Package ‘nmaINLA’

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Type Package
Title Network Meta-Analysis using Integrated Nested Laplace Approximations
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Description Performs network meta-analysis using integrated nested Laplace approximations ('INLA') which is described in Guenhan, Held, and Friede (2018) <doi:10.1002/jrsm.1285>. Includes methods to assess the heterogeneity and inconsistency in the network. Contains more than ten different network meta-analysis dataset. 'INLA' package can be obtained from <https://www.r-inla.org>.
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Author Burak Kuersad Guenhan [aut, cre]
  (<https://orcid.org/0000-0002-7454-8680>)
Maintainer Burak Kuersad Guenhan <burakgunhan@gmail.com>
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Description

Greco et al. (2013) considered four anaesthetic agents used in cardiac surgery (called here 1, 2, 3 and 4) and investigated through NMA.

Usage

Anestheticdat

Format

An object of class data.frame with 30 rows and 10 columns.

Source

Certolizumabdat

Data for the Certolizumab NMA-network discussed in Dias et al. (2013)

Description
Data are available from a review of trials of certolizumab pegol (CZP) for the treatment of rheumatoid arthritis in patients who had failed on disease-modifying antirheumatic drugs, including methotrexate (MTX). 20 Twelve MTX controlled trials were identified, comparing 6 different treatments with placebo. The primary outcome is improving by at least 50 of Rheumatology scale (ACR50) at 6 months. A trial-specific covariate, the mean disease duration in years for patients, is also given.

Usage
Certolizumabdat

Format
An object of class data.frame with 12 rows and 9 columns.

Source

CooperStrokedat

Data for the stroke prevention NMA-network discussed in Cooper et al. (2009)

Description
The stroke prevention dataset describes a network comparing 17 treatments with 26 trials.

Usage
CooperStrokedat

Format
A data frame with 26 observations on the following 17 variables.
r1  Number of events (responses) in the baseline treatment (treatment 1).
r2  Number of events (responses) in the second study arm treatment (treatment 2).
r3  Number of events (responses) in the third study arm treatment (treatment 3).
create_INLA_dat

Description

create_INLA_dat converts datasets in the one-study-per-row format to one-arm-per-row format, then adds indicator (dummy) variables for the basic contrasts, heterogeneity random effects and design-specific inconsistency random effects and for correlated multi-arm trials.

Usage

create_INLA_dat(
  dat = dat,
  armVars = c(treatment = "t", responders = "r", sampleSize = "n"),
  covariate = "cov",
  design = "des",
  nArmsVar = "na"
)
Arguments

dat Data in one-study-per-row format.

armVars Vector of per-arm variables The name of each component will be the column
name in the resulting dataset.

covariate Optional. Vector of study-specific covariate
design Optional. Vector of study-specific design. We refer design for the set of treat-
ments in each trial.
nArmsVar Variable holding the number of arms for each study.

Details

The resulting data.frame can be used as data argument in nma_inla.

Value

A data frame with the generated columns.

Author(s)

Burak Kuersad Guenhan, <burak.gunhan@med.uni-goettingen.de>, Rafael Sauter and Gert van Valkenhoef

See Also

gemtc::mtc.data.studyrow

Examples

data('Smokdat')
## Create the dataset suitable for INLA
SmokdatINLA <- create_INLA_dat(dat = Smokdat, armVars = c('treatment' = 't', 'responders' = 'r',
'sampleSize' = 'n'), nArmsVar = 'na')
## Check that the data are correct
print(SmokdatINLA)
Diabetesdat

Data for the Diabetes example in Senn et al. (2013)

Description
Results from 26 trials examining the effectiveness of glucose-lowering agents in patients with type 2 diabetes.

Usage
Diabetesdat

Format
An object of class data.frame with 26 rows and 11 columns.

Source
Dietaryfatdat  

*Data for the Dietary fat example in Dias et al. (2011)*

**Description**

In a Cochrane Review of randomised controlled trials to assess the effect of change in dietary fats on total and cardiovascular mortality, 104 data extracted was in the form of rates and given as the number of events per person-years observed.

**Usage**

Dietaryfatdat

**Format**

An object of class `data.frame` with 10 rows and 10 columns.

**Source**


Flourdat  

*Data for the Flour NMA example in Dias et al. (2010)*

**Description**

The flour dataset describes a network comparing 6 treatments with 130 trials. There are 121 pairwise comparisons, 8 three-arm trials and 1 four-arm trial. The main outcome is caries increment, as measured by the change in decayed, missing, and filled tooth surfaces (DMFS) in the permanent dentition of children. Data that are available for study i include the mean caries increment in trial i arm k, y ik, the number of patients at risk in each trial arm, n ik, the time that individuals are at risk in arm k of study i, t i (measured as the trial follow-up time, which is the same for both arms) and the interventions being compared.

**Usage**

Flourdat

**Format**

An object of class `data.frame` with 130 rows and 20 columns.
Source

IncDiabetesdat

Description
An example of network meta-analysis for binary outcomes with follow-up times reported.

Usage
IncDiabetesdat

Format
An object of class data.frame with 22 rows and 12 columns.

Details
This network meta-analysis is studied by Elliott and Meyer (2007) to assess the effects of antihypertensive agents on incident diabetes. Treatment IDs represent 1) diuretic; 2) placebo; 3) beta-blocker; 4) CCB; 5) ACE inhibitor; and 6) ARB.

Source

KussHeartdat

Description
Dataset for pairwise meta-analysis with many zero entries. Data is from a Cochrane review on postoperative stroke occurrence when comparing off-pump and on-pump coronary artery bypass grafting for ischemic heart disease. This data is used as an example in Kuss (2014).

Usage
KussHeartdat
**meta_inla**

**Format**

An object of class tbl_df (inherits from tbl.data.frame) with 60 rows and 4 columns.

**Source**


**Description**

`meta_inla` fits a pairwise meta-analysis model using INLA

**Usage**

```r
meta_inla(
  datINLA,
  fixed.par = c(0, 1000),
  tau.prior = "uniform",
  tau.par = c(0, 5),
  type = "FE",
  approach = "arm-level",
  mreg = FALSE,
  verbose = FALSE,
  inla.strategy = "simplified.laplace",
  improve.hyperpar.dz = 0.75,
  correct = FALSE,
  correct.factor = 10
)
```

**Arguments**

- `datINLA` An object of `create_INLA_dat_pair`
- `fixed.par` A numerical vector specifying the parameter of the normal prior density for mean treatment effect, first value is parameter for mean, second is for variance.
- `tau.prior` A string specifying the prior density for the heterogeneity standard deviation, options are 'uniform' for uniform prior and 'half-normal' for half-normal prior.
- `tau.par` A numerical vector specifying the parameter of the prior density for heterogeneity stddev.
  - `var.par = c(u,l)`: `u` is lower bound and `l` is upper bound when `var.prior = 'uniform'`
  - `var.par = c(m,v)`: `m` is mean and `v` is variance when `var.prior = 'uniform'`
meta_inla

type
A string indicating the type of the model, options are "FE", "RE".

approach
A string indicating the approach of the model, options are "summary-level", "arm-level".

mreg
Logical indicating whether covariate(s) should be incorporated to fit a meta-regression model, default FALSE.

verbose
Logical indicating whether the program should run in a verbose model, default FALSE.

inla.strategy
A string specifying the strategy to use for the approximations of INLA; one of 'gaussian', 'simplified.laplace' (default) or 'laplace', see ?INLA::control.inla.

improve.hyperpar.dz
Step length in the standardized scale used in the construction of the grid, default 0.75, see INLA::inla.hyperpar.

correct
Logical Add correction for the Laplace approximation, default FALSE, see INLA::inla.hyperpar.

correct.factor
Numerical Factor used in adjusting the correction factor if correct=TRUE, default 10, see INLA::inla.hyperpar.

Details

The following model types are supported

- FE, fixed-effect model
- RE, random effects model

Value

meta_inla returns a meta_inla object with components:

Examples

data('TBdat')
## Create the dataset suitable for INLA
TBdatINLA <- create_INLA_dat_pair(TBdat$TRT, TBdat$CON, TBdat$TRTTB, TBdat$CONTB)

## Fitting a random-effects model using arm-level approach
## Not run:
if(requireNamespace('INLA', quietly = TRUE)){
  require('INLA', quietly = TRUE)
  fit.TB.RE.INLA <- meta_inla(TBdatINLA, type = 'RE', approach = 'arm-level',
    tau.prior = 'uniform', tau.par = c(0, 5))
}

## End(Not run)
**Description**

An R package for performing network meta-analysis using INLA.

**Details**

Network meta-analysis is a generalization of pairwise meta-analysis to analyze networks of trials comparing two or more treatments simultaneously (Dias et al., 2011). Bayesian hierarchical models are commonly used for network meta-analysis (Dias et al., 2011). The default choice for performing inference within such models are Markov Chain Monte Carlo (MCMC), for example using BUGS-variants programs such as JAGS. A deterministic approach to do fully Bayesian inference for latent Gaussian models (LGMs) are integrated nested Laplace approximations (INLA) (Rue et al., 2009) which is a fast and accurate alternative to MCMC. INLA methodology is implemented as an R package INLA (<www.r-inla.org>). Sauter and Held (2015) has shown that INLA can be used for fitting many NMA models including fixed effect and consistency models, node-splitting models.

This package extends the INLA implementation of Sauter and Held (2015) to Jackson model (Jackson et al., 2014) and network meta-regression and extracts the features needed for NMA models from INLA R package and presents in an intuitive way (Guenhan et al., 2018). Currently, contrast-based network meta-analysis using trial-arm level data for datasets with binary, continuous, and survival outcomes are supported. Note that the installation of R package ‘INLA’ is compulsory for successful usage. The ‘INLA’ package can be obtained from <http://www.r-inla.org>. We recommend the testing version, which can be downloaded by running: install.packages("INLA",repos=c(getOption("repos"), INLA="https://inla.r-inla-download.org/R/testing"), dep=TRUE).

Type vignette("nmaINLA") to how to use this package.

The development version of nmaINLA is available on GitHub <https://github.com/gunhanb/nmaINLA>.

**Author(s)**

Burak Kuersad Guenhan <burakgunhan@gmail.com>

**Source**


Fitting a network meta-analysis model using INLA

Description

nma_inla fits a network meta-analysis model using INLA.

Usage

nma_inla(
  datINLA,  
  likelihood = NULL,  
  fixed.par = c(0, 1000),  
  tau.prior = "uniform",  
  tau.par = c(0, 5),  
  kappa.prior = "uniform",  
  kappa.par = c(0, 5),  
  mreg = FALSE,  
  type = "consistency",  
  verbose = FALSE,  
  inla.strategy = "simplified.laplace",  
  improve.hyperpar.dz = 0.75,  
  correct = FALSE,  
  correct.factor = 10,  
  improve.hyperpar = TRUE  
)

Arguments

datINLA An object of create_INLA_dat
likelihood The likelihood to be used.
fixed.par A numerical vector specifying the parameter of the normal prior density for basic parameters, first value is parameter for mean, second is for variance.
tau.prior A string specifying the prior density for the heterogeneity standard deviation, options are 'uniform' for uniform prior and 'half-normal' for half-normal prior.
tau.par A numerical vector specifying the parameter of the prior density for heterogeneity stdev.
  • var.par = c(u,l): u is lower bound and l is upper bound when var.prior = 'uniform'.

nma_inla


\( \text{var.par} = c(m, v) \): \( m \) is mean and \( v \) is variance when \( \text{var.prior} = \text{'half-normal'} \).

- **kappa.prior**: A string specifying the prior density for the inconsistency standard deviation, options are 'uniform' for uniform prior and 'half-normal' for half-normal prior.
- **kappa.par**: A numerical vector specifying the parameter of the prior density for inconsistency stddev. The definition of the priors is the same as for \( \text{tau.par} \).
- **mreg**: Logical indicating whether covariate(s) should be incorporated to fit a network meta-regression model, default FALSE.
- **type**: A string indicating the type of the model, options are "FE", "consistency" and "jackson".
- **verbose**: Logical indicating whether the program should run in a verbose model, default FALSE.
- **inla.strategy**: A string specifying the strategy to use for the approximations of INLA; one of 'gaussian', 'simplified.laplace' (default) or 'laplace', see ?INLA::control.inla.
- **improve.hyperpar.dz**: Step length in the standardized scale used in the construction of the grid, default 0.75, see INLA::inla.hyperpar. Not used if \( \text{mod} = \text{'FE'} \).
- **correct**: Logical Add correction for the Laplace approximation, default FALSE, see INLA::inla.hyperpar. Not used if \( \text{mod} = \text{'FE'} \).
- **correct.factor**: Numerical Factor used in adjusting the correction factor if \( \text{correct}=\text{TRUE} \), default 10, see INLA::inla.hyperpar. Not used if \( \text{mod} = \text{'FE'} \).
- **improve.hyperpar**: Improve the estimates of the posterior marginals for the hyperparameters of the model using the grid integration strategy, default TRUE. see INLA::inla.hyperpar.

**Details**

The following likelihood types are supported

- **normal**: for continuous (mean difference) data.
  - Required columns: [mean, std.err]
  - Result: relative mean difference
- **binomial**: for dichotomous data.
  - Required columns: [responders, sampleSize]
  - Result: log odds ratio
- **normal**: for event-rate (survival) data.
  - Required columns: [responders, exposure]
  - Result: log hazard ratio

The following model types are supported

- **FE**, ordinary fixed effect model, assuming homogeneity between trials (Dias et al., 2013)
- **consistency**, ordinary consistency model, assuming consistency in the network. (Jackson et al., 2014)
- **jackson**, the design-by-treatment interaction model with random inconsistency parameters. (Jackson et al., 2014)
`nma_inla` returns a `nma_inla` object.

**Examples**

```r
SmokdatINLA <- create_INLA_dat(dat = Smokdat,
  armVars = c('treatment' = 't', 'responders' = 'r',
  'sampleSize' = 'n'), nArmsVar = 'na')

## Not run:
## Fitting a consistency model
if(requireNamespace('INLA', quietly = TRUE)){
  require('INLA', quietly = TRUE)
  fit.Smok.cons.INLA <- nma_inla(SmokdatINLA, likelihood = 'binomial',
    type = 'consistency',
    tau.prior = 'uniform', tau.par = c(0, 5))
}

## End(Not run)
```

**Parkinsondat**

*Data for the Parkinson NMA-network discussed in Dias et al. (2013)*

**Description**

Data are the mean off-time reduction in patients given dopamine Agonists as adjunct therapy in Parkinson’s disease. The data available are the mean, standard deviation and number of patients in each trial arm, for 7 studies of five different drugs: placebo, coded 1, and five active drugs coded 2 to 5.

**Usage**

`Parkinsondat`

**Format**

An object of class `data.frame` with 7 rows and 11 columns.

**Source**

plot_nma

Plot a network plot

Description
Takes a create_INLA_dat output and plots a network graph.

Usage
plot_nma(
  s.id = "study",
  t.id = "treatment",
  data,
  title = "", 
  adjust.figsizex = 1.1,
  adjust.figsizey = 1.1
)

Arguments
s.id Variable holding the study IDs for each study. The default is "study".
t.id Variable holding the treatments for each study. The default is "treatment".
data A create_INLA_dat object.
title A character string indicating plot title.
adjust.figsizex a positive number used to adjust the plot width. The default is 1.1.
adjust.figsizey a positive number used to adjust the plot height. The default is 1.1.

Author(s)
Lifeng Lin, Jing Zhang, and Haitao Chu

Source
This function is taken from nma.networkplot function from pcnetmeta R package.

See Also
pcnetmeta::nma.networkplot
### print.nma_inla

**Print nmainla object**

**Description**

Takes an `nma_inla` object which is obtained by function `nma_inla` and print the model and data information such as model type used in the model.

**Usage**

```r
## S3 method for class 'nma_inla'
print(x, digits = 3, ...)
```

**Arguments**

- `x`: An `nma_inla` object.
- `digits`: An integer indicating the number of decimal places.
- `...`: Further arguments passed to or from other methods.

**Details**

The resulting data.frame can be used as data argument in `nma_inla`.

**Value**

The return value is invisible `NULL`.

---

### Smokdat

**Data for the smoking cessation NMA-network discussed in Dias et al. (2010)**

**Description**

The smoking cessation dataset describes a network comparing 4 treatments with 24 trials. There are 22 pairwise comparisons and 2 thee-arm trials.

**Usage**

`Smokdat`
**Strokedat**

**Format**

A data frame with 24 observations on the following 10 variables.

- r1 Number of events (responses) in the baseline treatment (treatment 1).
- r2 Number of events (responses) in the second study arm treatment (treatment 2).
- r3 Number of events (responses) in the third study arm treatment (treatment 3).
- n1 Total number of study participants in the baseline treatment (treatment 1).
- n2 Total number of study participants in the second study arm treatment (treatment 2).
- n3 Total number of study participants in the second study arm treatment (treatment 3).
- t1 Indicator variable identifying treatment 1.
- t2 Indicator variable identifying treatment 2.
- t3 Indicator variable identifying treatment 3.
- na Indicator with number of arms in trial.
- des Design, the set of treatments included in each study.

**Source**


**Strokedat**

Data for the Stroke NMA regression discussed in Batson et al. (2016)

**Description**

Dataset for network meta-regression of stroke prevention in Atrial Fibrillation. A total of 19 studies, and primary endpoint is reported ischaemic stroke. It includes 15 comparators which include fixed low dose warfarin with or without aspirin, aspirin monotherapy, aspirin plus clopidogrel, indobufen, idraparinux, triflusal and ximelagatran. Study level covariates are the proportion of patients with a previous stroke/TIA, proportion of males, mean age, and the duration of study.

**Usage**

Strokedat

**Format**

An object of class `data.frame` with 19 rows and 18 columns.

**Source**

**TBdat**  
*Trials investigating effectiveness of the BCG vaccine against TB*

**Description**

A dataset containing the results from 13 trials examining the efficacy of Bacillus Calmette-Guerin (BCG) vaccine against tuberculosis (TB).

**Usage**

TBdat

**Format**

A data frame with following columns

- **Trial**: Trial number
- **TRTTB**: number of TB events in treatment arm
- **TRT**: number of subjects in treatment arm
- **CONTB**: number of TB events in control arm
- **CON**: number of subjects in control arm
- **Latitude**: absolute latitude of the study location

**Source**


---

**Thrombdat**  
*Data for the thrombolytic NMA-network discussed in Dias et al. (2010)*

**Description**

The thrombolytic dataset describes a network comparing 9 treatments with 50 trials. There are 22 pairwise comparisons and 2 thee-arm trials.

**Usage**

Thrombdat
Format

A data frame with 50 observations on the following 11 variables.

- r1: Number of events (responses) in the baseline treatment (treatment 1).
- r2: Number of events (responses) in the second study arm treatment (treatment 2).
- r3: Number of events (responses) in the third study arm treatment (treatment 3).
- n1: Total number of study participants in the baseline treatment (treatment 1).
- n2: Total number of study participants in the second study arm treatment (treatment 2).
- n3: Total number of study participants in the second study arm treatment (treatment 3).
- t1: Indicator variable identifying treatment 1.
- t2: Indicator variable identifying treatment 2.
- t3: Indicator variable identifying treatment 3.
- na: Indicator with number of arms in trial.

Source


Woodsdat

Data for the Woods example in Woods et al. (2010)

Description

Count mortality statistics in randomised controlled trials of treatments for chronic obstructive pulmonary disease (Woods et al. (2010), Table 1)

Usage

Woodsdat

Format

An object of class data.frame with 3 rows and 14 columns.

Source

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