

Package ‘multinma’

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Title Bayesian Network Meta-Analysis of Individual and Aggregate Data

Version 0.2.1

Description Network meta-analysis and network meta-regression models for aggregate data, individual patient data, and mixtures of both individual and aggregate data using multilevel network meta-regression as described by Phillipppo et al. (2020) <doi:10.1111/rssa.12579>. Models are estimated in a Bayesian framework using 'Stan'.

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<https://github.com/dmpillippo/multinma>

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R topics documented:

multinma-package	3
.default	5
adapt_delta	5
add_integration	6
as.array.stan_nma	9
as.igraph.nma_data	10
as.stanfit	11
atrial_fibrillation	11
bcg_vaccine	12
blocker	13
combine_network	14
dgent	16
diabetes	17
dic	18
dietary_fat	19
distr	20
example_pso_mlnmr	21
example_smk_fe	23
example_smk_re	24
example_smk_ume	24
hta_psoriasis	25
is_network_connected	26
loo.stan_nma	27
mcmc_array-class	28
multi	29
nma	31
nma_data-class	37
nma_dic-class	38
nma_prior-class	39
nma_summary-class	39
pairs.stan_nma	40
parkinsons	41
plaque_psoriasis_ipd	42
plot.nma_data	43
plot.nma_dic	45
plot.nma_summary	47
plot_integration_error	50

plot_prior_posterior	51
posterior_ranks	52
predict.stan_nma	55
print.nma_data	58
print.nma_dic	58
print.nma_summary	59
print.stan_nma	60
priors	60
qbern	62
qgamma	62
qlogitnorm	63
relative_effects	64
RE_cor	66
set_agd_arm	67
set_agd_contrast	69
set_ipd	71
smoking	73
stan_nma-class	73
statins	74
summary.nma_prior	75
summary.stan_nma	76
theme_multinma	77
thrombolytics	78
transfusion	79

Index **80**

multinma-package	<i>multinma: A Package for Network Meta-Analysis of Individual and Aggregate Data in Stan</i>
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Description

An R package for performing network meta-analysis and network meta-regression with aggregate data, individual patient data, or mixtures of both.

Details

Network meta-analysis (NMA) combines (aggregate) data from multiple studies on multiple treatments in order to produce consistent estimates of relative treatment effects between each pair of treatments in the network (Dias et al. 2011).

Network meta-regression (NMR) extends NMA to include covariates, allowing adjustment for differences in effect-modifying variables between studies (Dias et al. 2011). NMR is typically performed using aggregate data (AgD), which lacks power and is prone to ecological bias. NMR with individual patient data (IPD) is the gold standard, if data are available.

Multilevel network meta-regression (ML-NMR) allows IPD and AgD to be incorporated together in a network meta-regression (Phillippo et al. 2020; Phillippo 2019). As in IPD NMR, an individual-level regression model is defined. AgD studies are then fitted by integrating the individual-level

model over the respective covariate distributions. This correctly links the two levels of the model (instead of "plugging in" mean covariate values), avoiding aggregation bias. Population-adjusted treatment effects (Phillippo et al. 2016) can be produced for any study population in the network, or for an external target population.

Models are estimated in a Bayesian framework using Stan (Carpenter et al. 2017). Quasi-Monte Carlo numerical integration based on Sobol' sequences is used for the integration in ML-NMR models, with a Gaussian copula to account for correlations between covariates (Phillippo et al. 2020; Phillippo 2019).

Getting Started

A good place to start is with the package vignettes which walk through example analyses, see `vignette("vignette_overview")` for an overview. The series of NICE Technical Support Documents on evidence synthesis gives a detailed introduction to network meta-analysis:

Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Reken S, Ades AE (2011). "NICE DSU Technical Support Documents 1-7: Evidence Synthesis for Decision Making." National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Multilevel network meta-regression is set out in the following methods paper:

Phillippo DM, Dias S, Ades AE, Belger M, Brnabic A, Schacht A, Saure D, Kadziola Z, Welton NJ (2020). "Multilevel Network Meta-Regression for population-adjusted treatment comparisons." *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, **183**(3), 1189–1210. doi: [10.1111/rssa.12579](https://doi.org/10.1111/rssa.12579), <https://doi.org/10.1111/rssa.12579>.

References

Carpenter B, Gelman A, Hoffman MD, Lee D, Goodrich B, Betancourt M, Brubaker M, Guo J, Li P, Riddell A (2017). "Stan: A Probabilistic Programming Language." *Journal of Statistical Software*, **76**(1). doi: [10.18637/jss.v076.i01](https://doi.org/10.18637/jss.v076.i01), <https://doi.org/10.18637/jss.v076.i01>.

Dias S, Sutton AJ, Welton NJ, Ades AE (2011). "NICE DSU Technical Support Document 3: Heterogeneity: subgroups, meta-regression, bias and bias-adjustment." National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Dias S, Welton NJ, Sutton AJ, Ades AE (2011). "NICE DSU Technical Support Document 2: A generalised linear modelling framework for pair-wise and network meta-analysis of randomised controlled trials." National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Phillippo DM (2019). *Calibration of Treatment Effects in Network Meta-Analysis using Individual Patient Data*. Ph.D. thesis, University of Bristol. Available from <https://research-information.bris.ac.uk/>.

Phillippo DM, Ades AE, Dias S, Palmer S, Abrams KR, Welton NJ (2016). "NICE DSU Technical Support Document 18: Methods for population-adjusted indirect comparisons in submission to NICE." National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Phillippo DM, Dias S, Ades AE, Belger M, Brnabic A, Schacht A, Saure D, Kadziola Z, Welton NJ (2020). "Multilevel Network Meta-Regression for population-adjusted treatment compar-

isons.” *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, **183**(3), 1189–1210. doi: [10.1111/rssa.12579](https://doi.org/10.1111/rssa.12579), <https://doi.org/10.1111/rssa.12579>.

.default	<i>Set default values</i>
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Description

The `.default()` function is used internally to mark certain values as default, so that the user may be notified when default values are being used. For example, choosing a default reference treatment for a network, or using default prior distributions. The function `.is_default()` checks whether an argument/object is set to a default value. Neither of these functions are intended to be called by the user.

Usage

```
.default(x = list())
.is_default(x)
```

Arguments

x An object

Value

For `.default()`, an identical object with additional attribute `.default`. For `.is_default()`, a logical value (TRUE or FALSE).

adapt_delta	<i>Target average acceptance probability</i>
-------------	--

Description

The Stan control argument `adapt_delta` sets the target average acceptance probability for the No-U-Turn Sampler (NUTS) used by Stan.

Details

The default value of `adapt_delta` used by `nma()` is 0.8 for fixed effect models, and 0.95 for random effects models.

You should not need to change `adapt_delta` unless you see a warning message about divergent transitions. Increasing `adapt_delta` from the default to a value closer to 1 means that Stan will use a smaller step size, making sampling slower but more robust, and resulting in fewer divergent transitions.

For more details see the Stan documentation available from <https://mc-stan.org/users/documentation/>.

add_integration *Add numerical integration points to aggregate data*

Description

The `add_integration()` generic creates numerical integration points using a Gaussian copula approach, as described in Phillippo et al. (2020). Methods are available for networks stored in `nma_data` objects, and for data frames. The function `unnest_integration()` unnests integration points stored in a data frame, to aid plotting or other exploration.

Usage

```
add_integration(x, ...)

## Default S3 method:
add_integration(x, ...)

## S3 method for class 'data.frame'
add_integration(x, ..., cor = NULL, n_int = 1000L, int_args = list())

## S3 method for class 'nma_data'
add_integration(x, ..., cor = NULL, n_int = 1000L, int_args = list())

unnest_integration(data)
```

Arguments

<code>x</code>	An <code>nma_data</code> object, as created by the <code>set_*</code> () functions or <code>combine_network()</code> , or data frame
<code>...</code>	Distributions for covariates, see "Details"
<code>cor</code>	Correlation matrix to use for generating the integration points. By default, this takes a weighted correlation matrix from all IPD studies. Rows and columns should match the order of covariates specified in <code>...</code>
<code>n_int</code>	Number of integration points to generate, default 1000
<code>int_args</code>	A named list of arguments to pass to <code>sobol()</code>
<code>data</code>	Data frame with nested integration points, stored in list columns as <code>.int_<variable name></code>

Details

The arguments passed to `...` specify distributions for the covariates. Argument names specify the name of the covariate, which should match a covariate name in the IPD (if IPD are present). The required marginal distribution is then specified using the function `distr()`.

Value

For the `nma_data` method, an object of class `nma_data`. For the `data.frame` method, the input data frame is returned (as a `tibble`) with an added column for each covariate (prefixed with `".int_"`), containing the numerical integration points nested as `length-n_int` vectors within each row. For `unnest_integration()`, a data frame with integration points unnested.

References

Phillippo DM, Dias S, Ades AE, Belger M, Brnabic A, Schacht A, Saure D, Kadziola Z, Welton NJ (2020). "Multilevel Network Meta-Regression for population-adjusted treatment comparisons." *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, **183**(3), 1189–1210. doi: [10.1111/rssa.12579](https://doi.org/10.1111/rssa.12579), <https://doi.org/10.1111/rssa.12579>.

Examples

```
## Plaque psoriasis ML-NMR - network setup and adding integration points
# Set up plaque psoriasis network combining IPD and AgD
library(dplyr)
pso_ipd <- filter(plaque_psoriasis_ipd,
                 studyc %in% c("UNCOVER-1", "UNCOVER-2", "UNCOVER-3"))

pso_agd <- filter(plaque_psoriasis_agd,
                 studyc == "FIXTURE")

head(pso_ipd)
head(pso_agd)

pso_ipd <- pso_ipd %>%
  mutate(# Variable transformations
         bsa = bsa / 100,
         prevsys = as.numeric(prevsys),
         psa = as.numeric(psa),
         weight = weight / 10,
         durnpso = durnpso / 10,
         # Treatment classes
         trtclass = case_when(trtn == 1 ~ "Placebo",
                              trtn %in% c(2, 3, 5, 6) ~ "IL blocker",
                              trtn == 4 ~ "TNFa blocker"),
         # Check complete cases for covariates of interest
         complete = complete.cases(durnpso, prevsys, bsa, weight, psa)
  )

pso_agd <- pso_agd %>%
  mutate(
    # Variable transformations
    bsa_mean = bsa_mean / 100,
    bsa_sd = bsa_sd / 100,
    prevsys = prevsys / 100,
    psa = psa / 100,
    weight_mean = weight_mean / 10,
    weight_sd = weight_sd / 10,
```

```

    durnpso_mean = durnpso_mean / 10,
    durnpso_sd = durnpso_sd / 10,
    # Treatment classes
    trtclass = case_when(trtn == 1 ~ "Placebo",
                        trtn %in% c(2, 3, 5, 6) ~ "IL blocker",
                        trtn == 4 ~ "TNFa blocker")
  )

# Exclude small number of individuals with missing covariates
pso_ipd <- filter(pso_ipd, complete)

pso_net <- combine_network(
  set_ipd(pso_ipd,
        study = studyc,
        trt = trtc,
        r = pasi75,
        trt_class = trtclass),
  set_agd_arm(pso_agd,
        study = studyc,
        trt = trtc,
        r = pasi75_r,
        n = pasi75_n,
        trt_class = trtclass)
)

# Print network details
pso_net

# Add integration points to the network
pso_net <- add_integration(pso_net,
  durnpso = distr(qgamma, mean = durnpso_mean, sd = durnpso_sd),
  prevsys = distr(qbern, prob = prevsys),
  bsa = distr(qlogitnorm, mean = bsa_mean, sd = bsa_sd),
  weight = distr(qgamma, mean = weight_mean, sd = weight_sd),
  psa = distr(qbern, prob = psa),
  n_int = 1000)

## Adding integration points to a data frame, e.g. for prediction
# Define a data frame of covariate summaries
new_agd_int <- data.frame(
  bsa_mean = 0.6,
  bsa_sd = 0.3,
  prevsys = 0.1,
  psa = 0.2,
  weight_mean = 10,
  weight_sd = 1,
  durnpso_mean = 3,
  durnpso_sd = 1)

# Adding integration points, using the weighted average correlation matrix
# computed for the plaque psoriasis network
new_agd_int <- add_integration(new_agd_int,

```



```

durnpso = distr(qgamma, mean = durnpso_mean, sd = durnpso_sd),
prevsys = distr(qbern, prob = prevsys),
bsa = distr(qlogitnorm, mean = bsa_mean, sd = bsa_sd),
weight = distr(qgamma, mean = weight_mean, sd = weight_sd),
psa = distr(qbern, prob = psa),
cor = pso_net$int_cor,
n_int = 1000)

new_agd_int

```

as.array.stan_nma *Convert samples into arrays, matrices, or data frames*

Description

Samples (post warm-up) from a `stan_nma` model object can be coerced into an array, matrix, or data frame.

Usage

```

## S3 method for class 'stan_nma'
as.array(x, ..., pars, include = TRUE)

## S3 method for class 'stan_nma'
as.data.frame(x, ..., pars, include = TRUE)

## S3 method for class 'stan_nma'
as.matrix(x, ..., pars, include = TRUE)

```

Arguments

<code>x</code>	A <code>stan_nma</code> object
<code>...</code>	Additional arguments passed to <code>as.array.stanfit()</code>
<code>pars</code>	Optional character vector of parameter names to include in output. If not specified, all parameters are used.
<code>include</code>	Logical, are parameters in <code>pars</code> to be included (TRUE, default) or excluded (FALSE)?

Value

The `as.array()` method produces a 3D array [Iteration, Chain, Parameter] containing posterior samples of each parameter (as class `mcmc_array`). This has the side effect of enabling `bayesplot` functions to seamlessly work on `stan_nma` objects.

The `as.data.frame()` method produces a data frame containing posterior samples of each parameter, combined over all chains.

The `as.matrix()` method produces a matrix containing posterior samples of each parameter, combined over all chains.

as.igraph.nma_data *Convert networks to graph objects*

Description

The method `as.igraph()` converts `nma_data` objects into the form used by the [igraph](#) package. The method `as_tbl_graph()` converts `nma_data` objects into the form used by the [ggraph](#) and [tidygraph](#) packages.

Usage

```
## S3 method for class 'nma_data'
as.igraph(x, ..., collapse = TRUE)
```

```
## S3 method for class 'nma_data'
as_tbl_graph(x, ...)
```

Arguments

<code>x</code>	An nma_data object to convert
<code>...</code>	Additional arguments
<code>collapse</code>	Logical, collapse edges over studies? Default TRUE, only one edge is produced for each comparison (by IPD or AgD study type) with a <code>.nstudy</code> attribute giving the number of studies making that comparison. If FALSE, repeated edges are added for each study making the comparison.

Value

An `igraph` object for `as.igraph()`, a `tbl_graph` object for `as_tbl_graph()`.

Examples

```
# Set up network of smoking cessation data
head(smoking)

smk_net <- set_agd_arm(smoking,
                     study = studyn,
                     trt = trtc,
                     r = r,
                     n = n,
                     trt_ref = "No intervention")

# Print details
smk_net

# Convert to igraph object
igraph::as.igraph(smk_net) # Edges combined by default
igraph::as.igraph(smk_net, collapse = FALSE) # Without combining edges
```

```
# Convert to tbl_graph object
tidygraph::as_tbl_graph(smkn_net) # Edges combined by default
tidygraph::as_tbl_graph(smkn_net, collapse = FALSE) # Without combining edges
```

as.stanfit

as.stanfit

Description

Attempt to turn an object into a [stanfit](#) object.

Usage

```
as.stanfit(x, ...)

## S3 method for class 'stan_nma'
as.stanfit(x, ...)

## Default S3 method:
as.stanfit(x, ...)
```

Arguments

x	an object
...	additional arguments

Value

A [stanfit](#) object.

atrial_fibrillation

Stroke prevention in atrial fibrillation patients

Description

Data frame containing the results of 26 trials comparing 17 treatments in 4 classes for the prevention of stroke in patients with atrial fibrillation (Cooper et al. 2009). The data are the corrected versions given by van Valkenhoef and Kuiper (2016).

Usage

```
atrial_fibrillation
```

Format

A data frame with 63 rows and 11 variables:

studyc study name
studyn numeric study ID
trtc treatment name
trtn numeric treatment code
trt_class treatment class
r number of events
n sample size
E person-years at risk
stroke proportion of individuals with prior stroke
year year of study publication
followup mean length of follow-up (years)

References

Cooper NJ, Sutton AJ, Morris D, Ades AE, Welton NJ (2009). “Addressing between-study heterogeneity and inconsistency in mixed treatment comparisons: Application to stroke prevention treatments in individuals with non-rheumatic atrial fibrillation.” *Statistics in Medicine*, **28**(14), 1861–1881. doi: [10.1002/sim.3594](https://doi.org/10.1002/sim.3594), <https://doi.org/10.1002/sim.3594>.

van Valkenhoef G, Kuiper J (2016). *gemtc: Network Meta-Analysis Using Bayesian Methods*. R package version 0.8-2, <https://CRAN.R-project.org/package=gemtc>.

bcg_vaccine

BCG vaccination

Description

Data frame containing the results of 13 trials comparing BCG vaccination to no vaccination for preventing tuberculosis (TB) (Dias et al. 2011; Berkey et al. 1995). The numbers of individuals diagnosed with TB in each arm during the study follow-up period are recorded. The absolute degrees latitude at which the study was conducted are also recorded.

Usage

bcg_vaccine

Format

A data frame with 26 rows and 6 variables:

studyn numeric study ID

trtn numeric treatment code

trtc treatment name

latitude absolute degrees latitude

r number diagnosed with TB

n sample size

References

Berkey CS, Hoaglin DC, Mosteller F, Colditz GA (1995). “A random-effects regression model for meta-analysis.” *Statistics in Medicine*, **14**(4), 395–411. doi: [10.1002/sim.4780140406](https://doi.org/10.1002/sim.4780140406), <https://doi.org/10.1002/sim.4780140406>.

Dias S, Sutton AJ, Welton NJ, Ades AE (2011). “NICE DSU Technical Support Document 3: Heterogeneity: subgroups, meta-regression, bias and bias-adjustment.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

blocker

Beta blockers to prevent mortality after MI

Description

Data frame containing the number of deaths in 22 trials comparing beta blockers vs. control for preventing mortality after myocardial infarction (Carlin 1992; Dias et al. 2011).

Usage

blocker

Format

A data frame with 44 rows and 5 variables:

studyn numeric study ID

trtn numeric treatment code

trtc treatment name

r total number of events

n total number of individuals

References

Carlin JB (1992). “Meta-analysis for 2 x 2 tables: A bayesian approach.” *Statistics in Medicine*, **11**(2), 141–158. doi: [10.1002/sim.4780110202](https://doi.org/10.1002/sim.4780110202), <https://doi.org/10.1002/sim.4780110202>.

Dias S, Welton NJ, Sutton AJ, Ades AE (2011). “NICE DSU Technical Support Document 2: A generalised linear modelling framework for pair-wise and network meta-analysis of randomised controlled trials.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

combine_network

Combine multiple data sources into one network

Description

Multiple data sources created using `set_ipd()`, `set_agd_arm()`, or `set_agd_contrast()` can be combined into a single network for analysis.

Usage

```
combine_network(..., trt_ref)
```

Arguments

<code>...</code>	multiple data sources, as defined using the <code>set_*</code> functions
<code>trt_ref</code>	reference treatment for the entire network, as a string (or coerced as such) referring to the levels of the treatment factor variable

Value

An object of class `nma_data`

See Also

`set_ipd()`, `set_agd_arm()`, and `set_agd_contrast()` for defining different data sources.
`print.nma_data()` for the print method displaying details of the network, and `plot.nma_data()` for network plots.

Examples

```
## Parkinson's - combining contrast- and arm-based data
studies <- parkinsons$studyn
(parkinsons_arm <- parkinsons[studies %in% 1:3, ])
(parkinsons_contr <- parkinsons[studies %in% 4:7, ])

park_arm_net <- set_agd_arm(parkinsons_arm,
                           study = studyn,
                           trt = trtn,
                           y = y,
```

```

      se = se,
      sample_size = n)

park_contr_net <- set_agd_contrast(parkinsons_contr,
                                study = studyn,
                                trt = trtn,
                                y = diff,
                                se = se_diff,
                                sample_size = n)

park_net <- combine_network(park_arm_net, park_contr_net)

# Print network details
park_net

# Plot network
plot(park_net, weight_edges = TRUE, weight_nodes = TRUE)

## Plaque Psoriasis - combining IPD and AgD in a network
# Set up plaque psoriasis network combining IPD and AgD
library(dplyr)
pso_ipd <- filter(plaque_psoriasis_ipd,
                 studyc %in% c("UNCOVER-1", "UNCOVER-2", "UNCOVER-3"))

pso_agd <- filter(plaque_psoriasis_agd,
                 studyc == "FIXTURE")

head(pso_ipd)
head(pso_agd)

pso_ipd <- pso_ipd %>%
  mutate(# Variable transformations
         bsa = bsa / 100,
         prevsys = as.numeric(prevsys),
         psa = as.numeric(psa),
         weight = weight / 10,
         durnpso = durnpso / 10,
         # Treatment classes
         trtclass = case_when(trtn == 1 ~ "Placebo",
                              trtn %in% c(2, 3, 5, 6) ~ "IL blocker",
                              trtn == 4 ~ "TNFa blocker"),
         # Check complete cases for covariates of interest
         complete = complete.cases(durnpso, prevsys, bsa, weight, psa)
  )

pso_agd <- pso_agd %>%
  mutate(
    # Variable transformations
    bsa_mean = bsa_mean / 100,
    bsa_sd = bsa_sd / 100,
    prevsys = prevsys / 100,
    psa = psa / 100,
    weight_mean = weight_mean / 10,
  )

```

```

weight_sd = weight_sd / 10,
durnpso_mean = durnpso_mean / 10,
durnpso_sd = durnpso_sd / 10,
# Treatment classes
trtclass = case_when(trtn == 1 ~ "Placebo",
                    trtn %in% c(2, 3, 5, 6) ~ "IL blocker",
                    trtn == 4 ~ "TNFa blocker")
)

# Exclude small number of individuals with missing covariates
pso_ipd <- filter(pso_ipd, complete)

pso_net <- combine_network(
  set_ipd(pso_ipd,
    study = studyc,
    trt = trtc,
    r = pasi75,
    trt_class = trtclass),
  set_agd_arm(pso_agd,
    study = studyc,
    trt = trtc,
    r = pasi75_r,
    n = pasi75_n,
    trt_class = trtclass)
)

# Print network details
pso_net

# Plot network
plot(pso_net, weight_nodes = TRUE, weight_edges = TRUE, show_trt_class = TRUE)

```

dgent

Generalised Student's t distribution (with location and scale)

Description

Density, distribution, and quantile function for the generalised t distribution with degrees of freedom df , shifted by location and scaled by scale.

Usage

```
dgent(x, df, location = 0, scale = 1)
```

```
pgent(q, df, location = 0, scale = 1)
```

```
qgent(p, df, location = 0, scale = 1)
```


Arguments

x, q	Vector of quantiles
df	Degrees of freedom, greater than zero
location	Location parameter
scale	Scale parameter, greater than zero
p	Vector of probabilities

Value

dgent() gives the density, pgent() gives the distribution function, qgent() gives the quantile function.

diabetes	<i>Incidence of diabetes in trials of antihypertensive drugs</i>
----------	--

Description

Data frame containing the number of new cases of diabetes in 22 trials of 6 antihypertensive drugs (Elliott and Meyer 2007; Dias et al. 2011). The trial duration (in years) is also recorded.

Usage

```
diabetes
```

Format

A data frame with 48 rows and 7 variables:

studyn numeric study ID
studyc study name
trtn numeric treatment code
trtc treatment name
r total number of events
n total number of individuals
time trial follow-up (years)

References

Dias S, Welton NJ, Sutton AJ, Ades AE (2011). “NICE DSU Technical Support Document 2: A generalised linear modelling framework for pair-wise and network meta-analysis of randomised controlled trials.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Elliott WJ, Meyer PM (2007). “Incident diabetes in clinical trials of antihypertensive drugs: a network meta-analysis.” *The Lancet*, **369**(9557), 201–207. doi: [10.1016/s01406736\(07\)601081](https://doi.org/10.1016/s01406736(07)601081), [https://doi.org/10.1016/s0140-6736\(07\)60108-1](https://doi.org/10.1016/s0140-6736(07)60108-1).

dic *Deviance Information Criterion (DIC)*

Description

Calculate the DIC for a model fitted using the `nma()` function.

Usage

```
dic(x, ...)
```

Arguments

x A fitted model object, inheriting class `stan_nma`
... Other arguments (not used)

Value

A `nma_dic` object.

See Also

`print.nma_dic()` for printing details, `plot.nma_dic()` for producing plots of residual deviance contributions.

Examples

```
## Smoking cessation

# Run smoking FE NMA example if not already available
if (!exists("smk_fit_FE")) example("example_smk_fe")

# Run smoking RE NMA example if not already available
if (!exists("smk_fit_RE")) example("example_smk_re")

# Compare DIC of FE and RE models
(smk_dic_FE <- dic(smk_fit_FE))
(smk_dic_RE <- dic(smk_fit_RE)) # substantially better fit

# Plot residual deviance contributions under RE model
plot(smk_dic_RE)

# Check for inconsistency using UME model

# Run smoking UME NMA example if not already available
if (!exists("smk_fit_RE_UME")) example("example_smk_ume")
```

```
# Compare DIC
smk_dic_RE
(smk_dic_RE_UME <- dic(smk_fit_RE_UME)) # no difference in fit

# Compare residual deviance contributions
plot(smk_dic_RE, smk_dic_RE_UME, show_uncertainty = FALSE)
```

dietary_fat

Reduced dietary fat to prevent mortality

Description

Data frame containing the number of deaths and person-years at risk in 10 trials comparing reduced fat diets vs. control (non-reduced fat diet) for preventing mortality (Hooper et al. 2000; Dias et al. 2011).

Usage

```
dietary_fat
```

Format

A data frame with 21 rows and 7 variables:

studyn numeric study ID

studyc study name

trtn numeric treatment code

trtc treatment name

r number of events

n number randomised

E person-years at risk

References

Dias S, Welton NJ, Sutton AJ, Ades AE (2011). “NICE DSU Technical Support Document 2: A generalised linear modelling framework for pair-wise and network meta-analysis of randomised controlled trials.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Hooper L, Summerbell CD, Higgins JPT, Thompson RL, Clements G, Capps N, Davey Smith G, Riemersma R, Ebrahim S (2000). “Reduced or modified dietary fat for preventing cardiovascular disease.” *Cochrane Database of Systematic Reviews*. ISSN 1465-1858, doi: [10.1002/14651858.CD002137](https://doi.org/10.1002/14651858.CD002137), <https://doi.org/10.1002/14651858.CD002137>.

distr	<i>Specify a general marginal distribution</i>
-------	--

Description

`distr()` is used within the function `add_integration()` to specify marginal distributions for the covariates, via a corresponding inverse CDF. It is also used in `predict.stan_nma()` to specify a distribution for the baseline response (intercept) when predicting absolute outcomes.

Usage

```
distr(qfun, ...)
```

Arguments

qfun	an inverse CDF, either as a function name or a string
...	parameters of the distribution as arguments to qfun, these will be quoted and evaluated later in the context of the aggregate data sources

Details

The function qfun should have a formal argument called p. This restriction serves as a crude check for inverse CDFs (e.g. an error will be given if `dnorm` is used instead of `qnorm`). If a user-written CDF is supplied, it must have an argument p which takes a vector of probabilities.

Value

An object of class `distr`.

See Also

`add_integration()` where `distr()` is used to specify marginal distributions for covariates to integrate over, and `predict.stan_nma()` where `distr()` is used to specify a distribution on the baseline response.

Examples

```
## Specifying marginal distributions for integration

df <- data.frame(x1_mean = 2, x1_sd = 0.5, x2 = 0.8)

# Distribution parameters are evaluated in the context of the data frame
add_integration(df,
  x1 = distr(qnorm, mean = x1_mean, sd = x1_sd),
  x2 = distr(qbern, prob = x2),
  cor = diag(2))
```

example_pso_mlnmr *Example plaque psoriasis ML-NMR*

Description

Calling `example("example_pso_mlnmr")` will run a ML-NMR model with the plaque psoriasis IPD and AgD, using the code in the Examples section below. The resulting `stan_nma` object `pso_fit` will then be available in the global environment.

Details

Plaque psoriasis ML-NMR for use in examples.

Examples

```
# Set up plaque psoriasis network combining IPD and AgD
library(dplyr)
pso_ipd <- filter(plaque_psoriasis_ipd,
                 studyc %in% c("UNCOVER-1", "UNCOVER-2", "UNCOVER-3"))

pso_agd <- filter(plaque_psoriasis_agd,
                 studyc == "FIXTURE")

head(pso_ipd)
head(pso_agd)

pso_ipd <- pso_ipd %>%
  mutate(# Variable transformations
         bsa = bsa / 100,
         prevsys = as.numeric(prevsys),
         psa = as.numeric(psa),
         weight = weight / 10,
         durnpso = durnpso / 10,
         # Treatment classes
         trtclass = case_when(trtn == 1 ~ "Placebo",
                              trtn %in% c(2, 3, 5, 6) ~ "IL blocker",
                              trtn == 4 ~ "TNFa blocker"),
         # Check complete cases for covariates of interest
         complete = complete.cases(durnpso, prevsys, bsa, weight, psa)
  )

pso_agd <- pso_agd %>%
  mutate(
    # Variable transformations
    bsa_mean = bsa_mean / 100,
    bsa_sd = bsa_sd / 100,
    prevsys = prevsys / 100,
    psa = psa / 100,
    weight_mean = weight_mean / 10,
    weight_sd = weight_sd / 10,
```

```

    durnpso_mean = durnpso_mean / 10,
    durnpso_sd = durnpso_sd / 10,
    # Treatment classes
    trtclass = case_when(trtn == 1 ~ "Placebo",
                        trtn %in% c(2, 3, 5, 6) ~ "IL blocker",
                        trtn == 4 ~ "TNFa blocker")
  )

# Exclude small number of individuals with missing covariates
pso_ipd <- filter(pso_ipd, complete)

pso_net <- combine_network(
  set_ipd(pso_ipd,
    study = studyc,
    trt = trtc,
    r = pasi75,
    trt_class = trtclass),
  set_agd_arm(pso_agd,
    study = studyc,
    trt = trtc,
    r = pasi75_r,
    n = pasi75_n,
    trt_class = trtclass)
)

# Print network details
pso_net

# Add integration points to the network
pso_net <- add_integration(pso_net,
  durnpso = distr(qgamma, mean = durnpso_mean, sd = durnpso_sd),
  prevsys = distr(qbern, prob = prevsys),
  bsa = distr(qlogitnorm, mean = bsa_mean, sd = bsa_sd),
  weight = distr(qgamma, mean = weight_mean, sd = weight_sd),
  psa = distr(qbern, prob = psa),
  n_int = 1000)

# Fitting a ML-NMR model.
# Specify a regression model to include effect modifier interactions for five
# covariates, along with main (prognostic) effects. We use a probit link and
# specify that the two-parameter Binomial approximation for the aggregate-level
# likelihood should be used. We set treatment-covariate interactions to be equal
# within each class. We narrow the possible range for random initial values with
# init_r = 0.1, since probit models in particular are often hard to initialise.
# Using the QR decomposition greatly improves sampling efficiency here, as is
# often the case for regression models.
pso_fit <- nma(pso_net,
  trt_effects = "fixed",
  link = "probit",
  likelihood = "bernoulli2",
  regression = ~(durnpso + prevsys + bsa + weight + psa)*.trt,
  class_interactions = "common",

```

```

      prior_intercept = normal(scale = 10),
      prior_trt = normal(scale = 10),
      prior_reg = normal(scale = 10),
      init_r = 0.1,
      QR = TRUE)
pso_fit

```

example_smk_fe

Example smoking FE NMA

Description

Calling `example("example_smk_fe")` will run a fixed effects NMA model with the smoking cessation data, using the code in the Examples section below. The resulting `stan_nma` object `smk_fit_FE` will then be available in the global environment.

Details

Smoking FE NMA for use in examples.

Examples

```

# Set up network of smoking cessation data
head(smoking)

smk_net <- set_agd_arm(smoking,
  study = studyn,
  trt = trtc,
  r = r,
  n = n,
  trt_ref = "No intervention")

# Print details
smk_net

# Fitting a fixed effect model
smk_fit_FE <- nma(smk_net,
  trt_effects = "fixed",
  prior_intercept = normal(scale = 100),
  prior_trt = normal(scale = 100))

smk_fit_FE

```

example_smk_re	<i>Example smoking RE NMA</i>
----------------	-------------------------------

Description

Calling `example("example_smk_re")` will run a random effects NMA model with the smoking cessation data, using the code in the Examples section below. The resulting `stan_nma` object `smk_fit_RE` will then be available in the global environment.

Details

Smoking RE NMA for use in examples.

Examples

```
# Set up network of smoking cessation data
head(smoking)

smk_net <- set_agd_arm(smoking,
                      study = studyn,
                      trt = trtc,
                      r = r,
                      n = n,
                      trt_ref = "No intervention")

# Print details
smk_net

# Fitting a random effects model
smk_fit_RE <- nma(smk_net,
                 trt_effects = "random",
                 prior_intercept = normal(scale = 100),
                 prior_trt = normal(scale = 100),
                 prior_het = normal(scale = 5))

smk_fit_RE
```

example_smk_ume	<i>Example smoking UME NMA</i>
-----------------	--------------------------------

Description

Calling `example("example_smk_ume")` will run an unrelated mean effects (inconsistency) NMA model with the smoking cessation data, using the code in the Examples section below. The resulting `stan_nma` object `smk_fit_RE_UME` will then be available in the global environment.

Details

Smoking UME NMA for use in examples.

Examples

```
# Set up network of smoking cessation data
head(smoking)

smk_net <- set_agd_arm(smoking,
                      study = studyn,
                      trt = trtc,
                      r = r,
                      n = n,
                      trt_ref = "No intervention")

# Print details
smk_net

# Fitting an unrelated mean effects (inconsistency) model
smk_fit_RE_UME <- nma(smk_net,
                     consistency = "ume",
                     trt_effects = "random",
                     prior_intercept = normal(scale = 100),
                     prior_trt = normal(scale = 100),
                     prior_het = normal(scale = 5))

smk_fit_RE_UME
```

 hta_psoriasis

HTA Plaque Psoriasis

Description

Data frame containing the results of 16 trials comparing 8 treatments for moderate-to-severe plaque psoriasis from an HTA report (Woolacott et al. 2006), analysed in TSD2 (Dias et al. 2011). Outcomes are success/failure to achieve 50%, 75%, or 90% reduction in symptoms on the Psoriasis Area and Severity Index (PASI) scale. Some studies report all three ordered outcomes, others only one or two. The latter are coded as missing values (see details).

Usage

```
hta_psoriasis
```

Format

A data frame with 39 rows and 9 variables:

studyn numeric study ID

studyc study name

year year of publication

trtn numeric treatment code

trtc treatment name

sample_size sample size in each arm

PASI50, PASI75, PASI90 ordered multinomial outcome counts (exclusive, see details)

Details

Outcome counts are "exclusive"; that is, for a study reporting all outcomes, the counts represent the categories $50 < \text{PASI} < 75$, $75 < \text{PASI} < 90$, and $90 < \text{PASI} < 100$, and are named by the lower end of the interval. (As opposed to "inclusive" counts, which would represent the overlapping categories $\text{PASI} > 50$, $\text{PASI} > 70$, and $\text{PASI} > 90$.) The count for the fourth category (the lowest), $0 < \text{PASI} < 50$, is equal to $\text{sample_size} - \text{PASI50} - \text{PASI75} - \text{PASI90}$.

Missing values are used where studies only report a subset of the outcomes. For a study reporting only two outcomes, say 50 and 75, the counts represent $50 < \text{PASI} < 75$ and $75 < \text{PASI} < 100$. For a study reporting only one outcome, say PASI 75, the count represents $75 < \text{PASI} < 100$.

References

Dias S, Welton NJ, Sutton AJ, Ades AE (2011). "NICE DSU Technical Support Document 2: A generalised linear modelling framework for pair-wise and network meta-analysis of randomised controlled trials." National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Woolacott N, Hawkins N, Mason A, Kainth A, Khadjesari Z, Bravo Vergel Y, Misso K, Light K, Chalmers R, Sculpher M, Riemsma R (2006). "Etanercept and efalizumab for the treatment of psoriasis: a systematic review." *Health Technology Assessment*, **10**(46). doi: [10.3310/hta10460](https://doi.org/10.3310/hta10460), <https://doi.org/10.3310/hta10460>.

is_network_connected *Check network connectedness*

Description

Check whether a network is connected - whether there is a path of study evidence linking every pair of treatments in the network.

Usage

is_network_connected(network)

Arguments

`network` An `nma_data` object, as created by the functions `set_*`() or `combine_network()`.

Details

Models will still run with disconnected networks. However, estimated relative effects between treatments across disconnected parts of the network will be entirely based on the prior distribution (typically very uncertain), as there is no information to update the prior distribution. Relative effects within each connected sub-network will be estimated as if each sub-network had been analysed separately.

Value

Logical TRUE or FALSE

Examples

```
## Smoking cessation
# Set up network of smoking cessation data
head(smoking)

smk_net <- set_agd_arm(smoking,
                     study = studyn,
                     trt = trtc,
                     r = r,
                     n = n,
                     trt_ref = "No intervention")

# Print details
smk_net

is_network_connected(smk_net) # TRUE, network is connected
## A disconnected network
disc_net <- set_agd_arm(smoking[smoking$studyn %in% c(15, 21), ],
                      study = studyn,
                      trt = trtc,
                      r = r,
                      n = n)
is_network_connected(disc_net) # FALSE, network is disconnected
disc_net
plot(disc_net)
```

Description

The `loo()` and `waic()` functions from the loo package may be called directly on `stan_nma` and `stan_mlnmr` objects.

Usage

```
## S3 method for class 'stan_nma'
loo(x, ...)

## S3 method for class 'stan_nma'
waic(x, ...)
```

Arguments

x An object of class `stan_nma` or `stan_mlnmr`
 ... Further arguments to `loo()` or `waic()`

mcmc_array-class

Working with 3D MCMC arrays

Description

3D MCMC arrays (Iterations, Chains, Parameters) are produced by `as.array()` methods applied to `stan_nma` or `nma_summary` objects.

Usage

```
## S3 method for class 'mcmc_array'
summary(object, ..., probs = c(0.025, 0.25, 0.5, 0.75, 0.975))

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

## S3 method for class 'mcmc_array'
names(x)

## S3 replacement method for class 'mcmc_array'
names(x) <- value
```

Arguments

... Further arguments passed to other methods
 probs Numeric vector of quantiles of interest
 x, object A 3D MCMC array of class `mcmc_array`
 value Character vector of replacement parameter names

Value

The `summary()` method returns a `nma_summary` object, the `print()` method returns `x` invisibly. The `names()` method returns a character vector of parameter names, and `names()<-` returns the object with updated parameter names.

Examples

```
## Smoking cessation

# Run smoking RE NMA example if not already available
if (!exists("smk_fit_RE")) example("example_smk_re")

# Working with arrays of posterior draws (as mcmc_array objects) is
# convenient when transforming parameters

# Transforming log odds ratios to odds ratios
LOR_array <- as.array(relative_effects(smk_fit_RE))
OR_array <- exp(LOR_array)

# mcmc_array objects can be summarised to produce a nma_summary object
smk_OR_RE <- summary(OR_array)

# This can then be printed or plotted
smk_OR_RE
plot(smk_OR_RE, ref_line = 1)

# Transforming heterogeneity SD to variance
tau_array <- as.array(smk_fit_RE, pars = "tau")
tausq_array <- tau_array^2

# Correct parameter names
names(tausq_array) <- "tausq"

# Summarise
summary(tausq_array)
```

multi

Multinomial outcome data

Description

This function aids the specification of multinomial outcome data when setting up a network with [set_agd_arm\(\)](#) or [set_ipd\(\)](#). It takes a set of columns (or, more generally, numeric vectors of the same length) of outcome counts in each category, and binds these together to produce a matrix.

Usage

```
multi(..., inclusive = FALSE, type = c("ordered", "competing"))
```

Arguments

... Two or more numeric columns (or vectors) of category counts. Argument names (optional) will be used to label the categories.

inclusive	Logical, are ordered category counts inclusive (TRUE) or exclusive (FALSE)? Default FALSE. Only used when ordered = TRUE. See details.
type	String, indicating whether categories are "ordered" or "competing". Currently only ordered categorical outcomes are supported by the modelling functions in this package.

Details

When specifying ordered categorical counts, these can either be given as *exclusive* counts (`inclusive = FALSE`, the default) where individuals are only counted in the highest category they achieve, or *inclusive* counts (`inclusive = TRUE`) where individuals are counted in every category up to and including the highest category achieved. (Competing outcomes, by nature, are always specified as exclusive counts.)

NA values can be used to indicate categories/cutpoints that were not measured.

Value

A matrix of (exclusive) category counts

Examples

```
# These two data sets specify the same ordered categorical data for outcomes
# r0 < r1 < r2, but the first uses the "inclusive" format and the second the
# "exclusive" format.
df_inclusive <- tibble::tribble(~r0, ~r1, ~r2,
                               1, 1, 1,
                               5, 4, 1,
                               5, 2, 2,
                               10, 5, 0,
                               5, 5, 0,
                               7, NA, 6, # Achieved r2 or not (no r1)
                               10, 4, NA) # Achieved r1 or not (no r2)

df_exclusive <- tibble::tribble(~r0, ~r1, ~r2,
                                0, 0, 1,
                                1, 3, 1,
                                3, 0, 2,
                                5, 5, 0,
                                0, 5, 0,
                                1, NA, 6, # Achieved r2 or not (no r1)
                                6, 4, NA) # Achieved r1 or not (no r2)

(r_inclusive <- with(df_inclusive, multi(r0, r1, r2, inclusive = TRUE)))
(r_exclusive <- with(df_exclusive, multi(r0, r1, r2, inclusive = FALSE)))

# Counts are always stored in exclusive format
stopifnot(isTRUE(all.equal(r_inclusive, r_exclusive)))

## HTA Plaque Psoriasis
library(dplyr)
```

```

# Ordered outcomes here are given as "exclusive" counts
head(hta_psoriasis)

# Calculate lowest category count (failure to achieve PASI 50)
pso_dat <- hta_psoriasis %>%
  mutate(`PASI<50` = sample_size - rowSums(cbind(PASI50, PASI75, PASI90), na.rm = TRUE))

# Set up network
pso_net <- set_agd_arm(pso_dat,
  study = paste(studyc, year),
  trt = trtc,
  r = multi(`PASI<50`, PASI50, PASI75, PASI90,
    inclusive = FALSE,
    type = "ordered"))

pso_net

```

nma

Network meta-analysis models

Description

The `nma` function fits network meta-analysis and (multilevel) network meta-regression models in Stan.

Usage

```

nma(
  network,
  consistency = c("consistency", "ume"),
  trt_effects = c("fixed", "random"),
  regression = NULL,
  class_interactions = c("common", "exchangeable", "independent"),
  likelihood = NULL,
  link = NULL,
  ...,
  prior_intercept = .default(normal(scale = 100)),
  prior_trt = .default(normal(scale = 10)),
  prior_het = .default(half_normal(scale = 5)),
  prior_het_type = c("sd", "var", "prec"),
  prior_reg = .default(normal(scale = 10)),
  prior_aux = .default(),
  QR = FALSE,
  center = TRUE,
  adapt_delta = NULL,
  int_thin = max(network$n_int%%10, 1)
)

```

Arguments

network	An <code>nma_data</code> object, as created by the functions <code>set_*</code> (), <code>combine_network()</code> , or <code>add_integration()</code>
consistency	Character string specifying the type of (in)consistency model to fit, currently either "consistency" or "ume"
trt_effects	Character string specifying either "fixed" or "random" effects
regression	A one-sided model formula, specifying the prognostic and effect-modifying terms for a regression model. Any references to treatment should use the <code>.trt</code> special variable, for example specifying effect modifier interactions as <code>variable:.trt</code> (see details).
class_interactions	Character string specifying whether effect modifier interactions are specified as "common", "exchangeable", or "independent".
likelihood	Character string specifying a likelihood, if unspecified will be inferred from the data (see details)
link	Character string specifying a link function, if unspecified will default to the canonical link (see details)
...	Further arguments passed to <code>sampling()</code> , such as <code>iter</code> , <code>chains</code> , <code>cores</code> , etc.
prior_intercept	Specification of prior distribution for the intercept
prior_trt	Specification of prior distribution for the treatment effects
prior_het	Specification of prior distribution for the heterogeneity (if <code>trt_effects = "random"</code>)
prior_het_type	Character string specifying whether the prior distribution <code>prior_het</code> is placed on the heterogeneity standard deviation τ ("sd", the default), variance τ^2 ("var"), or precision $1/\tau^2$ ("prec").
prior_reg	Specification of prior distribution for the regression coefficients (if regression formula specified)
prior_aux	Specification of prior distribution for the auxiliary parameter, if applicable (see details)
QR	Logical scalar (default FALSE), whether to apply a QR decomposition to the model design matrix
center	Logical scalar (default TRUE), whether to center the (numeric) regression terms about the overall means
adapt_delta	See adapt_delta for details
int_thin	A single integer value, the thinning factor for returning cumulative estimates of integration error

Details

When specifying a model formula in the regression argument, the usual formula syntax is available (as interpreted by `model.matrix()`). The only additional requirement here is that the special variable `.trt` should be used to refer to treatment. For example, effect modifier interactions should be specified as `variable:.trt`. Prognostic (main) effects and interactions can be included together

compactly as `variable*.trt`, which expands to `variable + variable:.trt` (plus `.trt`, which is already in the NMA model).

For the advanced user, the additional specials `.study` and `.trtclass` are also available, and refer to studies and (if specified) treatment classes respectively.

See [?priors](#) for details on prior specification. Default prior distributions are available, but may not be appropriate for the particular setting and will raise a warning if used. No attempt is made to tailor these defaults to the data provided. Please consider appropriate prior distributions for the particular setting, accounting for the scales of outcomes and covariates, etc. The function `plot_prior_posterior()` may be useful in examining the influence of the chosen prior distributions on the posterior distributions, and the `summary()` method for `nma_prior` objects prints prior intervals.

Value

`nma()` returns a `stan_nma` object, `nma.fit()` returns a `stanfit` object.

Likelihoods and link functions

Currently, the following likelihoods and link functions are supported for each data type:

Data type	Likelihood	Link function
Binary	bernoulli, bernoulli2	logit, probit, cloglog
Count	binomial, binomial2	logit, probit, cloglog
Rate	poisson	log
Continuous	normal	identity, log
Ordered	ordered	logit, probit, cloglog

The `bernoulli2` and `binomial2` likelihoods correspond to a two-parameter Binomial likelihood for arm-based AgD, which more closely matches the underlying Poisson Binomial distribution for the summarised aggregate outcomes in a ML-NMR model than the typical (one parameter) Binomial distribution (see Phillipppo et al. 2020).

When a `cloglog` link is used, including an offset for log follow-up time (i.e. `regression = ~offset(log(time))`) results in a model on the log hazard (see Dias et al. 2011).

Further details on each likelihood and link function are given by Dias et al. (2011).

Auxiliary parameters

Auxiliary parameters are only present in the following models.

Normal likelihood with IPD:

When a Normal likelihood is fitted to IPD, the auxiliary parameters are the arm-level standard deviations σ_{jk} on treatment k in study j .

Ordered multinomial likelihood:

When fitting a model to M ordered outcomes, the auxiliary parameters are the latent cutoffs between each category, $c_0 < c_1 < \dots < c_M$. Only c_2 to c_{M-1} are estimated; we fix $c_0 = -\infty$, $c_1 = 0$, and $c_M = \infty$. When specifying priors for these latent cutoffs, we choose to specify

priors on the *differences* $c_{m+1} - c_m$. Stan automatically truncates any priors so that the ordering constraints are satisfied.

References

Dias S, Welton NJ, Sutton AJ, Ades AE (2011). “NICE DSU Technical Support Document 2: A generalised linear modelling framework for pair-wise and network meta-analysis of randomised controlled trials.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Phillippo DM, Dias S, Ades AE, Belger M, Brnabic A, Schacht A, Saure D, Kadziola Z, Welton NJ (2020). “Multilevel Network Meta-Regression for population-adjusted treatment comparisons.” *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, **183**(3), 1189–1210. doi: [10.1111/rssa.12579](https://doi.org/10.1111/rssa.12579), <https://doi.org/10.1111/rssa.12579>.

Examples

```
## Smoking cessation NMA
# Set up network of smoking cessation data
head(smoking)

smk_net <- set_agd_arm(smoking,
                      study = studyn,
                      trt = trtc,
                      r = r,
                      n = n,
                      trt_ref = "No intervention")

# Print details
smk_net

# Fitting a fixed effect model
smk_fit_FE <- nma(smk_net,
                 trt_effects = "fixed",
                 prior_intercept = normal(scale = 100),
                 prior_trt = normal(scale = 100))

smk_fit_FE

# Fitting a random effects model
smk_fit_RE <- nma(smk_net,
                 trt_effects = "random",
                 prior_intercept = normal(scale = 100),
                 prior_trt = normal(scale = 100),
                 prior_het = normal(scale = 5))

smk_fit_RE
```

```

# Fitting an unrelated mean effects (inconsistency) model
smk_fit_RE_UME <- nma(smk_net,
  consistency = "ume",
  trt_effects = "random",
  prior_intercept = normal(scale = 100),
  prior_trt = normal(scale = 100),
  prior_het = normal(scale = 5))

smk_fit_RE_UME

## Plaque psoriasis ML-NMR
# Set up plaque psoriasis network combining IPD and AgD
library(dplyr)
pso_ipd <- filter(plaque_psoriasis_ipd,
  studyc %in% c("UNCOVER-1", "UNCOVER-2", "UNCOVER-3"))

pso_agd <- filter(plaque_psoriasis_agd,
  studyc == "FIXTURE")

head(pso_ipd)
head(pso_agd)

pso_ipd <- pso_ipd %>%
  mutate(# Variable transformations
    bsa = bsa / 100,
    prevsys = as.numeric(prevsys),
    psa = as.numeric(psa),
    weight = weight / 10,
    durnpso = durnpso / 10,
    # Treatment classes
    trtclass = case_when(trtn == 1 ~ "Placebo",
      trtn %in% c(2, 3, 5, 6) ~ "IL blocker",
      trtn == 4 ~ "TNFa blocker"),
    # Check complete cases for covariates of interest
    complete = complete.cases(durnpso, prevsys, bsa, weight, psa)
  )

pso_agd <- pso_agd %>%
  mutate(
    # Variable transformations
    bsa_mean = bsa_mean / 100,
    bsa_sd = bsa_sd / 100,
    prevsys = prevsys / 100,
    psa = psa / 100,
    weight_mean = weight_mean / 10,
    weight_sd = weight_sd / 10,
    durnpso_mean = durnpso_mean / 10,
    durnpso_sd = durnpso_sd / 10,
    # Treatment classes
    trtclass = case_when(trtn == 1 ~ "Placebo",
      trtn %in% c(2, 3, 5, 6) ~ "IL blocker",

```

```

        trtn == 4 ~ "TNFa blocker")
    )

# Exclude small number of individuals with missing covariates
pso_ipd <- filter(pso_ipd, complete)

pso_net <- combine_network(
  set_ipd(pso_ipd,
    study = studyc,
    trt = trtc,
    r = pasi75,
    trt_class = trtclass),
  set_agd_arm(pso_agd,
    study = studyc,
    trt = trtc,
    r = pasi75_r,
    n = pasi75_n,
    trt_class = trtclass)
)

# Print network details
pso_net

# Add integration points to the network
pso_net <- add_integration(pso_net,
  durnpso = distr(qgamma, mean = durnpso_mean, sd = durnpso_sd),
  prevsys = distr(qbern, prob = prevsys),
  bsa = distr(qlogitnorm, mean = bsa_mean, sd = bsa_sd),
  weight = distr(qgamma, mean = weight_mean, sd = weight_sd),
  psa = distr(qbern, prob = psa),
  n_int = 1000)

# Fitting a ML-NMR model.
# Specify a regression model to include effect modifier interactions for five
# covariates, along with main (prognostic) effects. We use a probit link and
# specify that the two-parameter Binomial approximation for the aggregate-level
# likelihood should be used. We set treatment-covariate interactions to be equal
# within each class. We narrow the possible range for random initial values with
# init_r = 0.1, since probit models in particular are often hard to initialise.
# Using the QR decomposition greatly improves sampling efficiency here, as is
# often the case for regression models.
pso_fit <- nma(pso_net,
  trt_effects = "fixed",
  link = "probit",
  likelihood = "bernoulli2",
  regression = ~(durnpso + prevsys + bsa + weight + psa)*.trt,
  class_interactions = "common",
  prior_intercept = normal(scale = 10),
  prior_trt = normal(scale = 10),
  prior_reg = normal(scale = 10),
  init_r = 0.1,
  QR = TRUE)

```

pso_fit

nma_data-class

The nma_data class

Description

The `nma_data` class contains the data for a NMA in a standard format, created using the functions `set_ipd()`, `set_agd_arm()`, `set_agd_contrast()`, or `combine_network()`. The sub-class `m1nmr_data` is created by the function `add_integration()`, and further contains numerical integration points for the aggregate data.

Details

Objects of class `nma_data` have the following components:

`agd_arm` data from studies with aggregate data (arm format)
`agd_contrast` data from studies with aggregate data (contrast format)
`ipd` data from studies with individual patient data
`treatments` treatment coding factor for entire network
`classes` treatment class coding factor (same length as `treatments` for entire network)
`studies` study coding factor for entire network
`outcome` outcome type for each data source, named list

The `agd_arm`, `agd_contrast`, and `ipd` components are tibbles with the following columns:

`.study` study (as factor)
`.trt` treatment (as factor)
`.trtclass` treatment class (as factor), if specified
`.y` continuous outcome
`.se` standard error (continuous)
`.r` event count (discrete)
`.n` event count denominator (discrete, `agd_arm` only)
`.E` time at risk (discrete)
`.surv` event/censoring time, of type `Surv` (time-to-event)
`.sample_size` sample size (`agd_*` only)
`...` other columns (typically covariates) from the original data frame

Objects of class `m1nmr_data` additionally have components:

`n_int` number of numerical integration points
`int_names` names of covariates with numerical integration points

`int_cor` correlation matrix for covariates used to generate numerical integration points

The `agd_arm` and `agd_contrast` tibbles have additional list columns with prefix `.int_`, one for each covariate, which contain the numerical integration points nested as length-`n_int` vectors within each row.

See Also

`print.nma_data()` for the print method displaying details of the network, and `plot.nma_data()` for network plots.

nma_dic-class

The nma_dic class

Description

The `nma_dic` class contains details of the Deviance Information Criterion (DIC), produced using the `dic()` function.

Details

Objects of class `nma_dic` have the following components:

`dic` The DIC value

`pd` The effective number of parameters

`resdev` The total residual deviance

`pointwise` A list of data frames containing the pointwise contributions for the IPD and AgD.

`resdev_array` A 3D MCMC array [Iterations, Chains, Parameters] of posterior residual deviance samples.

See Also

`dic()`, `print.nma_dic()`, `plot.nma_dic()`.

nma_prior-class	<i>The nma_prior class</i>
-----------------	----------------------------

Description

The `nma_prior` class is used to specify prior distributions.

Details

Objects of class `nma_prior` have the following components:

`dist` Distribution name

`fun` Name of constructor function, as string (e.g. "normal")

... Parameters of the distribution

The distribution parameters, specified as named components in ..., match those in the constructor functions (see [priors](#)).

nma_summary-class	<i>The nma_summary class</i>
-------------------	------------------------------

Description

The `nma_summary` class contains posterior summary statistics of model parameters or other quantities of interest, and the draws used to obtain these statistics.

Details

Objects of class `nma_summary` have the following components:

summary A data frame containing the computed summary statistics. If a regression model was fitted with effect modifier interactions with treatment, these summaries will be study-specific. In this case, the corresponding study population is indicated in a column named `.study`.

sims A 3D array [Iteration, Chain, Parameter] of MCMC simulations

studies (Optional) A data frame containing study information, printed along with the corresponding summary statistics if `summary` contains a `.study` column. Should have a matching `.study` column.

The following attributes may also be set:

xlab Label for x axis in plots, usually either "Treatment" or "Contrast".

ylab Label for y axis in plots, usually used for the scale e.g. "log Odds Ratio".

The subclass `nma_rank_probs` is used by the function `posterior_rank_probs()`, and contains posterior rank probabilities. This subclass does not have a `sims` component, as the rank probabilities are themselves posterior summaries of the ranks (i.e. they do not have a posterior distribution). The posterior ranks from which the rank probabilities are calculated may be obtained from `posterior_ranks()`.

pairs.stan_nma	<i>Matrix of plots for a stan_nma object</i>
----------------	--

Description

A `pairs()` method for `stan_nma` objects, which calls `bayesplot::mcmc_pairs()` on the underlying `stanfit` object.

Usage

```
## S3 method for class 'stan_nma'
pairs(x, ..., pars, include = TRUE)
```

Arguments

<code>x</code>	An object of class <code>stan_nma</code>
<code>...</code>	Other arguments passed to <code>bayesplot::mcmc_pairs()</code>
<code>pars</code>	Optional character vector of parameter names to include in output. If not specified, all parameters are used.
<code>include</code>	Logical, are parameters in <code>pars</code> to be included (TRUE, default) or excluded (FALSE)?

Value

A grid of `ggplot` objects produced by `bayesplot::mcmc_pairs()`.

Examples

```
## Not run:
## Parkinson's mean off time reduction
park_net <- set_agd_arm(parkinsons,
                      study = studyn,
                      trt = trtn,
                      y = y,
                      se = se,
                      sample_size = n)

# Fitting a RE model
park_fit_RE <- nma(park_net,
                  trt_effects = "random",
                  prior_intercept = normal(scale = 100),
                  prior_trt = normal(scale = 100),
                  prior_het = half_normal(scale = 5))

# We see a small number of divergent transition errors
# These do not go away entirely when adapt_delta is increased

# Try to diagnose with a pairs plot
```



```

pairs(park_fit_RE, pars = c("mu[4]", "d[3]", "delta[4: 3]", "tau"))

# Transforming tau onto log scale
pairs(park_fit_RE, pars = c("mu[4]", "d[3]", "delta[4: 3]", "tau"),
      transformations = list(tau = "log"))

# The divergent transitions occur in the upper tail of the heterogeneity
# standard deviation. In this case, with only a small number of studies, there
# is not very much information to estimate the heterogeneity standard deviation
# and the prior distribution may be too heavy-tailed. We could consider a more
# informative prior distribution for the heterogeneity variance to aid
# estimation.

## End(Not run)

```

parkinsons

Mean off-time reduction in Parkinson's disease

Description

Data frame containing the mean off-time reduction in patients given dopamine agonists as adjunct therapy in Parkinson's disease, from 7 trials comparing four active drugs and placebo (Dias et al. 2011).

Usage

```
parkinsons
```

Format

A data frame with 15 rows and 7 variables:

studyn numeric study ID
trtn numeric treatment code (placebo = 1)
y mean off-time reduction
se standard error
n sample size
diff mean difference vs. treatment in reference arm
se_diff standard error of mean difference, see details

Details

This dataset may be analysed using either an arm-based likelihood using `y` and `se`, or a contrast-based likelihood using `diff` and `se_diff` (or a combination of the two across different studies).

The contrast-based data is formatted as described in `set_agd_contrast()`. That is, for the chosen reference arm in each study, the mean difference `diff` is set to `NA`, and `se_diff` is set to the standard error `se` of the outcome on the reference arm.

References

Dias S, Welton NJ, Sutton AJ, Ades AE (2011). “NICE DSU Technical Support Document 2: A generalised linear modelling framework for pair-wise and network meta-analysis of randomised controlled trials.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

plaque_psoriasis_ipd *Plaque psoriasis data*

Description

Two data frames, `plaque_psoriasis_ipd` and `plaque_psoriasis_agd`, containing (simulated) individual patient data from four studies and aggregate data from five studies (Phillippo 2019). Outcomes are binary success/failure to achieve 75%, 90%, or 100% reduction in symptoms on the Psoriasis Area and Severity Index (PASI) scale.

Usage

`plaque_psoriasis_ipd`

`plaque_psoriasis_agd`

Format

The individual patient data are contained in a data frame `plaque_psoriasis_ipd` with 4118 rows, one per individual, and 16 variables:

studyc study name
trtc_long treatment name (long format)
trtc treatment name
trtn numeric treatment code
pasi75 binary PASI 75 outcome
pasi90 binary PASI 90 outcome
pasi100 binary PASI 100 outcome
age age (years)
bmi body mass index (BMI)
pasi_w0 PASI score at week 0
male male sex (TRUE or FALSE)
bsa body surface area (percent)
weight weight (kilograms)
durnpso duration of psoriasis (years)
prevsys previous systemic treatment (TRUE or FALSE)
psa psoriatic arthritis (TRUE or FALSE)

The aggregate data are contained in a data frame `plaque_psoriasis_agd` with 15 rows, one per study arm, and 26 variables:

studyc study name

trtc_long treatment name (long format)

trtc treatment name

trtn numeric treatment code

pasi75_r, pasi75_n PASI 75 outcome count and denominator

pasi90_r, pasi90_n PASI 75 outcome count and denominator

pasi100_r, pasi100_n PASI 75 outcome count and denominator

sample_size_w0 sample size at week zero

age_mean, age_sd mean and standard deviation of age (years)

bmi_mean, bmi_sd mean and standard deviation of BMI

pasi_w0_mean, pasi_w0_sd mean and standard deviation of PASI score at week 0

male percentage of males

bsa_mean, bsa_sd mean and standard deviation of body surface area (percent)

weight_mean, weight_sd mean and standard deviation of weight (kilograms)

durnpso_mean, durnpso_sd mean and standard deviation of duration of psoriasis (years)

prevsys percentage of individuals with previous systemic treatment

psa percentage of individuals with psoriatic arthritis

An object of class `data.frame` with 15 rows and 26 columns.

References

Phillippo DM (2019). *Calibration of Treatment Effects in Network Meta-Analysis using Individual Patient Data*. Ph.D. thesis, University of Bristol. Available from <https://research-information.bris.ac.uk/>.

plot.nma_data

Network plots

Description

Create a network plot from a `nma_data` network object.

Usage

```
## S3 method for class 'nma_data'
plot(
  x,
  ...,
  layout,
  circular,
  weight_edges = TRUE,
  weight_nodes = FALSE,
  show_trt_class = FALSE
)
```

Arguments

x	A <code>nma_data</code> object to plot
...	Additional arguments passed to <code>ggraph()</code> and on to the layout function
layout	The type of layout to create. Any layout accepted by <code>ggraph()</code> may be used, including all of the layout functions provided by <code>igraph</code> .
circular	Whether to use a circular representation. See <code>ggraph()</code> .
weight_edges	Weight edges by the number of studies? Default is TRUE.
weight_nodes	Weight nodes by the total sample size? Default is FALSE.
show_trt_class	Colour treatment nodes by class, if <code>trt_class</code> is set? Default is FALSE.

Details

The default is equivalent to `layout = "linear"` and `circular = TRUE`, which places the treatment nodes on a circle in the order defined by the treatment factor variable. An alternative layout which may give good results for simple networks is `"sugiyama"`, which attempts to minimise the number of edge crossings.

`weight_nodes = TRUE` requires that sample sizes have been specified for any aggregate data in the network, using the `sample_size` option of `set_agd_*`().

Value

A ggplot object, as produced by `ggraph()`.

Examples

```
## Stroke prevention in atrial fibrillation
# Setting up the network
af_net <- set_agd_arm(atrial_fibrillation,
  study = studyc,
  trt = abbreviate(trtc, minlength = 3),
  r = r,
  n = n,
  trt_class = trt_class)

af_net
```

```

# Basic plot
plot(af_net)

# Turn off weighting edges by number of studies
plot(af_net, weight_edges = FALSE)

# Turn on weighting nodes by sample size
plot(af_net, weight_nodes = TRUE)

# Colour treatment nodes by class
plot(af_net, weight_nodes = TRUE, show_trt_class = TRUE)

# Output may be customised using standard ggplot commands
# For example, to display the legends below the plot:
plot(af_net, weight_nodes = TRUE, show_trt_class = TRUE) +
  ggplot2::theme(legend.position = "bottom",
                 legend.box = "vertical",
                 legend.margin = ggplot2::margin(0, 0, 0, 0),
                 legend.spacing = ggplot2::unit(0.5, "lines"))

# Choosing a different ggraph layout, hiding some legends
plot(af_net, weight_nodes = TRUE, show_trt_class = TRUE,
     layout = "star") +
  ggplot2::guides(edge_width = "none", size = "none")

```

plot.nma_dic

Plots of model fit diagnostics

Description

The `plot()` method for `nma_dic` objects produced by `dic()` produces several useful diagnostic plots for checking model fit and model comparison. Further detail on these plots and their interpretation is given by Dias et al. (2011).

Usage

```

## S3 method for class 'nma_dic'
plot(
  x,
  y,
  ...,
  show_uncertainty = TRUE,
  stat = "pointinterval",
  orientation = c("vertical", "horizontal", "x", "y")
)

```

Arguments

x	A nma_dic object
y	(Optional) A second nma_dic object, to produce "dev-dev" plots for model comparison.
...	Additional arguments passed on to other methods
show_uncertainty	Logical, show uncertainty with a ggdist plot stat? Default TRUE.
stat	Character string specifying the ggdist plot stat to use if show_uncertainty = TRUE, default "pointinterval". If y is provided, currently only "pointinterval" is supported.
orientation	Whether the ggdist geom is drawn horizontally ("horizontal") or vertically ("vertical"). Only used for residual deviance plots, default "vertical".

Details

When a single nma_dic object is given, a plot of the residual deviance contribution for each data point is produced. For a good fitting model, each data point is expected to have a residual deviance of 1; larger values indicate data points that are fit poorly by the model.

When two nma_dic objects are given, a "dev-dev" plot comparing the residual deviance contributions under each model is produced. Data points with residual deviance contributions lying on the line of equality are fit equally well under either model. Data points lying below the line of equality indicate better fit under the second model (y); conversely, data points lying above the line of equality indicate better fit under the first model (x). A common use case is to compare a standard consistency model (fitted using `nma()` with consistency = "consistency") with an unrelated mean effects (UME) inconsistency model (fitted using `nma()` with consistency = "ume"), to check for potential inconsistency.

See Dias et al. (2011) for further details.

Value

A ggplot object.

References

Dias S, Welton NJ, Sutton AJ, Ades AE (2011). "NICE DSU Technical Support Document 2: A generalised linear modelling framework for pair-wise and network meta-analysis of randomised controlled trials." National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Examples

```
## Smoking cessation

# Run smoking FE NMA example if not already available
if (!exists("smk_fit_FE")) example("example_smk_fe")

# Run smoking RE NMA example if not already available
```

```

if (!exists("smk_fit_RE")) example("example_smk_re")

# Compare DIC of FE and RE models
(smk_dic_FE <- dic(smk_fit_FE))
(smk_dic_RE <- dic(smk_fit_RE)) # substantially better fit

# Plot residual deviance contributions under RE model
plot(smk_dic_RE)

# Further customisation is possible using ggplot commands
# For example, highlighting data points with residual deviance above a certain threshold
plot(smk_dic_RE) +
  ggplot2::aes(colour = ifelse(..y.. > 1.5, "darkorange", "black")) +
  ggplot2::scale_colour_identity()

# Or by posterior probability, for example here a central probability of 0.6
# corresponds to a lower tail probability of  $(1 - 0.6)/2 = 0.2$ 
plot(smk_dic_RE, .width = c(0.6, 0.95)) +
  ggplot2::aes(colour = ifelse(..ymin.. > 1, "darkorange", "black")) +
  ggplot2::scale_colour_identity()

# Check for inconsistency using UME model

# Run smoking UME NMA example if not already available
if (!exists("smk_fit_RE_UME")) example("example_smk_ume")

# Compare DIC
smk_dic_RE
(smk_dic_RE_UME <- dic(smk_fit_RE_UME)) # no difference in fit

# Compare residual deviance contributions with a "dev-dev" plot
plot(smk_dic_RE, smk_dic_RE_UME)

# By default the dev-dev plot can be a little cluttered
# Hiding the credible intervals
plot(smk_dic_RE, smk_dic_RE_UME, show_uncertainty = FALSE)

# Changing transparency
plot(smk_dic_RE, smk_dic_RE_UME, point_alpha = 0.5, interval_alpha = 0.1)

```

plot.nma_summary

Plots of summary results

Description

The plot method for nma_summary objects is used to produce plots of parameter estimates (when called on a stan_nma object or its summary), relative effects (when called on the output of `relative_effects()`),

absolute predictions (when called on the output of `predict.stan_nma()`), posterior ranks and rank probabilities (when called on the output of `posterior_ranks()` or `posterior_rank_probs()`).

Usage

```
## S3 method for class 'nma_summary'
plot(
  x,
  ...,
  stat = "pointinterval",
  orientation = c("horizontal", "vertical", "y", "x"),
  ref_line = NA_real_
)

## S3 method for class 'nma_parameter_summary'
plot(
  x,
  ...,
  stat = "pointinterval",
  orientation = c("horizontal", "vertical", "y", "x"),
  ref_line = NA_real_
)

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

Arguments

<code>x</code>	A <code>nma_summary</code> object
<code>...</code>	Additional arguments passed on to the underlying <code>ggdist</code> plot stat, see Details
<code>stat</code>	Character string specifying the <code>ggdist</code> plot stat to use, default "pointinterval"
<code>orientation</code>	Whether the <code>ggdist</code> geom is drawn horizontally ("horizontal") or vertically ("vertical"), default "horizontal"
<code>ref_line</code>	Numeric vector of positions for reference lines, by default no reference lines are drawn

Details

Plotting is handled by `ggplot2` and the stats and geoms provided in the `ggdist` package. As a result, the output is very flexible. Any plotting stats provided by `ggdist` may be used, via the argument `stat`. The default uses `ggdist::stat_pointinterval()`, to produce medians and 95% Credible Intervals with 66% inner bands. Additional arguments in `...` are passed to the `ggdist` stat, to customise the output. For example, to produce means and Credible Intervals, specify `point_interval = mean_qi`. To produce an 80% Credible Interval with no inner band, specify `.width = c(0, 0.8)`.

Alternative stats can be specified to produce different summaries. For example, specify `stat = "[half]eye"` to produce (half) eye plots, or `stat = "histinterval"` to produce histograms with intervals.

A full list of options and examples is found in the `ggdist` vignette `vignette("slabinterval", package = "ggdist")`.

A `ggplot` object is returned which can be further modified through the usual `ggplot2` functions to add further aesthetics, geoms, themes, etc.

Value

A `ggplot` object.

Examples

```
## Smoking cessation

# Run smoking RE NMA example if not already available
if (!exists("smk_fit_RE")) example("example_smk_re")

# Produce relative effects
smk_releff_RE <- relative_effects(smk_fit_RE)
plot(smk_releff_RE, ref_line = 0)

# Customise plot options
plot(smk_releff_RE, ref_line = 0, stat = "halfeye")

# Further customisation is possible with ggplot commands
plot(smk_releff_RE, ref_line = 0, stat = "halfeye", slab_alpha = 0.6) +
  ggplot2::aes(slab_fill = ifelse(..x.. < 0, "darkred", "grey60"))

# Produce posterior ranks
smk_rank_RE <- posterior_ranks(smk_fit_RE, lower_better = FALSE)
plot(smk_rank_RE)

# Produce rank probabilities
smk_rankprob_RE <- posterior_rank_probs(smk_fit_RE, lower_better = FALSE)
plot(smk_rankprob_RE)

# Produce cumulative rank probabilities
smk_cumrankprob_RE <- posterior_rank_probs(smk_fit_RE, lower_better = FALSE,
                                          cumulative = TRUE)
plot(smk_cumrankprob_RE)

# Further customisation is possible with ggplot commands
plot(smk_cumrankprob_RE) +
  ggplot2::facet_null() +
  ggplot2::aes(colour = Treatment)
```

 plot_integration_error

Plot numerical integration error

Description

For ML-NMR models, plot the estimated numerical integration error over the entire posterior distribution, as the number of integration points increases. See (Phillippo et al. 2020; Phillippo 2019) for details.

Usage

```
plot_integration_error(
  x,
  ...,
  stat = "violin",
  orientation = c("vertical", "horizontal", "x", "y"),
  show_expected_rate = TRUE
)
```

Arguments

x	An object of type <code>stan_mlnmr</code>
...	Additional arguments passed to the <code>ggdist</code> plot stat.
stat	Character string specifying the <code>ggdist</code> plot stat used to summarise the integration error over the posterior. Default is "violin", which is equivalent to "eye" with some cosmetic tweaks.
orientation	Whether the <code>ggdist</code> geom is drawn horizontally ("horizontal") or vertically ("vertical"), default "vertical"
show_expected_rate	Logical, show typical convergence rate $1/N$? Default TRUE.

Details

The total number of integration points is set by the `n_int` argument to `add_integration()`, and the intervals at which integration error is estimated are set by the `int_thin` argument to `nma()`. The typical convergence rate of Quasi-Monte Carlo integration (as used here) is $1/N$, which by default is displayed on the plot output.

The integration error at each thinning interval N_{thin} is estimated for each point in the posterior distribution by subtracting the final estimate (using all `n_int` points) from the estimate using only the first N_{thin} points.

Value

A `ggplot` object.

Examples

```
## Plaque psoriasis ML-NMR

# Run plaque psoriasis ML-NMR example if not already available
if (!exists("pso_fit")) example("example_pso_mlnmr")

# Plot numerical integration error
plot_integration_error(pso_fit)
```

plot_prior_posterior *Plot prior vs posterior distribution*

Description

Produce plots comparing the prior and posterior distributions of model parameters.

Usage

```
plot_prior_posterior(
  x,
  ...,
  prior = NULL,
  post_args = list(),
  prior_args = list(),
  overlay = c("prior", "posterior"),
  ref_line = NA_real_
)
```

Arguments

x	A stan_nma object
...	Additional arguments passed on to methods
prior	Character vector selecting the prior and posterior distribution(s) to plot. May include "intercept", "trt", "het", "reg", or "aux", as appropriate.
post_args	List of arguments passed on to ggplot2::geom_histogram to control plot output for the posterior distribution
prior_args	List of arguments passed on to ggplot2::geom_path to control plot output for the prior distribution. Additionally, n controls the number of points the density curve is evaluated at (default 500), and p_limits controls the endpoints of the curve as quantiles (default c(.001, .999)).
overlay	String, should prior or posterior be shown on top? Default "prior".
ref_line	Numeric vector of positions for reference lines, by default no reference lines are drawn

Details

Prior distributions are displayed as lines, posterior distributions are displayed as histograms.

Value

A ggplot object.

Examples

```
## Smoking cessation NMA

# Run smoking RE NMA example if not already available
if (!exists("smk_fit_RE")) example("example_smk_re")

# Plot prior vs. posterior, by default all parameters are plotted
plot_prior_posterior(smk_fit_RE)

# Plot prior vs. posterior for heterogeneity SD only
plot_prior_posterior(smk_fit_RE, prior = "het")

# Customise plot
plot_prior_posterior(smk_fit_RE, prior = "het",
                     prior_args = list(colour = "darkred", size = 2),
                     post_args = list(alpha = 0.6))
```

posterior_ranks

Treatment rankings and rank probabilities

Description

Produce posterior treatment rankings and rank probabilities from a fitted NMA model. When a meta-regression is fitted with effect modifier interactions with treatment, these will differ by study population.

Usage

```
posterior_ranks(
  x,
  newdata = NULL,
  study = NULL,
  lower_better = TRUE,
  probs = c(0.025, 0.25, 0.5, 0.75, 0.975),
  summary = TRUE
)
```

```
posterior_rank_probs(
  x,
  newdata = NULL,
  study = NULL,
  lower_better = TRUE,
  cumulative = FALSE
)
```

Arguments

x	A <code>stan_nma</code> object created by <code>nma()</code>
newdata	Only used if a regression model is fitted. A data frame of study details, one row per study, giving the covariate values at which to produce relative effects. Column names must match variables in the regression model. If <code>NULL</code> , relative effects are produced for all studies in the network.
study	Column of <code>newdata</code> which specifies study names, otherwise studies will be labelled by row number.
lower_better	Logical, are lower treatment effects better (<code>TRUE</code> ; default) or higher better (<code>FALSE</code>)? See details.
probs	Numeric vector of quantiles of interest to present in computed summary, default <code>c(0.025, 0.25, 0.5, 0.75, 0.975)</code>
summary	Logical, calculate posterior summaries? Default <code>TRUE</code> .
cumulative	Logical, return cumulative rank probabilities? Default is <code>FALSE</code> , return posterior probabilities of each treatment having a given rank. If <code>TRUE</code> , cumulative posterior rank probabilities are returned for each treatment having a given rank or better.

Details

The function `posterior_ranks()` produces posterior rankings, which have a distribution (e.g. mean/median rank and 95% Credible Interval). The function `posterior_rank_probs()` produces rank probabilities, which give the posterior probabilities of being ranked first, second, etc. out of all treatments.

The argument `lower_better` specifies whether lower treatment effects or higher treatment effects are preferred. For example, with a negative binary outcome lower (more negative) log odds ratios are preferred, so `lower_better = TRUE`. Conversely, for example, if treatments aim to increase the rate of a positive outcome then `lower_better = FALSE`.

Value

A `nma_summary` object if `summary = TRUE`, otherwise a list containing a 3D MCMC array of samples and (for regression models) a data frame of study information.

See Also

`plot.nma_summary()` for plotting the ranks and rank probabilities.

Examples

```
## Smoking cessation

# Run smoking RE NMA example if not already available
if (!exists("smk_fit_RE")) example("example_smk_re")

# Produce posterior ranks
smk_rank_RE <- posterior_ranks(smk_fit_RE, lower_better = FALSE)
smk_rank_RE
plot(smk_rank_RE)

# Produce rank probabilities
smk_rankprob_RE <- posterior_rank_probs(smk_fit_RE, lower_better = FALSE)
smk_rankprob_RE
plot(smk_rankprob_RE)

# Produce cumulative rank probabilities
smk_cumrankprob_RE <- posterior_rank_probs(smk_fit_RE, lower_better = FALSE,
                                           cumulative = TRUE)
smk_cumrankprob_RE
plot(smk_cumrankprob_RE)

# Further customisation is possible with ggplot commands
plot(smk_cumrankprob_RE) +
  ggplot2::facet_null() +
  ggplot2::aes(colour = Treatment)

## Plaque psoriasis ML-NMR

# Run plaque psoriasis ML-NMR example if not already available
if (!exists("pso_fit")) example("example_pso_mlnmr")

# Produce population-adjusted rankings for all study populations in
# the network

# Ranks
pso_rank <- posterior_ranks(pso_fit)
pso_rank
plot(pso_rank)

# Rank probabilities
pso_rankprobs <- posterior_rank_probs(pso_fit)
pso_rankprobs
plot(pso_rankprobs)

# Cumulative rank probabilities
pso_cumrankprobs <- posterior_rank_probs(pso_fit, cumulative = TRUE)
pso_cumrankprobs
plot(pso_cumrankprobs)
```

```

# Produce population-adjusted rankings for a different target
# population
new_agd_means <- data.frame(
  bsa = 0.6,
  prevsys = 0.1,
  psa = 0.2,
  weight = 10,
  durnpso = 3)

# Ranks
posterior_ranks(pso_fit, newdata = new_agd_means)

# Rank probabilities
posterior_rank_probs(pso_fit, newdata = new_agd_means)

# Cumulative rank probabilities
posterior_rank_probs(pso_fit, newdata = new_agd_means,
  cumulative = TRUE)

```

predict.stan_nma *Predictions of absolute effects from NMA models*

Description

Obtain predictions of absolute effects from NMA models fitted with `nma()`. For example, if a model is fitted to binary data with a logit link, predicted outcome probabilities or log odds can be produced.

Usage

```

## S3 method for class 'stan_nma'
predict(
  object,
  ...,
  baseline = NULL,
  newdata = NULL,
  study = NULL,
  trt_ref = NULL,
  type = c("link", "response"),
  level = c("aggregate", "individual"),
  probs = c(0.025, 0.25, 0.5, 0.75, 0.975),
  summary = TRUE
)

```

Arguments

object	A stan_nma object created by <code>nma()</code> .
...	Additional arguments (not used).

baseline	An optional <code>distr()</code> distribution for the baseline response (i.e. intercept) on the linear predictor scale, about which to produce absolute effects. For example, in a model with a logit link, this would be a distribution for the baseline log odds of an event. If NULL, predictions are produced using the baseline response for each study in the network with IPD or arm-based AgD.
newdata	Only required if a regression model is fitted and <code>baseline</code> is specified. A data frame of covariate details, for which to produce predictions. Column names must match variables in the regression model. If <code>type = "aggregate"</code> this should either be a data frame with integration points as produced by <code>add_integration()</code> (one row per study), or a data frame with individual covariate values (one row per individual) which are summarised over. If <code>type = "individual"</code> this should be a data frame of individual covariate values, one row per individual. If NULL, predictions are produced for all studies with IPD and/or arm-based AgD in the network, depending on the value of <code>type</code> .
study	Column of <code>newdata</code> which specifies study names or IDs. When not specified: if <code>newdata</code> contains integration points produced by <code>add_integration()</code> , studies will be labelled sequentially by row; otherwise data will be assumed to come from a single study.
trt_ref	Treatment to which the baseline response distribution refers, if <code>baseline</code> is specified. By default, the baseline response distribution will refer to the network reference treatment. Coerced to character string.
type	Whether to produce predictions on the "link" scale (the default, e.g. log odds) or "response" scale (e.g. probabilities).
level	The level at which predictions are produced, either "aggregate" (the default), or "individual". If <code>baseline</code> is not specified, predictions are produced for all IPD studies in the network if <code>type</code> is "individual" or "aggregate", and for all arm-based AgD studies in the network if <code>type</code> is "aggregate".
probs	Numeric vector of quantiles of interest to present in computed summary, default <code>c(0.025, 0.25, 0.5, 0.75, 0.975)</code>
summary	Logical, calculate posterior summaries? Default TRUE.

Value

A `nma_summary` object if `summary = TRUE`, otherwise a list containing a 3D MCMC array of samples and (for regression models) a data frame of study information.

See Also

`plot.nma_summary()` for plotting the predictions.

Examples

```
## Smoking cessation

# Run smoking RE NMA example if not already available
if (!exists("smk_fit_RE")) example("example_smk_re")
```



```

# Predicted log odds of success in each study in the network
predict(smkn_fit_RE)

# Predicted probabilities of success in each study in the network
predict(smkn_fit_RE, type = "response")

# Predicted probabilities in a population with a baseline log odds of
# response on No Intervention given a Normal distribution with mean -2
# and SD 0.15
(smkn_pred_RE <- predict(smkn_fit_RE,
                        baseline = distr(qnorm, mean = -2, sd = 0.15),
                        type = "response"))
plot(smkn_pred_RE, ref_line = c(0, 1))

## Plaque psoriasis ML-NMR

# Run plaque psoriasis ML-NMR example if not already available
if (!exists("pso_fit")) example("example_pso_mlnmr")

# Predicted probabilities of response in each study in the network
(pso_pred <- predict(pso_fit, type = "response"))
plot(pso_pred, ref_line = c(0, 1))

# Predicted probabilities of response in a new target population, with means
# and SDs or proportions given by
new_agd_int <- data.frame(
  bsa_mean = 0.6,
  bsa_sd = 0.3,
  prevsys = 0.1,
  psa = 0.2,
  weight_mean = 10,
  weight_sd = 1,
  durnpso_mean = 3,
  durnpso_sd = 1
)

# We need to add integration points to this data frame of new data
# We use the weighted mean correlation matrix computed from the IPD studies
new_agd_int <- add_integration(new_agd_int,
                              durnpso = distr(qgamma, mean = durnpso_mean, sd = durnpso_sd),
                              prevsys = distr(qbern, prob = prevsys),
                              bsa = distr(qlogitnorm, mean = bsa_mean, sd = bsa_sd),
                              weight = distr(qgamma, mean = weight_mean, sd = weight_sd),
                              psa = distr(qbern, prob = psa),
                              cor = pso_net$int_cor,
                              n_int = 1000)

# Predicted probabilities of achieving PASI 75 in this target population, given
# a Normal(-1.75, 0.08^2) distribution on the baseline probit-probability of

```

```
# response on Placebo (at the reference levels of the covariates), are given by
(pso_pred_new <- predict(pso_fit,
                        type = "response",
                        newdata = new_agd_int,
                        baseline = distr(qnorm, -1.75, 0.08)))
plot(pso_pred_new, ref_line = c(0, 1))
```

```
print.nma_data      Print nma_data objects
```

Description

Print details of networks stored as `nma_data` objects, as created by `set_ipd()`, `set_agd_arm()`, `set_agd_contrast()`, or `combine_network()`.

Usage

```
## S3 method for class 'nma_data'
print(x, ..., n = 10)

## S3 method for class 'mlnmr_data'
print(x, ..., n = 10)
```

Arguments

<code>x</code>	<code>nma_data</code> object
<code>...</code>	other options (not used)
<code>n</code>	number of studies of each type to print

```
print.nma_dic      Print DIC details
```

Description

Print details of DIC model fit statistics, computed by `dic()` function.

Usage

```
## S3 method for class 'nma_dic'
print(x, digits = 1, ...)
```

Arguments

<code>x</code>	An object of class <code>nma_dic</code>
<code>digits</code>	An integer passed to <code>round()</code>
<code>...</code>	Ignored

Value

x is returned invisibly.

```
print.nma_summary      Methods for nma_summary objects
```

Description

The `as.data.frame()`, `as_tibble()`, and `as.tibble()` methods return the posterior summary statistics in a data frame or tibble. The `as.matrix()` method returns a matrix of posterior draws. The `as.array()` method returns a 3D array [Iteration, Chain, Parameter] of posterior draws (as class `mcmc_array`).

Usage

```
## S3 method for class 'nma_summary'
print(x, ..., digits = 2, pars, include = TRUE)
```

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

```
## S3 method for class 'nma_summary'
as.tibble(x, ...)
```

```
## S3 method for class 'nma_summary'
as_tibble(x, ...)
```

```
## S3 method for class 'nma_summary'
as.array(x, ...)
```

```
## S3 method for class 'nma_summary'
as.matrix(x, ...)
```

```
## S3 method for class 'nma_rank_probs'
as.array(x, ...)
```

```
## S3 method for class 'nma_rank_probs'
as.matrix(x, ...)
```

Arguments

x	A <code>nma_summary</code> object
...	Additional arguments passed on to other methods
digits	Integer number of digits to display
pars	Character vector of parameters to display in the printed summary
include	Logical, are parameters named in <code>pars</code> included (TRUE) or excluded (FALSE)

Value

A `data.frame` for `as.data.frame()`, a `tbl_df` for `as.tibble()` and `as_tibble()`, a `matrix` for `as.matrix()`, and an `mcmc_array` for `as.array()`.

The `print()` method returns `x` invisibly.

See Also

[plot.nma_summary\(\)](#)

<code>print.stan_nma</code>	<i>Print stan_nma objects</i>
-----------------------------	-------------------------------

Description

Print `stan_nma` objects

Usage

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

Arguments

<code>x</code>	A stan_nma object
<code>...</code>	Further arguments passed to print.stanfit()

<code>priors</code>	<i>Prior distributions</i>
---------------------	----------------------------

Description

These functions are used to specify prior distributions for the model parameters.

Usage

```
normal(location = 0, scale)
```

```
half_normal(scale)
```

```
log_normal(location, scale)
```

```
cauchy(location = 0, scale)
```

```
half_cauchy(scale)
```

```

student_t(location = 0, scale, df)

half_student_t(scale, df)

exponential(scale = 1/rate, rate = 1/scale)

flat()

```

Arguments

location	Prior location. Typically prior mean (see details).
scale	Prior scale. Typically prior standard deviation (see details).
df	Prior degrees of freedom.
rate	Prior rate.

Details

The location and scale parameters are typically the prior mean and standard deviation, with the following exceptions:

- For the Cauchy distribution location is the prior median and scale is the prior scale.
- For the log-Normal distribution, location and scale are the prior mean and standard deviation of the logarithm.

Compatibility with model parameters:

The following table summarises which prior distributions may be used with which model parameters. Essentially, priors that take only non-negative values (e.g. half-Normal) may only be used for non-negative parameters (heterogeneity SD/variance/precision, and any auxiliary parameter). If a real-valued prior distribution is specified for a non-negative parameter, it will be truncated at 0 to be non-negative.

	Intercept prior_intercept	Treatment effects prior_trt	Heterogeneity prior_
Normal normal()	Yes	Yes	Yes
half-Normal half_normal()	-	-	Yes
log-Normal log_normal()	-	-	Yes
Cauchy cauchy()	Yes	Yes	Yes
half-Cauchy half_cauchy()	-	-	Yes
Student t student_t()	Yes	Yes	Yes
half-Student t half_student_t()	-	-	Yes
Exponential exponential()	-	-	Yes
Flat flat()	Yes	Yes	Yes

The flat() prior is a special case where no prior information is added to the model, resulting in an implicit flat uniform prior distribution over the entire support for a parameter. This will be an improper prior if the parameter is unbounded, and is not generally advised. See the [Stan user's guide](#) for more details.

Value

Object of class [nma_prior](#).

See Also

[summary.nma_prior\(\)](#) for summarising details of prior distributions. [plot_prior_posterior\(\)](#) for plots comparing the prior and posterior distributions of model parameters.

<code>qbern</code>	<i>The Bernoulli Distribution</i>
--------------------	-----------------------------------

Description

The quantile function `qbern` for a Bernoulli distribution, with success probability `prob`. This is equivalent to `qbinom(p, 1, prob)`.

Usage

```
qbern(p, prob, lower.tail = TRUE, log.p = FALSE)
```

```
pbern(q, prob, lower.tail = TRUE, log.p = FALSE)
```

```
dbern(x, prob, log = FALSE)
```

Arguments

<code>p</code>	vector of probabilities
<code>prob</code>	probability of success
<code>lower.tail</code> , <code>log.p</code> , <code>log</code>	see stats::Binomial
<code>x</code> , <code>q</code>	vector of quantiles

<code>qgamma</code>	<i>The Gamma distribution</i>
---------------------	-------------------------------

Description

We provide convenient extensions of the `[dpq]gamma` functions, which allow the distribution to be specified in terms of its mean and standard deviation, instead of shape and rate/scale.

Usage

```

qgamma(
  p,
  shape,
  rate = 1,
  scale = 1/rate,
  lower.tail = TRUE,
  log.p = FALSE,
  mean,
  sd
)

dgamma(x, shape, rate = 1, scale = 1/rate, log = FALSE, mean, sd)

pgamma(
  q,
  shape,
  rate = 1,
  scale = 1/rate,
  lower.tail = TRUE,
  log.p = FALSE,
  mean,
  sd
)

```

Arguments

p vector of probabilities
shape, rate, scale, log, lower.tail, log.p
 see [stats::GammaDist](#)
mean, sd mean and standard deviation, overriding shape and rate or scale if specified
x, q vector of quantiles

qlogitnorm

The logit Normal distribution

Description

We provide convenient extensions of the [dpq]logitnorm functions in the package [logitnorm](#), which allow the distribution to be specified in terms of its mean and standard deviation, instead of its logit-mean and logit-sd.

Usage

```
qlogitnorm(p, mu = 0, sigma = 1, ..., mean, sd)
```

```
dlogitnorm(x, mu = 0, sigma = 1, ..., mean, sd)
```

```
plogitnorm(q, mu = 0, sigma = 1, ..., mean, sd)
```

Arguments

p, x	vector of quantiles
mu, sigma, ...	see logitnorm
mean, sd	mean and standard deviation, overriding mu and sigma if specified
q	vector of probabilities

relative_effects	<i>Relative treatment effects</i>
------------------	-----------------------------------

Description

Generate (population-average) relative treatment effects. If a ML-NMR or meta-regression model was fitted, these are specific to each study population.

Usage

```
relative_effects(  
  x,  
  newdata = NULL,  
  study = NULL,  
  all_contrasts = FALSE,  
  trt_ref = NULL,  
  probs = c(0.025, 0.25, 0.5, 0.75, 0.975),  
  summary = TRUE  
)
```

Arguments

x	A stan_nma object created by nma()
newdata	Only used if a regression model is fitted. A data frame of study details, one row per study, giving the covariate values at which to produce relative effects. Column names must match variables in the regression model. If NULL, relative effects are produced for all studies in the network.
study	Column of newdata which specifies study names, otherwise studies will be labelled by row number.
all_contrasts	Logical, generate estimates for all contrasts (TRUE), or just the "basic" contrasts against the network reference treatment (FALSE)? Default FALSE.

trt_ref	Reference treatment to construct relative effects against, if all_contrasts = FALSE. By default, relative effects will be against the network reference treatment. Coerced to character string.
probs	Numeric vector of quantiles of interest to present in computed summary, default <code>c(0.025, 0.25, 0.5, 0.75, 0.975)</code>
summary	Logical, calculate posterior summaries? Default TRUE.

Value

A `nma_summary` object if `summary = TRUE`, otherwise a list containing a 3D MCMC array of samples and (for regression models) a data frame of study information.

See Also

`plot.nma_summary()` for plotting the relative effects.

Examples

```
## Smoking cessation

# Run smoking RE NMA example if not already available
if (!exists("smk_fit_RE")) example("example_smk_re")

# Produce relative effects
smk_releff_RE <- relative_effects(smk_fit_RE)
smk_releff_RE
plot(smk_releff_RE, ref_line = 0)

# Relative effects for all pairwise comparisons
relative_effects(smk_fit_RE, all_contrasts = TRUE)

# Relative effects against a different reference treatment
relative_effects(smk_fit_RE, trt_ref = "Self-help")

# Transforming to odds ratios
# We work with the array of relative effects samples
LOR_array <- as.array(smk_releff_RE)
OR_array <- exp(LOR_array)

# mcmc_array objects can be summarised to produce a nma_summary object
smk_OR_RE <- summary(OR_array)

# This can then be printed or plotted
smk_OR_RE
plot(smk_OR_RE, ref_line = 1)

## Plaque psoriasis ML-NMR

# Run plaque psoriasis ML-NMR example if not already available
```

```

if (!exists("pso_fit")) example("example_pso_mlnmr")

# Produce population-adjusted relative effects for all study populations in
# the network
pso_releff <- relative_effects(pso_fit)
pso_releff
plot(pso_releff, ref_line = 0)

# Produce population-adjusted relative effects for a different target
# population
new_agd_means <- data.frame(
  bsa = 0.6,
  prevsys = 0.1,
  psa = 0.2,
  weight = 10,
  durnpso = 3)

relative_effects(pso_fit, newdata = new_agd_means)

```

RE_cor

Random effects structure

Description

Use RE_cor to generate the random effects correlation matrix, under the assumption of common heterogeneity variance (i.e. all within-study correlations are 0.5). Use which_RE to return a vector of IDs for the RE deltas (0 means no RE delta on this arm).

Usage

```
RE_cor(study, trt, contrast, type = c("reftrt", "blshift"))
```

```
which_RE(study, trt, contrast, type = c("reftrt", "blshift"))
```

Arguments

study	A vector of study IDs (integer, character, or factor)
trt	A factor vector of treatment codes (or coercible as such), with first level indicating the reference treatment
contrast	A logical vector, of the same length as study and trt, indicating whether the corresponding data are in contrast rather than arm format.
type	Character string, whether to generate RE structure under the "reference treatment" parameterisation, or the "baseline shift" parameterisation.

Value

For `RE_cor()`, a correlation matrix of dimension equal to the number of random effects deltas (excluding those that are set equal to zero).

For `which_RE()`, an integer vector of IDs indexing the rows and columns of the correlation matrix returned by `RE_cor()`.

Examples

```
RE_cor(smoking$studyn, smoking$trtn, contrast = rep(FALSE, nrow(smoking)))
RE_cor(smoking$studyn, smoking$trtn, contrast = rep(FALSE, nrow(smoking)), type = "blshift")
which_RE(smoking$studyn, smoking$trtn, contrast = rep(FALSE, nrow(smoking)))
which_RE(smoking$studyn, smoking$trtn, contrast = rep(FALSE, nrow(smoking)), type = "blshift")
```

 set_agd_arm

Set up arm-based aggregate data

Description

Set up a network containing arm-based aggregate data (AgD), such as event counts or mean outcomes on each arm. Multiple data sources may be combined once created using [combine_network\(\)](#).

Usage

```
set_agd_arm(
  data,
  study,
  trt,
  y = NULL,
  se = NULL,
  r = NULL,
  n = NULL,
  E = NULL,
  sample_size = NULL,
  trt_ref = NULL,
  trt_class = NULL
)
```

Arguments

<code>data</code>	a data frame
<code>study</code>	column of data specifying the studies, coded using integers, strings, or factors
<code>trt</code>	column of data specifying treatments, coded using integers, strings, or factors
<code>y</code>	column of data specifying a continuous outcome
<code>se</code>	column of data specifying the standard error for a continuous outcome
<code>r</code>	column of data specifying a binary or Binomial outcome count

n	column of data specifying Binomial outcome numerator
E	column of data specifying the total time at risk for Poisson outcomes
sample_size	column of data giving the sample size in each arm. Optional, see details.
trt_ref	reference treatment for the network, as a single integer, string, or factor. If not specified, a reasonable well-connected default will be chosen (see details).
trt_class	column of data specifying treatment classes, coded using integers, strings, or factors. By default, no classes are specified.

Details

By default, `trt_ref = NULL` and a network reference treatment will be chosen that attempts to maximise computational efficiency and stability. If an alternative reference treatment is chosen and the model runs slowly or has low effective sample size (ESS) this may be the cause - try letting the default reference treatment be used instead. Regardless of which treatment is used as the network reference at the model fitting stage, results can be transformed afterwards: see the `trt_ref` argument of [relative_effects\(\)](#) and [predict.stan_nma\(\)](#).

The `sample_size` argument is optional, but when specified:

- Enables automatic centering of predictors (`center = TRUE`) in [nma\(\)](#) when a regression model is given for a network combining IPD and AgD
- Enables production of study-specific relative effects, rank probabilities, etc. for studies in the network when a regression model is given
- Nodes in [plot.nma_data\(\)](#) may be weighted by sample size

If a Binomial outcome is specified and `sample_size` is omitted, `n` will be used as the sample size by default. If a Multinomial outcome is specified and `sample_size` is omitted, the sample size will be determined automatically from the supplied counts by default.

All arguments specifying columns of data accept the following:

- A column name as a character string, e.g. `study = "studyc"`
- A bare column name, e.g. `study = studyc`
- `dplyr::mutate()` style semantics for inline variable transformations, e.g. `study = paste(author, year)`

Value

An object of class `nma_data`

See Also

[set_ipd\(\)](#) for individual patient data, [set_agd_contrast\(\)](#) for contrast-based aggregate data, and [combine_network\(\)](#) for combining several data sources in one network.

[print.nma_data\(\)](#) for the print method displaying details of the network, and [plot.nma_data\(\)](#) for network plots.

Examples

```
# Set up network of smoking cessation data
head(smoking)

smk_net <- set_agd_arm(smoking,
                     study = studyn,
                     trt = trtc,
                     r = r,
                     n = n,
                     trt_ref = "No intervention")

# Print details
smk_net

# Plot network
plot(smk_net)
```

set_agd_contrast	<i>Set up contrast-based aggregate data</i>
------------------	---

Description

Set up a network containing contrast-based aggregate data (AgD), i.e. summaries of relative effects between treatments such as log Odds Ratios. Multiple data sources may be combined once created using `combine_network()`.

Usage

```
set_agd_contrast(
  data,
  study,
  trt,
  y = NULL,
  se = NULL,
  sample_size = NULL,
  trt_ref = NULL,
  trt_class = NULL
)
```

Arguments

data	a data frame
study	column of data specifying the studies, coded using integers, strings, or factors
trt	column of data specifying treatments, coded using integers, strings, or factors
y	column of data specifying a continuous outcome
se	column of data specifying the standard error for a continuous outcome

sample_size	column of data giving the sample size in each arm. Optional, see details.
trt_ref	reference treatment for the network, as a single integer, string, or factor. If not specified, a reasonable well-connected default will be chosen (see details).
trt_class	column of data specifying treatment classes, coded using integers, strings, or factors. By default, no classes are specified.

Details

Each study should have a single reference/baseline treatment, against which relative effects in the other arm(s) are given. For the reference arm, include a data row with continuous outcome y equal to NA. If a study has three or more arms (so two or more relative effects), set the standard error se for the reference arm data row equal to the standard error of the mean outcome on the reference arm (this determines the covariance of the relative effects, when expressed as differences in mean outcomes between arms).

All arguments specifying columns of data accept the following:

- A column name as a character string, e.g. `study = "studyc"`
- A bare column name, e.g. `study = studyc`
- `dplyr::mutate()` style semantics for inline variable transformations, e.g. `study = paste(author, year)`

By default, `trt_ref = NULL` and a network reference treatment will be chosen that attempts to maximise computational efficiency and stability. If an alternative reference treatment is chosen and the model runs slowly or has low effective sample size (ESS) this may be the cause - try letting the default reference treatment be used instead. Regardless of which treatment is used as the network reference at the model fitting stage, results can be transformed afterwards: see the `trt_ref` argument of [relative_effects\(\)](#) and [predict.stan_nma\(\)](#).

The `sample_size` argument is optional, but when specified:

- Enables automatic centering of predictors (`center = TRUE`) in [nma\(\)](#) when a regression model is given for a network combining IPD and AgD
- Enables production of study-specific relative effects, rank probabilities, etc. for studies in the network when a regression model is given
- Nodes in [plot.nma_data\(\)](#) may be weighted by sample size

Value

An object of class `nma_data`

See Also

[set_ipd\(\)](#) for individual patient data, [set_agd_arm\(\)](#) for arm-based aggregate data, and [combine_network\(\)](#) for combining several data sources in one network.

[print.nma_data\(\)](#) for the print method displaying details of the network, and [plot.nma_data\(\)](#) for network plots.

Examples

```
# Set up network of Parkinson's contrast data
head(parkinsons)

park_net <- set_agd_contrast(parkinsons,
                            study = studyn,
                            trt = trtn,
                            y = diff,
                            se = se_diff,
                            sample_size = n)

# Print details
park_net

# Plot network
plot(park_net)
```

set_ipd

Set up individual patient data

Description

Set up a network containing individual patient data (IPD). Multiple data sources may be combined once created using [combine_network\(\)](#).

Usage

```
set_ipd(
  data,
  study,
  trt,
  y = NULL,
  r = NULL,
  E = NULL,
  trt_ref = NULL,
  trt_class = NULL
)
```

Arguments

data	a data frame
study	column of data specifying the studies, coded using integers, strings, or factors
trt	column of data specifying treatments, coded using integers, strings, or factors
y	column of data specifying a continuous outcome
r	column of data specifying a binary outcome or Poisson outcome count
E	column of data specifying the total time at risk for Poisson outcomes

trt_ref	reference treatment for the network, as a single integer, string, or factor. If not specified, a reasonable well-connected default will be chosen (see details).
trt_class	column of data specifying treatment classes, coded using integers, strings, or factors. By default, no classes are specified.

Details

By default, `trt_ref = NULL` and a network reference treatment will be chosen that attempts to maximise computational efficiency and stability. If an alternative reference treatment is chosen and the model runs slowly or has low effective sample size (ESS) this may be the cause - try letting the default reference treatment be used instead. Regardless of which treatment is used as the network reference at the model fitting stage, results can be transformed afterwards: see the `trt_ref` argument of [relative_effects\(\)](#) and [predict.stan_nma\(\)](#).

All arguments specifying columns of data accept the following:

- A column name as a character string, e.g. `study = "studyc"`
- A bare column name, e.g. `study = studyc`
- `dplyr::mutate()` style semantics for inline variable transformations, e.g. `study = paste(author, year)`

Value

An object of class `nma_data`

See Also

[set_agd_arm\(\)](#) for arm-based aggregate data, [set_agd_contrast\(\)](#) for contrast-based aggregate data, and [combine_network\(\)](#) for combining several data sources in one network.

[print.nma_data\(\)](#) for the print method displaying details of the network, and [plot.nma_data\(\)](#) for network plots.

Examples

```
# Set up network of plaque psoriasis IPD
head(plaque_psoriasis_ipd)

pso_net <- set_ipd(plaque_psoriasis_ipd,
                  study = studyc,
                  trt = trtc,
                  r = pasi75)

# Print network details
pso_net

# Plot network
plot(pso_net)

# Setting a different reference treatment
set_ipd(plaque_psoriasis_ipd,
        study = studyc,
        trt = trtc,
```



```
r = pasi75,
trt_ref = "PBO")
```

smoking	<i>Smoking cessation data</i>
---------	-------------------------------

Description

Data frame containing the results of 24 trials of 4 smoking cessation treatments (Hasselblad 1998; Dias et al. 2011).

Usage

```
smoking
```

Format

A data frame with 50 rows and 5 variables:

studyn numeric study ID

trtn numeric treatment code

trtc treatment name

r total number of events

n total number of individuals

References

Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Ades AE (2011). “NICE DSU Technical Support Document 4: Inconsistency in networks of evidence based on randomised controlled trials.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Hasselblad V (1998). “Meta-analysis of Multitreatment Studies.” *Medical Decision Making*, **18**(1), 37–43. doi: [10.1177/0272989x9801800110](https://doi.org/10.1177/0272989x9801800110), <https://doi.org/10.1177/0272989x9801800110>.

stan_nma-class	<i>The stan_nma class</i>
----------------	---------------------------

Description

The `stan_nma` and `stan_mlnmr` classes contains the results from running a model with the function `nma()`.

Details

Objects of class `stan_nma` and `stan_mlnmr` have the following components:

`network` The network data from which the model was run (class `nma_data` for `stan_nma`, or class `mlnmr_data` for `stan_mlnmr`)

`stanfit` The `stanfit` object returned by calling `sampling()` for the model

`trt_effects` Whether fixed or random effects were used (character string)

`consistency` The consistency/inconsistency model used (character string)

`regression` The regression model used (formula)

`class_interactions` If treatment classes and a regression model are specified, the model used for interactions within each class (common, exchangeable, or independent)

`xbar` A named vector of values used for centering

`likelihood` The likelihood used (character string)

`link` The link function used (character string)

`priors` A list containing the priors used (as `nma_prior` objects)

The `stan_mlnmr` sub-class inherits from `stan_nma`, and differs only in the class of the network object.

statins

Statins for cholesterol lowering

Description

Data frame containing the results of 19 trials comparing statins to placebo or usual care (Dias et al. 2011). The number of deaths (all-cause mortality) are recorded. In some studies the aim was primary prevention (patients had no previous heart disease), and in others the aim was secondary prevention (patients had previous heart disease).

Usage

`statins`

Format

A data frame with 38 rows and 7 variables:

studyn numeric study ID

studyc study name

trtn numeric treatment code

trtc treatment name

prevention primary or secondary prevention study

r number of deaths

n sample size

References

Dias S, Sutton AJ, Welton NJ, Ades AE (2011). “NICE DSU Technical Support Document 3: Heterogeneity: subgroups, meta-regression, bias and bias-adjustment.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

summary.nma_prior	<i>Summary of prior distributions</i>
-------------------	---------------------------------------

Description

Print a summary of prior distribution details.

Usage

```
## S3 method for class 'nma_prior'
summary(object, ..., probs = c(0.5, 0.95), digits = 2, trunc = NULL)
```

Arguments

object	Prior distribution as a nma_prior object
...	Additional arguments, not used
probs	Numeric vector of probabilities to calculate prior intervals
digits	Number of digits to display
trunc	Optional numeric vector of length 2, giving the truncation limits of the prior distribution. Useful if a real-valued prior is assigned to a positive-valued parameter, then trunc = c(0, Inf) will give the correct prior intervals. By default, truncation is not used.

Value

A data frame is returned invisibly, giving the prior intervals

Examples

```
summary(normal(location = 0, scale = 1))
summary(half_normal(scale = 1))
summary(log_normal(location = -3.93, scale = 1.51))

# Truncation limits may be set, for example to restrict a prior to positive values
summary(normal(location = 0.5, scale = 1), trunc = c(0, Inf))
```

summary.stan_nma *Posterior summaries from stan_nma objects*

Description

Posterior summaries of model parameters in stan_nma objects may be produced using the `summary()` method and plotted with the `plot()` method. NOTE: To produce relative effects, absolute predictions, or posterior ranks, see [relative_effects\(\)](#), [predict.stan_nma\(\)](#), [posterior_ranks\(\)](#), [posterior_rank_probs\(\)](#).

Usage

```
## S3 method for class 'stan_nma'
summary(object, ..., pars, include, probs = c(0.025, 0.25, 0.5, 0.75, 0.975))

## S3 method for class 'stan_nma'
plot(
  x,
  ...,
  pars,
  include,
  stat = "pointinterval",
  orientation = c("horizontal", "vertical", "y", "x"),
  ref_line = NA_real_
)
```

Arguments

...	Additional arguments passed on to other methods
pars, include	See rstan::extract()
probs	Numeric vector of specifying quantiles of interest, default <code>c(0.025, 0.25, 0.5, 0.75, 0.975)</code>
x, object	A stan_nma object
stat	Character string specifying the ggdist plot stat to use, default "pointinterval"
orientation	Whether the ggdist geom is drawn horizontally ("horizontal") or vertically ("vertical"), default "horizontal"
ref_line	Numeric vector of positions for reference lines, by default no reference lines are drawn
summary	Logical, calculate posterior summaries? Default TRUE.

Details

The `plot()` method is a shortcut for `plot(summary(stan_nma))`. For details of plotting options, see [plot.nma_summary\(\)](#).

Value

A `nma_summary` object

See Also

`plot.nma_summary()`, `relative_effects()`, `predict.stan_nma()`, `posterior_ranks()`, `posterior_rank_probs()`

Examples

```
## Smoking cessation

# Run smoking RE NMA example if not already available
if (!exists("smk_fit_RE")) example("example_smk_re")

# Summary and plot of all model parameters
summary(smk_fit_RE)
plot(smk_fit_RE)

# Summary and plot of heterogeneity tau only
summary(smk_fit_RE, pars = "tau")
plot(smk_fit_RE, pars = "tau")

# Customising plot output
plot(smk_fit_RE,
     pars = c("d", "tau"),
     stat = "halfeye",
     ref_line = 0)
```

theme_multinma

Plot theme for multinma plots

Description

A simple ggplot2 theme for plots in the multinma package.

Usage

```
theme_multinma(...)
```

Arguments

... Arguments passed to `ggplot2::theme_light()`

Value

A ggplot2 theme

See Also

```
ggplot2::theme(), ggplot2::theme_set()
```

Examples

```
library(ggplot2)
theme_set(theme_multinma())
```

thrombolytics	<i>Thrombolytic treatments data</i>
---------------	-------------------------------------

Description

Data frame containing the results of 50 trials of 8 thrombolytic drugs (streptokinase, SK; alteplase, t-PA; accelerated alteplase, Acc t-PA; streptokinase plus alteplase, SK+tPA; reteplase, r-PA; tenecteplase, TNK; urokinase, UK; anistreplase, ASPAC) plus per-cutaneous transluminal coronary angioplasty (PTCA) (Boland et al. 2003; Lu and Ades 2006; Dias et al. 2011). The number of deaths in 30 or 35 days following acute myocardial infarction are recorded.

Usage

```
thrombolytics
```

Format

A data frame with 50 rows and 5 variables:

studyn numeric study ID
trtn numeric treatment code
trtc treatment name
r total number of events
n total number of individuals

References

Boland A, Dunder Y, Bagust A, Haycox A, Hill R, Mota RM, Walley T, Dickson R (2003). “Early thrombolysis for the treatment of acute myocardial infarction: a systematic review and economic evaluation.” *Health Technology Assessment*, 7(15). doi: [10.3310/hta7150](https://doi.org/10.3310/hta7150), <https://doi.org/10.3310/hta7150>.

Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Ades AE (2011). “NICE DSU Technical Support Document 4: Inconsistency in networks of evidence based on randomised controlled trials.” National Institute for Health and Care Excellence. <http://nicedsu.org.uk/>.

Lu GB, Ades AE (2006). “Assessing evidence inconsistency in mixed treatment comparisons.” *Journal of the American Statistical Association*, 101(474), 447–459. doi: [10.1198/016214505000001302](https://doi.org/10.1198/016214505000001302), <https://doi.org/10.1198/016214505000001302>.

transfusion	<i>Granulocyte transfusion in patients with neutropenia or neutrophil dysfunction</i>
-------------	---

Description

Data frame containing the number of deaths in 6 trials comparing transfusion of granulocytes (white blood cells) to control (Stanworth et al. 2005). Previously used to demonstrate informative prior distributions for the heterogeneity variance by Turner et al. (2012).

Usage

```
transfusion
```

Format

A data frame with 12 rows and 4 variables:

studyc study name

trtc treatment name

r total number of deaths

n total number of individuals

References

Stanworth S, Massey E, Hyde C, Brunskill SJ, Navarette C, Lucas G, Marks D, Paulus U (2005). “Granulocyte transfusions for treating infections in patients with neutropenia or neutrophil dysfunction.” *Cochrane Database of Systematic Reviews*. ISSN 1465-1858, doi: [10.1002/14651858.CD005339](https://doi.org/10.1002/14651858.CD005339), <https://doi.org/10.1002/14651858.CD005339>.

Turner RM, Davey J, Clarke MJ, Thompson SG, Higgins JPT (2012). “Predicting the extent of heterogeneity in meta-analysis, using empirical data from the Cochrane Database of Systematic Reviews.” *International Journal of Epidemiology*, **41**(3), 818–827. doi: [10.1093/ije/dys041](https://doi.org/10.1093/ije/dys041), <https://doi.org/10.1093/ije/dys041>.

Index

- * **datasets**
 - [atrial_fibrillation](#), 11
 - [bcg_vaccine](#), 12
 - [blocker](#), 13
 - [diabetes](#), 17
 - [dietary_fat](#), 19
 - [hta_psoriasis](#), 25
 - [parkinsons](#), 41
 - [plaque_psoriasis_ipd](#), 42
 - [smoking](#), 73
 - [statins](#), 74
 - [thrombolytics](#), 78
 - [transfusion](#), 79
- * **examples**
 - [example_pso_mlnmr](#), 21
 - [example_smk_fe](#), 23
 - [example_smk_re](#), 24
 - [example_smk_ume](#), 24
- [.default](#), 5
- [.is_default \(.default\)](#), 5
- [?priors](#), 33
- [adapt_delta](#), 5, 32
- [add_integration](#), 6
- [add_integration\(\)](#), 20, 37, 50, 56
- [as.array.nma_rank_probs](#)
 - [\(print.nma_summary\)](#), 59
- [as.array.nma_summary](#)
 - [\(print.nma_summary\)](#), 59
- [as.array.stan_nma](#), 9
- [as.array.stanfit\(\)](#), 9
- [as.data.frame.nma_summary](#)
 - [\(print.nma_summary\)](#), 59
- [as.data.frame.stan_nma](#)
 - [\(as.array.stan_nma\)](#), 9
- [as.igraph.nma_data](#), 10
- [as.matrix.nma_rank_probs](#)
 - [\(print.nma_summary\)](#), 59
- [as.matrix.nma_summary](#)
 - [\(print.nma_summary\)](#), 59
- [as.matrix.stan_nma \(as.array.stan_nma\)](#), 9
- [as.stanfit](#), 11
- [as.tibble.nma_summary](#)
 - [\(print.nma_summary\)](#), 59
- [as_tbl_graph.nma_data](#)
 - [\(as.igraph.nma_data\)](#), 10
- [as_tibble.nma_summary](#)
 - [\(print.nma_summary\)](#), 59
- [atrial_fibrillation](#), 11
- [bayesplot](#), 9
- [bayesplot::mcmc_pairs\(\)](#), 40
- [bcg_vaccine](#), 12
- [blocker](#), 13
- [cauchy \(priors\)](#), 60
- [combine_network](#), 14
- [combine_network\(\)](#), 37, 58, 67–72
- [dbern \(qbern\)](#), 62
- [dgamma \(qgamma\)](#), 62
- [dgent](#), 16
- [diabetes](#), 17
- [dic](#), 18
- [dic\(\)](#), 38, 45, 58
- [dietary_fat](#), 19
- [distr](#), 20, 20
- [distr\(\)](#), 6, 56
- [dlogitnorm \(qlogitnorm\)](#), 63
- [example_pso_mlnmr](#), 21
- [example_smk_fe](#), 23
- [example_smk_re](#), 24
- [example_smk_ume](#), 24
- [exponential \(priors\)](#), 60
- [flat \(priors\)](#), 60
- [ggdist](#), 48
- [ggdist::stat_pointinterval\(\)](#), 48

- ggplot2, 48, 49
- ggplot2::geom_histogram, 51
- ggplot2::geom_path, 51
- ggplot2::theme(), 78
- ggplot2::theme_light(), 77
- ggplot2::theme_set(), 78
- ggraph, 10
- ggraph(), 44

- half_cauchy (priors), 60
- half_normal (priors), 60
- half_student_t (priors), 60
- hta_psoriasis, 25

- igraph, 10, 44
- is_network_connected, 26

- log_normal (priors), 60
- logitnorm, 63, 64
- loo (loo.stan_nma), 27
- loo(), 27, 28
- loo.stan_nma, 27

- mcmc_array, 9, 59
- mcmc_array (mcmc_array-class), 28
- mcmc_array-class, 28
- mlnmr_data, 74
- mlnmr_data (nma_data-class), 37
- mlnmr_data-class (nma_data-class), 37
- model.matrix(), 32
- multi, 29
- multinma (multinma-package), 3
- multinma-package, 3

- names.mcmc_array (mcmc_array-class), 28
- names<- .mcmc_array (mcmc_array-class), 28

- nma, 31
- nma(), 5, 18, 46, 50, 53, 55, 64, 68, 70, 73
- nma_data, 7, 10, 14, 44, 58, 68, 70, 72, 74
- nma_data (nma_data-class), 37
- nma_data-class, 37
- nma_dic, 18, 45, 58
- nma_dic (nma_dic-class), 38
- nma_dic-class, 38
- nma_prior, 62, 74
- nma_prior (nma_prior-class), 39
- nma_prior-class, 39
- nma_rank_probs (nma_summary-class), 39

- nma_summary, 28, 53, 56, 65, 77
- nma_summary (nma_summary-class), 39
- nma_summary-class, 39
- normal (priors), 60

- pairs(), 40
- pairs.stan_nma, 40
- parkinsons, 41
- pbern (qbern), 62
- pgamma (qgamma), 62
- pgent (dgent), 16
- plaque_psoriasis
 - (plaque_psoriasis_ipd), 42
- plaque_psoriasis_agd
 - (plaque_psoriasis_ipd), 42
- plaque_psoriasis_ipd, 42
- plogitnorm (qlogitnorm), 63
- plot.nma_data, 43
- plot.nma_data(), 14, 38, 68, 70, 72
- plot.nma_dic, 45
- plot.nma_dic(), 18, 38
- plot.nma_parameter_summary
 - (plot.nma_summary), 47
- plot.nma_rank_probs (plot.nma_summary), 47
- plot.nma_summary, 47
- plot.nma_summary(), 53, 56, 60, 65, 76, 77
- plot.stan_nma (summary.stan_nma), 76
- plot_integration_error, 50
- plot_prior_posterior, 51
- plot_prior_posterior(), 33, 62
- posterior_rank_probs (posterior_ranks), 52
- posterior_rank_probs(), 39, 48, 76, 77
- posterior_ranks, 52
- posterior_ranks(), 39, 48, 76, 77
- predict.stan_nma, 55
- predict.stan_nma(), 20, 48, 68, 70, 72, 76, 77
- print.mcmc_array (mcmc_array-class), 28
- print.mlnmr_data (print.nma_data), 58
- print.nma_data, 58
- print.nma_data(), 14, 38, 68, 70, 72
- print.nma_dic, 58
- print.nma_dic(), 18, 38
- print.nma_summary, 59
- print.stan_nma, 60
- print.stanfit(), 60
- priors, 39, 60

qbern, 62
qgamma, 62
qgent (dgent), 16
qlogitnorm, 63

RE_cor, 66
relative_effects, 64
relative_effects(), 47, 68, 70, 72, 76, 77
round(), 58
rstan::extract(), 76

sampling(), 32, 74
set_agd_arm, 67
set_agd_arm(), 14, 29, 37, 58, 70, 72
set_agd_contrast, 69
set_agd_contrast(), 14, 37, 41, 58, 68, 72
set_ipd, 71
set_ipd(), 14, 29, 37, 58, 68, 70
smoking, 73
sobol(), 6
stan_mlnmr, 27, 28
stan_mlnmr (stan_nma-class), 73
stan_nma, 18, 27, 28, 33, 60
stan_nma (stan_nma-class), 73
stan_nma-class, 73
stanfit, 11, 33
statins, 74
stats::Binomial, 62
stats::GammaDist, 63
student_t (priors), 60
summary(), 33
summary.mcmc_array (mcmc_array-class),
28
summary.nma_prior, 75
summary.nma_prior(), 62
summary.stan_nma, 76

theme_multinma, 77
thrombolytics, 78
tibble, 7
tidygraph, 10
transfusion, 79

unnest_integration (add_integration), 6

waic (loo.stan_nma), 27
waic(), 27, 28
which_RE (RE_cor), 66