicator specifying whether or not to parametrically sample exposure_true,

exposure_mis, outcome_true and outcome_mis. If semiparametric == TRUE, it is assumed that the missing data pattern is conditionally independent of these variables given covariates. Provided nboot > 0, the missing data pattern and covariates are sampled nonparametrically. semiparametric is ignored if nboot

== 0.

optim_args arguments passed onto optim if called. See Details below for more information.

force_optim logical indicator specifying whether or not to force the optim function to be

called

sp scalar shrinkage parameter in the interval (0, Inf). Values closer to zero result

in greater shrinkage of the estimated odds ratio to unity; sp == Inf results in no

shrinkage.

print logical indicator specifying whether or not to print the output.

Details

This function is an implementation of the weighting method described by Penning de Vries et al. (2018). The method defaults to the estimator proposed by Gravel and Platt (2018) in the absence of exposure misclassification.

The function assumes that the exposure or the outcome has a misclassified version. An error is issued when both outcome_mis and exposure_mis are set to NULL.

Provided force_optim = FALSE, ipwm is considerably more efficient when the optim function is not invoked; i.e., when (1) exposure_mis = NULL and the formula for outcome_true does not contain stats::terms involving outcome_mis or exposure_true, (2) outcome_mis = NULL and the formula for exposure_true does not contain stats::terms involving exposure_mis or outcome_true, or (3) all(is.na(data[,exposure_true]) == is.na(data[,outcome_true])) and the formulas for exposure_true and outcome_true do not contain stats::terms involving exposure_mis or outcome_mis. In these cases, ipwm uses iteratively reweighted least squares via the glm function for maximum likelihood estimation. In all other cases, optim_args is passed on to optim for optimisation of the joint likelihood of outcome_true, outcome_mis, exposure_true and exposure_mis.

Value

ipwm returns an object of class ipwm. The returned object is a list containing the following elements:

logOR the estimated log odds ratio;

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call the matched function call.

If nboot != 0, the list also contains

SE a bootstrap estimate of the standard error for the estimator of the log odds ratio;

CI a bootstrap percentile confidence interval for the log odds ratio.

Author(s)

Bas B. L. Penning de Vries, <b.1.penning_de_vries@lumc.nl>

References

Gravel, C. A., & Platt, R. W. (2018). Weighted estimation for confounded binary outcomes subject to misclassification. *Statistics in medicine*, 37(3), 425-436. https://doi.org/10.1002/sim.7522

Penning de Vries, B. B. L., van Smeden, M., & Groenwold, R. H. H. (2020). A weighting method for simultaneous adjustment for confounding and joint exposure-outcome misclassifications. *Statistical Methods in Medical Research*, 0(0), 1-15. https://doi.org/10.1177/0962280220960172

```
data(sim) # simulated data on 10 covariates, exposure A and outcome Y.
formulas <- list(</pre>
 Y \sim A + L1 + L2 + L3 + L4 + L5 + L6 + L7 + L8 + L9 + L10 + B + Z
 A \sim L1 + L2 + L3 + L4 + L5 + L6 + L7 + L8 + L9 + L10 + B + Z
 Z \sim L1 + L2 + L3 + L4 + L5 + L6 + L7 + L8 + L9 + L10 + B,
 B ~ L1 + L2 + L3 + L4 + L5 + L6 + L7 + L8 + L9 + L10
)
## Not run:
ipwm_out <- ipwm(</pre>
 formulas = formulas,
 data = sim,
 outcome_true = "Y",
 outcome_mis = "Z",
 exposure_true = "A"
 exposure_mis = "B",
 nboot = 200,
 sp = 1e6
)
ipwm_out
## End(Not run)
```

8 MeasError

MeasError	Create a Measurement Error Object
-----------	-----------------------------------

Description

This function creates a measurement error object, usually used as a covariate or the outcome in the formula argument of mecor if one wants to correct for the measurement error in that variable using a reference variable or a replicate measure.

Usage

```
MeasError(substitute, reference, replicate, differential)
```

Arguments

substitute a vector containing the error-prone measure

a vector containing the reference measure assumed without measurement error

a vector or matrix with replicates of the error-prone measure with classical measurement error. This can either be replicates obtained by using the same measurement method as the substitute measure (replicates study) or replicates using a different measurement method than the substitute measure (calibration study).

differential a vector containing the variable to which the measurement error is differential.

Value

MeasError returns an object of class "MeasError".

An object of class MeasError is a list containing the substitute and reference (and replicate or differential if applicable) variables and has attributes input (the name of the substitute and reference or replicate and differential (if applicable) variables) and call (the matched call).

Author(s)

```
Linda Nab, <1.nab@lumc.nl>
```

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MeasErrorExt

Create an External Measurement Error Object

Description

This function creates an external measurement error object, usually used as a covariate or the outcome in the formula argument of mecor if one wants to correct for the measurement error in that variable using external data or externally estimated coefficients of the calibration model (covariate-measurement error) or measurement error model (outcome-measurement error)

Usage

```
MeasErrorExt(substitute, model)
```

Arguments

substitute a vector containing the error-prone measure

model a fitted linear model of class lm or a named list. The list contains a vector

named coef: the coefficients of the calibration model or measurement error model and an optional matrix named vcov: the variance-covariance matrix of

the coefficients

Value

MeasErrorExt returns an object of class "MeasErrorExt".

An object of class MeasErrorExt is a list containing the substitute variable and the fitted calibration model or measurement error model and has attributes input (the name of the substitute variable) and call (the matched call).

Author(s)

```
Linda Nab, <1.nab@lumc.nl>
```

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Examples

```
## measurement error in a outcome:
# external outcome-validation study
data(haemoglobin ext)
# calibration model
calmod_fit <- lm(capillary ~ venous, data = haemoglobin)</pre>
# the external covariate-validation study can be used to correct for the
# measurement error in X_star in the dataset 'icvs', using the fitted
# calibration model
data(haemoglobin)
with (haemoglobin, MeasErrorExt(substitute = capillary,
                                model = calmod_fit))
# identical to:
calmod_coef <- coefficients(calmod_fit)</pre>
calmod_vcov <- vcov(calmod_fit)</pre>
with (haemoglobin, MeasErrorExt(substitute = capillary,
                                model = list(coef = calmod_coef,
                                              vcov = calmod_vcov)))
# when no external data is available, guesstimations of the coefficients of
# the calibration model can be used instead:
with (haemoglobin, MeasErrorExt(substitute = capillary,
                                 model = list(coef = c('(Intercept)' = -7,
                                                        venous' = 1.1)))
```

MeasErrorRandom

Create a Random Measurement Error Object

Description

This function creates a random measurement error object, usually used as a covariate in the formula argument of mecor if one wants to correct for random measurement error in that variable

Usage

```
MeasErrorRandom(substitute, variance)
```

Arguments

substitute a vector containing the error-prone measure

variance a numeric quantifying the assumed variance of the random measurement error

Value

MeasErrorRandom returns an object of class "MeasErrorRandom".

An object of class MeasErrorRandom is a list containing the substitute variable, the assumed variance of the random measurement error in that variable and, the attributes input (the name of the substitute variable) and call (the matched call).

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Author(s)

```
Linda Nab, <1.nab@lumc.nl>
```

Examples

```
## random measurement error in a covariate:
# internal covariate-validation study
data(bloodpressure)
with(bloodpressure, MeasErrorRandom(sbp30, variance = 0.25))
```

mecor

mecor: a Measurement Error Correction Package

Description

mecor provides correction methods for measurement error in a continuous covariate or outcome in linear regression models with a continuous outcome

Usage

```
mecor(formula, data, method = "standard", B = 0)
```

Arguments

formula an object of class formula (or one that is coerced to that class): a symbolic

description of the regression model containing a MeasError, MeasErrorExt or

MeasErrorRandom object in one of the covariates or the outcome.

data a data.frame, list or environment (or object coercible by as.data.frame to a data

frame) containing the variables in the model specified in formula.

method a character string indicating the method used to correct for the measurement

error, either "standard" (regression calibration for covariate measurement error and method of moments for outcome measurement error), "efficient" (efficient regression calibration for covariate measurement error and efficient method of moments for outcome measurement error), "valregcal" (validation regression calibration) or "mle" (maximum likelihood estimation). Defaults to "standard".

B number of bootstrap samples, defaults to 0.

Value

mecor returns an object of class "mecor".

An object of class mecor is a list containing the following components:

corfit a list containing the corrected fit, including the coefficients of the corrected fit

(coef) and the variance—covariance matrix of the coefficients of the corrected fit obtained by the delta method (vcov), and more depending on the method used.

uncorfit an lm.fit object of the uncorrected fit.

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Author(s)

Linda Nab, <1.nab@lumc.nl>

References

- L. Nab, R.H.H. Groenwold, P.M.J. Welsing, and M. van Smeden. Measurement error in continuous endpoints in randomised trials: problems and solutions
- L. Nab, M. van Smeden, R.H. Keogh, and R.H.H. Groenwold. mecor: an R package for measurement error correction in linear models with continuous outcomes

```
## measurement error in a covariate/outcome:
# internal covariate-validation study
data(vat)
out <-
mecor(ir_ln ~ MeasError(wc, reference = vat) + sex + age + tbf,
      data = vat,
      method = "standard",
      B = 999)
# replicates study
data(bloodpressure)
mecor(creatinine ~ MeasError(sbp30, replicate = cbind(sbp60, sbp120)) + age,
      data = bloodpressure,
      method = "mle")
# outcome-calibration study
data(sodium)
mecor(MeasError(recall, replicate = cbind(urinary1, urinary2)) ~ diet,
      data = sodium.
      method = "efficient")
# external outcome-validation study
data(haemoglobin_ext)
calmod_fit <- lm(capillary ~ venous, data = haemoglobin_ext)</pre>
data(haemoglobin) # suppose reference venous is not available
mecor(MeasErrorExt(capillary, model = calmod_fit) ~ supplement,
      data = haemoglobin)
# sensitivity analyses
data(vat) # suppose reference vat is not available
# guesstimate the coefficients of the calibration model:
mecor(ir_ln \sim MeasErrorExt(wc, model = list(coef = c(0.2, 0.5, -1.3, 0, 0.6))) + sex + age + tbf,
      data = vat)
# assume random measurement error in wc of magnitude 0.25:
mecor(ir_ln ~ MeasErrorRandom(wc, variance = 0.25) + sex + age + tbf,
      data = vat)
data(bloodpressure) # suppose replicates sbp60 and sbp60 are not available
mecor(creatinine ~ MeasErrorRandom(sbp30, variance = 25) + age,
      data = bloodpressure)
## differential measurement error in the outcome:
# internal outcome-validation study
mecor(MeasError(capillary, reference = venous, differential = supplement) ~ supplement,
```

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```
data = haemoglobin,
method = "standard")
```

sim

Simulated dataset for the ipwm function

Description

A simulated dataset containing 5000 observations of the covariates L1-L10, the true exposure A and true outcome Y, and the misclassified exposure B and misclassified outcome Z.

Usage

sim

Format

A data frame with 5000 rows and 14 variables:

- L1 covariate, binary
- L2 covariate, continuous
- L3 covariate, binary
- L4 covariate, continuous
- L5 covariate, binary
- L6 covariate, binary
- L7 covariate, continuous
- L8 covariate, binary
- L9 covariate, binary
- L10 covariate, continuous
- A exposure, binary
- Y outcome, binary
- B misclassified exposure, binary
- **Z** misclassified outcome, binary

```
data("sim", package = "mecor")
```

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sodium

TONE sodium data [outcome-calibration study]

Description

Self-reported sodium intake and urinary sodium in the TONE study, a randomized controlled trial designed to investigate whether a reduction in sodium intake results in satisfactory blood pressure control. Two replicate urinary sodium measures were available in 50% of the subjects included in the trial.

Usage

sodium

Format

A data frame with 1000 rows and 4 variables:

recall Sodium intake measured by a 24h recall (mg)

diet Usual diet or sodium-lowering diet (0 = usual, 1 = sodium-lowering)

urinary1 Sodium intake measured in urine (1st measure, mg)

urinary2 Sodium intake measured in urine (2nd measure, mg)

Details

This is a simulated data set inspired by the TONE study <doi: 10.1016/1047-2797(94)00056-y>. A motivating example using the example data can be found here: <doi:10.1002/sim.7011>

References

Lawrence J Appel, Mark Espeland, Paul K Whelton, Therese Dolecek, Shiriki Kumanyika, William B Applegate, Walter H Ettinger, John B Kostis, Alan C Wilson, Clifton Lacy, and Stephen T Miller. Trial of Nonpharmacologic Intervention in the Elderly (TONE). Design and rationale of a blood pressure control trial. Annals of Epidemiology (1995). <doi: 10.1016/1047-2797(94)00056-y>

Ruth H Keogh, Raymond J Carroll, Janet A Tooze, Sharon I Kirkpatrick, Laurence S Freedman. Statistical issues related to dietary intake as the response variable in intervention trials. Statistics in Medicine (2016). <doi:10.1002/sim.7011>

```
data("sodium", package = "mecor")
```

summary.mecor 15

summary.mecor Summarizing Measurement Error Correction
--

Description

summary method for class "mecor"

Usage

```
## S3 method for class 'mecor'
summary(object, alpha = 0.05, zerovar = FALSE, fieller = FALSE, ...)
```

Arguments

object	an object of class "mecor", a result of a call to mecor.
alpha	probability of obtaining a type II error.
zerovar	a boolean indicating whether standard errors and confidence intervals using the zerovariance method must be added to the summary object.
fieller	a boolean indicating whether confidence intervals using the fieller method must be added to the summary object.
	additional arguments affecting the summary produced

Value

The function summary mecor returns a list of summary statistics of the fitted corrected model and fitted uncorrected model.

call the matched call
c summary of the corrected fit
uc summary of the uncorrected fit
B number of bootstrap replicates used
alpha alpha level used

See Also

The model fitting function mecor, summary

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```
summary(mecor_fit, zerovar = TRUE, fieller = TRUE)
summary(mecor_fit, alpha = 0.10)
```

vat

NEO visceral adipose tissue data [internal covariate-validation study]

Description

Insulin resistance, waist circumference, sex, age, total body fat and visceral adipose tissue of 650 individuals from the Netherlands Epidemiology of Obesity (NEO) study. Visceral adipose tissue measurements were taken of approximately 40% of the individuals, at random.

Usage

vat

Format

A data frame with 650 rows and 6 variables:

ir_ln Natural logarithm of insulin resistance (fasting glucose (mmol/L) x fasting insulin (mU/L) / 22.5)

wc Waist circumference (standardised, cm)

sex Sex (0 = male, 1 = female)

age Age (years)

tbf Total body fat (standardised, %)

vat Visceral adipose tissue (standardised, cm^2)

Details

This is a simulated data set inspired by the NEO data <doi:10.1007/s10654-013-9801-3>. A motivating example using the example data can be found here: <doi:10.1093/aje/kwab114>

References

Renee de Mutsert, Martin den Heijer, Ton J Rabelink, Johannes WA Smit, Johannes A Romijn, Johan W Jukema, Albert de Roos, Christa M Cobbaert, Margreet Kloppenburg, Saskia le Cessie, Saskia Middeldorp, Frits R Rosendaal. The Netherlands epidemiology of obesity (NEO) study: Study design and data collection. European Journal of Epidemiology (2013). <doi:10.1007/s10654-013-9801-3>

Linda Nab, Maarten van Smeden, Renee de Mutsert, Frits R Rosendaal, and Rolf HH Groenwold. Sampling strategies for internal validation samples for exposure measurement error correction: A study of visceral adipose tissue measures replaced by waist circumference measures. American Journal of Epidemiology (2021). <doi:10.1093/aje/kwab114>

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Examples

```
data("vat", package = "mecor")
```

vat_ext

Visceral adipose tissue external data [external covariate-validation study]

Description

Waist circumference, visceral adipose tissue, sex, age, and total body fat of 100 individuals

Usage

```
vat_ext
```

Format

A data frame with 100 rows and 5 variables:

```
wc Waist circumference (standardised, cm)
```

vat Visceral adipose tissue (standardised, cm^2)

sex Sex (0 = male, 1 = female)

age Age (years)

tbf Total body fat (standardised, %)

Details

This is a simulated data set accompanying the dataset "vat", that is inspired by the NEO data <doi:10.1007/s10654-013-9801-3>. A motivating example using the example data can be found here: <doi:10.1093/aje/kwab114>

References

Renee de Mutsert, Martin den Heijer, Ton J Rabelink, Johannes WA Smit, Johannes A Romijn, Johan W Jukema, Albert de Roos, Christa M Cobbaert, Margreet Kloppenburg, Saskia le Cessie, Saskia Middeldorp, Frits R Rosendaal. The Netherlands epidemiology of obesity (NEO) study: Study design and data collection. European Journal of Epidemiology (2013). <doi:10.1007/s10654-013-9801-3>

Linda Nab, Maarten van Smeden, Renee de Mutsert, Frits R Rosendaal, and Rolf HH Groenwold. Sampling strategies for internal validation samples for exposure measurement error correction: A study of visceral adipose tissue measures replaced by waist circumference measures. American Journal of Epidemiology (2021). <doi:10.1093/aje/kwab114>

```
data("vat_ext", package = "mecor")
```

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