# Package: gemtc (via r-universe)

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Title Network Meta-Analysis Using Bayesian Methods

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Description Network meta-analyses (mixed treatment comparisons) in the Bayesian framework using JAGS. Includes methods to assess heterogeneity and inconsistency, and a number of standard visualizations. van Valkenhoef et al. (2012) [<doi:10.1002/jrsm.1054>](https://doi.org/10.1002/jrsm.1054); van Valkenhoef et al. (2015) [<doi:10.1002/jrsm.1167>](https://doi.org/10.1002/jrsm.1167).

**Depends** R ( $>= 3.5.0$ ), coda ( $>= 0.13$ )

**Imports** igraph  $(>= 1.0)$ , meta  $(>= 2.1)$ , plyr  $(>= 1.8)$ , graphics,  $grDevices, stats, utilise, grid, rjags (>= 4-0), trunc norm,$ Rglpk, forcats  $(>= 0.5.0)$ 

**Suggests** test that  $(>= 0.8)$ , Matrix

#### URL <https://github.com/gertvv/gemtc>

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LazyData true

Collate 'anohe.R' 'arrayize.R' 'blobbogram.R' 'template.R' 'code.R' 'data.R' 'deviance.R' 'forest.R' 'solveLP.R' 'inits.R' 'likelihoods.R' 'll-helper.counts.R' 'll.binom.cloglog.R' 'll.binom.log.R' 'll.binom.logit.R' 'll.call.R' 'll.normal.identity.R' 'll.poisson.log.R' 'minimum.diameter.spanning.tree.R' 'mtc.data.studyrow.R' 'mtc.hy.prior.R' 'mtc.model.R' 'mtc.model.consistency.R' 'mtc.model.nodesplit.R' 'mtc.model.regression.R' 'mtc.model.ume.R' 'mtc.model.use.R' 'mtc.network.R' 'stopIfNotConsistent.R' 'mtc.result.R' 'mtc.run.R' 'nodesplit.R' 'plotCovariateEffect.R' 'priors.R' 'rank.probability.R' 'regression.R' 'relative.effect.R' 'relative.effect.table.R'

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# **Contents**



<span id="page-1-1"></span>gemtc-package *GeMTC: Network meta-analysis in R*

# Description

An R package for performing network meta-analyses (mixed treatment comparisons).

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#### Details

Network meta-analysis, or mixed treatment comparison (MTC) is a technique to meta-analyze networks of trials comparing two or more treatments at the same time [Dias et al. 2013a]. Using a Bayesian hierarchical model, all direct and indirect comparisons are taken into account to arrive at a single consistent estimate of the effect of all included treatments based on all included studies.

This package allows the automated generation of network meta-analysis models [van Valkenhoef et al. 2012], inclusing both fixed effect and random effects network meta-analysis, node-splitting models to identify inconsistency, and network meta-regression models. Models are estimated using JAGS (through the rjags package).

It is possible to get reproducible results, but as JAGS uses its own pseudo-random number generator, this is somewhat more involved. See [mtc.model](#page-17-1) for details.

The source for GeMTC is available under the GPL-3 on [Github.](https://github.com/gertvv/gemtc)

### Author(s)

Gert van Valkenhoef

#### References

S. Dias, N.J. Welton, D.M. Caldwell, and A.E. Ades (2010), *Checking consistency in mixed treatment comparison meta-analysis*, Statistics in Medicine 29(7-8, Sp. Iss. SI):932-944. [\[doi:10.1002/sim.3767\]](https://doi.org/10.1002/sim.3767)

S. Dias, A.J. Sutton, A.E. Ades, and N.J. Welton (2013a), *A Generalized Linear Modeling Framework for Pairwise and Network Meta-analysis of Randomized Controlled Trials*, Medical Decision Making 33(5):607-617. [\[doi:10.1177/0272989X12458724\]](https://doi.org/10.1177/0272989X12458724)

S. Dias, A.J. Sutton, N.J. Welton, and A.E. Ades (2013b), *Heterogeneity - Subgroups, Meta-Regression, Bias, and Bias-Adjustment*, Medical Decision Making 33(5):618-640. [\[doi:10.1177/0272989X13485157\]](https://doi.org/10.1177/0272989X13485157)

S. Dias, N.J. Welton, A.J. Sutton, D.M. Caldwell, G. Lu, and A.E. Ades (2013c), *Inconsistency in Networks of Evidence Based on Randomized Controlled Trials*, Medical Decision Making 33(5):641- 656. [\[doi:10.1177/0272989X12455847\]](https://doi.org/10.1177/0272989X12455847)

A. Gelman, A. Jakulin, M. Grazia Pittau, Y.-S. Su (2008), *A weakly informative default prior distribution for logistic and other regression models*, The Annals of Applied Statistics 2(4):1360-1383. [\[doi:10.1214/08AOAS191\]](https://doi.org/10.1214/08-AOAS191)

R.M. Turner, J. Davey, M.J. Clarke, S.G. Thompson, J.P.T. Higgins (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)

G. van Valkenhoef, G. Lu, B. de Brock, H. Hillege, A.E. Ades, and N.J. Welton (2012), *Automating network meta-analysis*, Research Synthesis Methods 3(4):285-299. [\[doi:10.1002/jrsm.1054\]](https://doi.org/10.1002/jrsm.1054)

G. van Valkenhoef, S. Dias, A.E. Ades, and N.J. Welton (2015), *Automated generation of nodesplitting models for assessment of inconsistency in network meta-analysis*, Research Synthesis Methods, accepted manuscript. [\[doi:10.1002/jrsm.1167\]](https://doi.org/10.1002/jrsm.1167)

G. van Valkenhoef et al. (draft), *Modeling inconsistency as heterogeneity in network meta-analysis*, draft manuscript.

### <span id="page-3-0"></span>4 atrialFibrillation

D.E. Warn, S.G. Thompson, and D.J. Spiegelhalter (2002), *Bayesian random effects meta-analysis of trials with binary outcomes: methods for the absolute risk difference and relative risk scales*, Statistics in Medicine 21(11):1601-1623. [\[doi:10.1002/sim.1189\]](https://doi.org/10.1002/sim.1189)

#### See Also

[mtc.network](#page-22-1), [mtc.model](#page-17-1), [mtc.run](#page-26-1)

#### Examples

```
# Load the example network and generate a consistency model:
model <- mtc.model(smoking, type="consistency")
# Load pre-generated samples instead of runing the model:
## Not run: results <- mtc.run(model, thin=10)
results <- readRDS(system.file("extdata/luades-smoking-samples.rds", package="gemtc"))
# Print a basic statistical summary of the results:
summary(results)
## Iterations = 5010:25000
## Thinning interval = 10
## Number of chains = 4
## Sample size per chain = 2000
##
## 1. Empirical mean and standard deviation for each variable,
## plus standard error of the mean:
##
## Mean SD Naive SE Time-series SE
## d.A.B 0.4965 0.4081 0.004563 0.004989
## d.A.C 0.8359 0.2433 0.002720 0.003147
## d.A.D 1.1088 0.4355 0.004869 0.005280
## sd.d 0.8465 0.1913 0.002139 0.002965
##
## 2. Quantiles for each variable:
##
## 2.5% 25% 50% 75% 97.5%
## d.A.B -0.2985 0.2312 0.4910 0.7530 1.341
## d.A.C 0.3878 0.6720 0.8273 0.9867 1.353
## d.A.D 0.2692 0.8197 1.0983 1.3824 2.006
## sd.d 0.5509 0.7119 0.8180 0.9542 1.283
```
<span id="page-3-1"></span>atrialFibrillation *Prevention of stroke in atrial fibrillation patients*

#### Description

A dataset of 25 trials investigating 17 treatments for stroke prevention in atrial fibrillation patients. The main outcome is the number of patients with a stroke, and a covariate captures the proportion of patients with a prior stroke.

# <span id="page-4-0"></span>blobbogram 5

Data are take from Table 1 of Cooper et al. (2009), with the following corrections applied: SPAF 3 and AFASAK 2 do not have a treatment 13 arm, and SPAF 1 does not contain treatment 5, but treatment 6. Thanks to prof. Cooper for providing the original analysis dataset.

#### Format

A network meta-regression dataset containing 60 rows of arm-based data (responders and sample size).

#### Source

Cooper et al. (2009), *Adressing between-study heterogeneity and inconsistency in mixed treatment comparisons: Application to stroke prevention treatments in individuals with non-rheumatic atrial fibrillation*, Statistics in Medicine 28:1861-1881. [\[doi:10.1002/sim.3594\]](https://doi.org/10.1002/sim.3594)

#### Examples

```
# Build a model similar to Model 4(b) from Cooper et al. (2009):
classes <- list("control"=c("01"),
                "anti-coagulant"=c("02","03","04","09"),
                "anti-platelet"=c("05","06","07","08","10","11","12","16","17"),
                "mixed"=c("13","14","15"))
regressor <- list(coefficient='shared',
                  variable='stroke',
                  classes=classes)
model <- mtc.model(atrialFibrillation,
                   type="regression",
                   regressor=regressor,
                   om.scale=10)
## Not run:
result <- mtc.run(model)
## End(Not run)
```
blobbogram *Plot a blobbogram (AKA forest plot)*

# Description

blobbogram is a flexible function for creating blobbograms (forest plots), making no specific assumptions about the data being plotted. It supports column and row grouping as well as pagination.

#### Usage

```
blobbogram(data, id.label="Study", ci.label="Mean (95% CI)",
    left.label=NULL, right.label=NULL, center.label=NULL,
   log.scale=FALSE, xlim=NULL, styles=NULL,
```
# 6 blobbogram

```
grouped=TRUE, group.labels=NULL,
columns=NULL, column.labels=NULL,
column.groups=NULL, column.group.labels=NULL,
digits=2,
ask=dev.interactive(orNone=TRUE),
draw.no.effect=TRUE)
```
forest(x, ...)

# Arguments



# blobbogram 7

# Details

The forest function is a generic S3 method (definition compatible with the meta package). This package defines methods for mtc.result and mtc.relative.effect.table.

The blobbogram function creates a blobbogram (forest plot) from the given data (point estimates and confidence intervals) and meta-data (labels, column specifications, column groups, row groups, styles) using the grid package. If the plot would not fit the device's graphics region, the content is broken up into multiple plots generated in sequence (pagination).

The data argument is given as a data frame containing the following columns:

- id: identifier (label) for this row.
- group (optional): row group this row belongs to (indexes into the group.labels argument).
- pe: point estimate.
- ci.l: lower confidence interval limit.
- ci.u: upper confidence interval limit.
- style: the style to apply to this row (defined in the styles argument).

Additional user-defined columns can be specified using the columns and column.labels arguments.

The styles argument is given as a data frame containing the following columns:

- style: name of the style.
- weight: font weight.
- pe.style: symbol to draw for the point estimate ("circle" or "square", currently).

# Value

None.

# Note

This method should not be considered stable. We intend to generalize it further and possibly provide it in a separate package. The interface may change at any time.

#### Author(s)

Gert van Valkenhoef, Joël Kuiper

# See Also

meta::forest, grid::Grid

#### Examples

```
data <- read.table(textConnection('
id group pe ci.l ci.u style value.A value.B
"Study 1" 1 0.35 0.08 0.92 "normal" "2/46" "7/46"
"Study 2" 1 0.43 0.15 1.14 "normal" "4/50" "8/49"
"Study 3" 2 0.31 0.07 0.74 "normal" "2/97" "10/100"
"Study 4" 2 0.86 0.34 2.90 "normal" "9/104" "6/105"
                 0.33  0.10  0.72  "normal" "4/74"  "14/74"
"Study 6" 2 0.47 0.23 0.91 "normal" "11/120" "22/129"
"Pooled" NA 0.42 0.15 1.04 "pooled" NA NA
'), header=TRUE)
data$pe <- log(data$pe)
data$ci.l <- log(data$ci.l)
data$ci.u <- log(data$ci.u)
blobbogram(data, group.labels=c('GROUP 1', 'GROUP 2'),
   columns=c('value.A', 'value.B'), column.labels=c('r/n', 'r/n'),
   column.groups=c(1, 2), grouped=TRUE,
   column.group.labels=c('Intervention', 'Control'),
   id.label="Trial", ci.label="Odds Ratio (95% CrI)", log.scale=TRUE)
```
blocker *Beta blockers to prevent mortality after myocardial infarction*

#### Description

A dataset of 22 trials investigating beta blockers versus control to prevent mortality after myocardial infarction. Number of events and sample size.

#### Format

A meta-analysis dataset containing 44 rows of arm-based data (responders and sample size).

#### Source

S. Dias, A.J. Sutton, A.E. Ades, and N.J. Welton (2013a), *A Generalized Linear Modeling Framework for Pairwise and Network Meta-analysis of Randomized Controlled Trials*, Medical Decision Making 33(5):607-617. [\[doi:10.1177/0272989X12458724\]](https://doi.org/10.1177/0272989X12458724)

J.B. Carlin (1992), *Meta-analysis for 2 × 2 tables: a Bayesian approach*, Statistics in Medicine 11(2):141-158. [\[doi:10.1002/sim.4780110202\]](https://doi.org/10.1002/sim.4780110202)

<span id="page-7-0"></span>

# <span id="page-8-1"></span><span id="page-8-0"></span>Description

A dataset of 12 trials investigating 6 treatments and placebo for rheumatoid arthritis. The main outcome is the number of patients who improved by at least 50% on the American College of Rheumatology scale (ACR50) at 6 Months. A covariate is present for the mean disease duration at baseline (years).

#### Format

A network meta-regression dataset containing 24 rows of arm-based data (responders and sample size).

#### Source

S. Dias, A.J. Sutton, N.J. Welton, and A.E. Ades (2013b), *Heterogeneity - Subgroups, Meta-Regression, Bias, and Bias-Adjustment*, Medical Decision Making 33(5):618-640. [\[doi:10.1177/0272989X13485157\]](https://doi.org/10.1177/0272989X13485157)

#### Examples

```
# Run RE regression model with informative heterogeneity prior
regressor <- list(coefficient='shared',
                  variable='diseaseDuration',
                  control='Placebo')
# sd ~ half-Normal(mean=0, sd=0.32)
hy.prior <- mtc.hy.prior(type="std.dev", distr="dhnorm", 0, 9.77)
model <- mtc.model(certolizumab,
                   type="regression",
                   regressor=regressor,
                   hy.prior=hy.prior)
## Not run:
result <- mtc.run(model)
## End(Not run)
```
<span id="page-9-0"></span>

#### **Description**

A dataset of 111 trials investigating 12 treatments for major depression on treatment response. Treatment response was defined as a reduction of at least 50% from the baseline score on the HAM-D or MADRS at week 8 (or, if not available, another time between week 6 and 12).

#### Format

A network meta-analysis dataset containing 224 rows of arm-based data (responders and sample size).

# Source

Cipriani et al. (2009), *Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis*, Lancet 373(9665):746-758. [\[doi:10.1016/S01406736\(09](https://doi.org/10.1016/S0140-6736%2809%2960046-5))60046- [5\]](https://doi.org/10.1016/S0140-6736%2809%2960046-5)

dietfat *Effects of low-fat diets on mortality*

#### **Description**

A dataset of 10 trials investigating low-fat diet versus control diet for mortality. Number of events and exposure in person-years.

#### Format

A meta-analysis dataset containing 20 rows of arm-based data (responders, exposure, and sample size).

#### Source

S. Dias, A.J. Sutton, A.E. Ades, and N.J. Welton (2013a), *A Generalized Linear Modeling Framework for Pairwise and Network Meta-analysis of Randomized Controlled Trials*, Medical Decision Making 33(5):607-617. [\[doi:10.1177/0272989X12458724\]](https://doi.org/10.1177/0272989X12458724)

Hooper et al. (2000), *Reduced or modified dietary fat for preventing cardiovascular disease*, Cochrane Database of Systematic Reviews 2:CD002137. [\[doi:10.1002/14651858.CD002137\]](https://doi.org/10.1002/14651858.CD002137)

<span id="page-10-1"></span><span id="page-10-0"></span>hfPrevention *Statins versus placebo in primary and secondary prevention of heart failure*

#### Description

A dataset of 19 trials comparing statins versus placebo or usual care for cholesterol lowering. The main outcome is the number of deaths. Trials are either primary prevention (no previous heart disease; secondary = 0) or secondary prevention (previous heart disease; secondary = 1).

# Format

A meta-regression dataset containing 38 rows of arm-based data (responders and sample size).

#### Source

S. Dias, A.J. Sutton, N.J. Welton, and A.E. Ades (2013b), *Heterogeneity - Subgroups, Meta-Regression, Bias, and Bias-Adjustment*, Medical Decision Making 33(5):618-640. [\[doi:10.1177/0272989X13485157\]](https://doi.org/10.1177/0272989X13485157)

#### Examples

```
# Build a model similar to Program 1(a) from Dias et al. (2013b):
regressor <- list(coefficient='shared',
                  variable='secondary',
                  control='control')
model <- mtc.model(hfPrevention,
                   type="regression",
                   regressor=regressor,
                   hy.prior=mtc.hy.prior("std.dev", "dunif", 0, 5))
## Not run:
result <- mtc.run(model)
## End(Not run)
```
ll.call *Call a likelihood/link-specific function*

#### **Description**

GeMTC implements various likelihood/link combinations. Functionality specific to the likelihood/link is handled by methods with names ending in .<likelihood>.<link>. This convenience function calls such methods.

# <span id="page-11-0"></span>Usage

ll.call(fnName, model, ...)

# Arguments



#### Details

The following methods currently need to be implemented to implement a likelihood/link:

- mtc.arm.mle: calculates a (corrected) maximum likelihood estimate for an arm-level effect. Used to generate starting values.
- mtc.rel.mle: calculates a (corrected) maximum likelihood estimate for a relative effect. Used to generate starting values.
- mtc.code.likelihood: generates JAGS code implementing the likelihood.
- scale.log: returns TRUE if plots should use the log scale.
- scale.name: returns the user-facing name of the outcome metric.
- scale.limit.inits: returns an upper and lower bound for the initial values, because some initial values might trigger boundary conditions such as probability 0 or 1 for the binomial.
- required.columns.ab: returns the required columns for arm-based data.

The first two methods can now also be used to selectively apply continuity corrections in case the maximum likelihood estimates are used for other purposes. mtc.arm.mle has an additional k=0.5 argument to specify the correction factor. mtc.rel.mle has arguments correction.force=TRUE to force application of the continuity correction even if unnecessary, correction.type="constant" to specify the type of correction (specify "reciprocal") for a correction proportional to the reciprocal of the size of the other arm, and correction.magnitude=1 to specify the (total) magnitude of the correction. These corrections apply only for count data, and will be ignored for continuous likelihood/links.

# Value

The return value of the called function.

#### Author(s)

Gert van Valkenhoef

#### See Also

[mtc.model](#page-17-1)

#### <span id="page-12-0"></span>mtc.anohe 13

#### Examples

```
# The "model" may be a stub.
model <- list(likelihood="poisson", link="log")
ll.call("scale.name", model)
# "Hazard Ratio"
ll.call("mtc.arm.mle", model, c('responders'=12, 'exposure'=80))
# mean sd
#-1.8562980 0.1118034
```
mtc.anohe *Analysis of heterogeneity (ANOHE)*

#### Description

(EXPERIMENTAL) Generate an analysis of heterogeneity for the given network. Three types of model are estimated: unrelated study effects, unrelated mean effects, and consistency. Output of the summary function can passed to plot for a visual representation.

# Usage

mtc.anohe(network, ...)

#### Arguments



#### Details

Analysis of heterogeneity is intended to be a unified set of statistics and a visual display that allows the simultaneous assessment of both heterogeneity and inconsistency in network meta-analysis [\[van](#page-1-1) [Valkenhoef et al. 2014b \(draft\)\].](#page-1-1)

mtc.anohe returns the MCMC results for all three types of model. To get appropriate summary statistics, call summary() on the results object. The summary can be plotted.

To control parameters of the MCMC estimation, see [mtc.run](#page-26-1). To specify the likelihood/link or to control other model parameters, see [mtc.model](#page-17-1). The ... arguments are first matched against [mtc.run](#page-26-1), and those that do not match are passed to [mtc.model](#page-17-1).

#### Value

For mtc. anohe: an object of class mtc. anohe. This is a list with the following elements:



<span id="page-13-0"></span>result.cons The result for the consistency model (see [mtc.run](#page-26-1)).

For summary: an object of class mtc.anohe.summary. This is a list with the following elements:



# Note

This method should not be considered stable. It is an experimental feature and heavily work in progress. The interface may change at any time.

# Author(s)

Gert van Valkenhoef, Joël Kuiper

#### See Also

[mtc.model](#page-17-1) [mtc.run](#page-26-1)

<span id="page-13-1"></span>mtc.data.studyrow *Convert one-study-per-row datasets*

# Description

Converts datasets in the one-study-per-row format to one-arm-per-row format used by GeMTC

#### Usage

```
mtc.data.studyrow(data,
  armVars=c('treatment'='t', 'responders'='r', 'sampleSize'='n'),
  nArmsVar='na',
  studyVars=c(),
  studyNames=1:nrow(data),
  treatmentNames=NA,
  patterns=c('%s..', '%s..%d.'))
```
#### <span id="page-14-0"></span>Arguments



# Details

Maps the one-study-per-row format that is widely used and convenient for BUGS models to the one-arm-per-row format used by GeMTC. As the primary purpose is to input datasets from BUGS models, the defaults work for the standard BUGS data table format. In most cases, it should be possible to just copy/paste the BUGS data table (without the final 'END') and read.table it into R, then apply mtc.data.studyrow. In many cases, the resulting table can be processed directly by [mtc.network](#page-22-1).

# Value

A data table with the requested columns.

#### Author(s)

Gert van Valkenhoef

#### See Also

[mtc.network](#page-22-1)

# Examples

## Example taken from the NICE DSU TSD series in Evidence Synthesis, #2 ## Dopamine agonists for the treatment of Parkinson's

# Read the bugs-formatted data data.src <- read.table(textConnection(' t[,1] t[,2] t[,3] y[,1] y[,2] y[,3] se[,1] se[,2] se[,3] na[] 1 3 NA -1.22 -1.53 NA 0.504 0.439 NA 2 1 2 NA -0.7 -2.4 NA 0.282 0.258 NA 2 1 2 4 -0.3 -2.6 -1.2 0.505 0.510 0.478 3 3 4 NA -0.24 -0.59 NA 0.265 0.354 NA 2 3 4 NA -0.73 -0.18 NA 0.335 0.442 NA 2

```
4 5 NA -2.2 -2.5 NA 0.197 0.190 NA 2
4 5 NA -1.8 -2.1 NA 0.200 0.250 NA 2'), header=TRUE)
# Convert the data, setting treatment names
data <- mtc.data.studyrow(data.src,
  armVars=c('treatment'='t', 'mean'='y', 'std.err'='se'),
  treatmentNames=c('Placebo', 'DA1', 'DA2', 'DA3', 'DA4'))
# Check that the data are correct
print(data)
# Create a network
network <- mtc.network(data)
```
<span id="page-15-1"></span>mtc.deviance *Inspect residual deviance*

# Description

Inspect the posterior residual deviance and summarize it using plots

#### Usage

```
mtc.deviance(result)
```

```
mtc.devplot(x, ...)
mtc.levplot(x, ...)
```

```
## S3 method for class 'mtc.deviance'
plot(x, auto.layout=TRUE, ...)
```
# Arguments



# Details

mtc.devplot will generate a stem plot of the posterior deviance per arm (if there are only arm-based data) or the mean per data point deviance per study (if there are contrast-based data).

mtc.levplot will plot the leverage versus the square root of the residual deviance (mean per data point for each study).

The generic plot function will display both on a single page (unless auto.layout=FALSE).

<span id="page-15-0"></span>

# <span id="page-16-0"></span>mtc.hy.prior 17

# Value

mtc.deviance returns the deviance statistics of a mtc.result.

#### Author(s)

Gert van Valkenhoef

# See Also

[mtc.run](#page-26-1)

<span id="page-16-1"></span>mtc.hy.prior *Set priors for the heterogeneity parameter*

# Description

These functions generate priors for the heterogeneity parameter in [mtc.model](#page-17-1). Priors can be set explicitly or, for outcomes on the log odds-ratio scale, based on empirical research.

#### Usage

```
mtc.hy.prior(type, distr, ...)
```
mtc.hy.empirical.lor(outcome.type, comparison.type)

comparisons).

# Arguments



# <span id="page-17-0"></span>Details

The generated prior is a list, the structure of which may change without notice. It can be converted to JAGS compatible code using as.character.

Empirical priors for the log odds-ratio (LOR) are taken from [\[Turner et al. 2012\].](#page-1-1)

# Value

A value to be passed to [mtc.model](#page-17-1).

#### Author(s)

Gert van Valkenhoef

#### See Also

[mtc.model](#page-17-1)

#### Examples

```
# NOTE: the mtc.run commands below are for illustrative purposes, such a small
# number of iterations should obviously not be used in practice.
# set a uniform prior standard deviation
model1 <- mtc.model(smoking, hy.prior=mtc.hy.prior("std.dev", "dunif", 0, 2))
result <- mtc.run(model1, n.adapt=10, n.iter=10)
# set an empirical (log-normal) prior on the variance
model2 <- mtc.model(smoking, hy.prior=mtc.hy.empirical.lor("subjective", "non-pharma"))
result <- mtc.run(model2, n.adapt=10, n.iter=10)
# set a gamma prior on the precision
model3 <- mtc.model(smoking, hy.prior=mtc.hy.prior("prec", "dgamma", 0.01, 0.01))
result <- mtc.run(model3, n.adapt=10, n.iter=10)
```
<span id="page-17-1"></span>

mtc.model *Generate network meta-analysis models*

#### **Description**

The mtc.model function generates network meta-analysis models from an mtc.network object.

#### Usage

```
mtc.model(network, type = "consistency", factor = 2.5, n.chain = 4,
  likelihood=NULL, link=NULL, linearModel="random",
  om.scale=NULL, hy.prior=mtc.hy.prior("std.dev", "dunif", 0, "om.scale"),
  re.prior.sd=15 * om.scale, dic=TRUE, powerAdjust=NA, ...)
```
#### <span id="page-18-0"></span>mtc.model 19

# Arguments



# Details

The mtc.model function generates an object of S3 class mtc.model, which can be visualized by the generic plot function or summarized by the generic summary function.

These likelihood/links are supported:

- normal/identity: for continuous (mean difference) data. Required columns: [mean, std.err] or [mean, std.dev, sampleSize]. Result: relative mean difference.
- binom/logit: for dichotomous data. Required columns [responders, sampleSize]. Result: (log) odds ratio.
- binom/log: for dichotomous data. Required columns [responders, sampleSize]. Result: (log) risk ratio.
- <span id="page-19-0"></span>• binom/cloglog: for rate (survival) data - equal follow-up in each arm. Required columns [responders, sampleSize]. Result: (log) hazard ratio.
- poisson/log: for rate (survival) data. Required columns [responders, exposure]. Result: (log) hazard ratio.

Most likelihood/links follow [\[Dias et al. 2013a\],](#page-1-1) and the binom/log model follows [\[Warn et al.](#page-1-1) [2002\].](#page-1-1)

The following model types are supported:

- consistency: ordinary consistency model. No additional parameters. [\[Dias et al. 2013a, van](#page-1-1) [Valkenhoef et al. 2012\]](#page-1-1)
- nodesplit: node-splitting model. Removes both arms used to estimate the direct evidence from the network of indirect evidence, rather than just one of those arms. This means that three-arm trials do not contribute any evidence in the network of indirect evidence. When relative effect data are present, these are transformed appropriately (using an assumption of normality) to enable this direct/indirect evidence split. Additional parameters: t1 and t2, which indicate the comparison to be split. [\[Dias et al. 2010, van Valkenhoef et al. 2015\]](#page-1-1)
- regression: meta-regression model. Additional parameters: regressor, which indicates how to structure the treatment-interaction model for the regression. See below for details.
- use: unrelated study effects. Models the effects within each study as if the studies are independent. No additional parameters. [\[van Valkenhoef et al. \(draft\)\]](#page-1-1)
- ume: unrelated mean effects. Models the effects within each comparison as if they are independent. Does not properly handle multi-arm trials, and warns when they are present in the network. No additional parameters. [\[Dias et al. 2013b, van Valkenhoef et al. \(draft\)\]](#page-1-1)

Regressor specification: a list with elements: variable, coefficient, and either control or classes. The variable is the name of the covariate to include in the regression analysis, and must be a column of the studies data frame in the network. The regressor variable is automatically centered and standardized using the method recommended by [Gelman et al. \(2008\).](#page-1-1) The coefficient indicates the type of treatment-interaction model: "shared", "unrelated", or "exchangeable". control, if specified, must be the ID of a treatment in the network. All other treatments have a coefficient relative to the control, which can be the same for all treatments ("shared"), different for all treatments ("unrelated") or exchangeable between treatments ("exchangeable"). classes is a named list of treatment classes, the first of which will act as the control class. Each class is a vector of treatment IDs from the network. Only "shared" coefficients can currently be used, meaning a single coefficient per class (except the control class). See also [atrialFibrillation](#page-3-1), [certolizumab](#page-8-1), and [hfPrevention](#page-10-1) for examples of meta-regression analyses.

Studies can be downweighted by using the powerAdjust argument, which applies a variance inflation (also known as "power prior") to the likelihood. This allows a weight  $\alpha_i \in [0, 1]$  to be specified for each study i. The log-likelihood will be multiplied by a factor  $\alpha_i$ , or equivalently for normal distributions the variance will be multiplied by  $1/\alpha_i$ . Setting  $\alpha_i = 0$  will completely exclude that study, whereas setting  $\alpha_i = 1$  will weight it fully. Essentially, down-weighted models modify the data and hence model fit statistics such as DIC can not be compared between models with different weightings.

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# Value

An object of class mtc.model. The following elements are descriptive:



These elements determine the model run by JAGS:



These latter fields can be modified to alter the statistical model, but such changes may break the model or assumptions made elsewhere in the package.

# Visualization

Calling the generic plot method on an S3 mtc.model object will show a graph with the treatments as vertices and the comparisons as edges. The lines with solid arrows represent basic parameters, and the other lines represent comparisons that are not associated with any parameter but do have direct evidence from trials.

The example code will generate the following graph:

<span id="page-21-0"></span>

The default layout algorithm is igraph::layout.circle, other layout algorithms can be used by passing them as an optional argument called layout to plot. The igraph::layout.fruchterman.reingold algorithm also seems to produce nice results and may be better for large graphs.

#### Reproducible results

It is possible to get reproducible results, but as JAGS uses its own pseudo-random number generator, this is somewhat more involved.

mtc.model generates random numbers using the R functions (for example to generate initial values). Therefore, set.seed must be called before calling mtc.model.

Then, before calling mtc.run, the random number generator type and seed must be set for each of the chains. This can be done as documented in jags.model, by setting the .RNG.name and .RNG.seed for each chain in model\$inits. See below for an example.

#### Author(s)

Gert van Valkenhoef, Joël Kuiper

#### See Also

[mtc.network](#page-22-1), [mtc.run](#page-26-1)

# Examples

```
# Random effects consistency model for Parkinson network
model <- mtc.model(parkinson)
plot(model)
summary(model)
```
# Fixed effect meta-regression for heart failure prevention regressor <- list(coefficient='shared',

```
variable='secondary',
                  control='control')
model <- mtc.model(hfPrevention,
                   type="regression",
                   regressor=regressor,
                  linearModel="fixed")
# Reproducible results
# Set the R RNG seed
set.seed(42)
model <- mtc.model(parkinson, likelihood='normal', link='identity')
# By default, the model will have 4 chains - generate a seed for each
seeds <- sample.int(4, n = .Machine$integer.max)
# Apply JAGS RNG settings to each chain
model$inits <- mapply(c, model$inits, list(
 list(.RNG.name="base::Wichmann-Hill", .RNG.seed=seeds[1]),
 list(.RNG.name="base::Marsaglia-Multicarry", .RNG.seed=seeds[2]),
 list(.RNG.name="base::Super-Duper", .RNG.seed=seeds[3]),
 list(.RNG.name="base::Mersenne-Twister", .RNG.seed=seeds[4])), SIMPLIFY=FALSE)
```
<span id="page-22-1"></span>mtc.network *Create an mtc.network*

# Description

Creates an object of class mtc.network

#### Usage

```
mtc.network(data.ab=data, treatments=NULL, description="Network",
            data.re=NULL, studies=NULL, data=NULL)
```
## S3 method for class 'mtc.network' plot(x, layout=igraph::layout.circle, dynamic.edge.width=TRUE, use.description=FALSE, ...)

#### Arguments



<span id="page-23-0"></span>

# Details

One-arm trials are automatically removed, which results in a warning.

Also see [mtc.data.studyrow](#page-13-1) for a convenient way to import data from the one-study-per-row format, which is very popular for BUGS code.

# Value

For mtc.network, an object of the class mtc.network which is a list containing:



These are cleaned up and standardized versions of the arguments provided, or generated defaults for 'treatments' if the argument was omitted.

# Author(s)

Gert van Valkenhoef, Joël Kuiper

# See Also

[mtc.data.studyrow](#page-13-1), [mtc.model](#page-17-1)

# <span id="page-24-0"></span>mtc.nodesplit 25

#### Examples

```
# Create a new network by specifying all information.
treatments <- read.table(textConnection('
 id description
 A "Treatment A"
 B "Treatment B"
 C "Treatment C"'), header=TRUE)
data <- read.table(textConnection('
 study treatment responders sampleSize
 01 A 2 100
 01 B 5 100
 02 B 6 110
 02 C 1 110
 03 A 3 60
 03 C 4 80
 03 B 7 80'), header=TRUE)
network <- mtc.network(data, description="Example", treatments=treatments)
plot(network)
# Create a new network by specifying only the data.
data <- read.table(textConnection('
 study treatment mean std.dev sampleSize
 01 A -1.12 0.6 15
 01 B -1.55 0.5 16
 02 A -0.8 0.7 33
 02 B -1.1 0.5 31'), header=TRUE)
network <- mtc.network(data)
# Print the network
print(network)
## MTC dataset: Network
## study treatment mean std.dev sampleSize
## 1 1 A -1.12 0.6 15
## 2 1 B -1.55 0.5 16
## 3 2 A -0.80 0.7 33
## 4 2 B -1.10 0.5 31
```
mtc.nodesplit *Node-splitting analysis of inconsistency*

# **Description**

Generate and run an ensemble of node-splitting models, results of which can be jointly summarized and plotted.

#### Usage

```
mtc.nodesplit(network, comparisons=mtc.nodesplit.comparisons(network), ...)
mtc.nodesplit.comparisons(network)
```
#### <span id="page-25-0"></span>Arguments



# Details

mtc.nodesplit returns the MCMC results for all relevant node-splitting models [\[van Valkenhoef et](#page-1-1) [al. 2015\].](#page-1-1) To get appropriate summary statistics, call summary() on the results object. The summary can be plotted. See [mtc.model](#page-17-1) for details on how the node-splitting models are generated.

To control parameters of the MCMC estimation, see [mtc.run](#page-26-1). To specify the likelihood/link or to control other model parameters, see [mtc.model](#page-17-1). The ... arguments are first matched against [mtc.run](#page-26-1), and those that do not match are passed to [mtc.model](#page-17-1).

mtc.nodesplit.comparisons returns a data frame enumerating all comparisons that can reasonably be split (i.e. have independent indirect evidence).

# Value

For mtc.nodesplit: an object of class mtc.nodesplit. This is a list with the following elements:



### Author(s)

Gert van Valkenhoef, Joël Kuiper

# See Also

[mtc.model](#page-17-1) [mtc.run](#page-26-1)

#### <span id="page-26-0"></span>mtc.run 27

#### Examples

```
# Run all relevant node-splitting models
## Not run: result.ns <- mtc.nodesplit(parkinson, thin=50)
# (read results from file instead of running:)
result.ns <- readRDS(system.file('extdata/parkinson.ns.rds', package='gemtc'))
# List the individual models
names(result.ns)
# Time series plots and convergence diagnostics for d.A.C model
plot(result.ns$d.A.C)
gelman.diag(result.ns$d.A.C, multivariate=FALSE)
# Overall summary and plot
summary.ns <- summary(result.ns)
print(summary.ns)
plot(summary.ns)
```
mtc.run *Running an* mtc.model *using an MCMC sampler*

#### <span id="page-26-2"></span>Description

The function mtc.run is used to generate samples from a object of type mtc.model using a MCMC sampler. The resulting mtc.result object can be coerced to an mcmc.list for further analysis of the dataset using the coda package.

#### Usage

```
mtc.run(model, sampler = NA, n.adapt = 5000, n.iter = 20000, thin = 1)
## S3 method for class 'mtc.result'
summary(object, ...)
## S3 method for class 'mtc.result'
plot(x, \ldots)## S3 method for class 'mtc.result'
forest(x, use.description=FALSE, ...)
## S3 method for class 'mtc.result'
print(x, \ldots)## S3 method for class 'mtc.result'
as.mcmc.list(x, \ldots)
```
# **Arguments**

model An object of S3 class mtc.model describing a network meta-analysis model.

sampler Deprecated: gemtc now only supports the JAGS sampler. Specifying a sampler will result in a warning or error. This argument will be removed in future versions.

<span id="page-27-0"></span>28 mtc.run and the contract of the contract of



# Value

An object of class mtc.result. This is a list with the following elements:



The object can be coerced to an mcmc. list from the coda package by the generic S3 method as.mcmc.list.

#### Analysis of the results

Convergence of the model can be assessed using methods from the coda package. For example the Brooks-Gelman-Rubin method (coda::gelman.diag, coda::gelman.plot). The summary also provides useful information, such as the MCMC error and the time series and densities given by plot should also be inspected.

The forest function can provide forest plots for mtc.result objects. This is especially useful in combination with the [relative.effect](#page-31-1) function that can be used to calculate relative effects compared to any baseline for consistency models. The [rank.probability](#page-30-1) function calculates rank probabilities for consistency models.

# Author(s)

Gert van Valkenhoef, Joël Kuiper

# See Also

```
mtc.model
relative.effect.table, relative.effect, rank.probability
coda::gelman.diag, coda::gelman.plot
```
#### <span id="page-28-0"></span>parkinson 29

#### Examples

```
model <- mtc.model(smoking)
## Not run: results <- mtc.run(model, thin=10)
results <- readRDS(system.file("extdata/luades-smoking-samples.rds", package="gemtc"))
# Convergence diagnostics
gelman.plot(results)
# Posterior summaries
summary(results)
## Iterations = 5010:25000
## Thinning interval = 10
## Number of chains = 4
## Sample size per chain = 2000
##
## 1. Empirical mean and standard deviation for each variable,
## plus standard error of the mean:
##
## Mean SD Naive SE Time-series SE
## d.A.B 0.4965 0.4081 0.004563 0.004989
## d.A.C 0.8359 0.2433 0.002720 0.003147
## d.A.D 1.1088 0.4355 0.004869 0.005280
## sd.d 0.8465 0.1913 0.002139 0.002965
##
## 2. Quantiles for each variable:
##
## 2.5% 25% 50% 75% 97.5%
## d.A.B -0.2985 0.2312 0.4910 0.7530 1.341
## d.A.C 0.3878 0.6720 0.8273 0.9867 1.353
## d.A.D 0.2692 0.8197 1.0983 1.3824 2.006
## sd.d 0.5509 0.7119 0.8180 0.9542 1.283
plot(results) # Shows time-series and density plots of the samples
forest(results) # Shows a forest plot
```
parkinson *Mean off-time reduction in Parkinson's disease*

#### Description

A dataset of seven trials investigating four treatments and placebo for Parkinson's disease. The outcome is mean off-time reduction.

#### Format

• parkinson: A network meta-analysis dataset containing fifteen rows of arm-based data (mean, standard deviation, and sample size).

- parkinson\_diff: A network meta-analysis dataset containing fifteen rows of contrast-based data.
- parkinson\_shared: A network meta-analysis dataset containing mixed arm-based and contrastbased data.

#### Source

Franchini et al. (2012), *Accounting for correlation in network meta-analysis with multi-arm trials*, Research Synthesis Methods, 3(2):142-160. [\[doi:10.1002/jrsm.1049\]](https://doi.org/10.1002/jrsm.1049)

plotCovariateEffect *Plot treatment effects versus covariate values*

# Description

The plot will show the median treatment effect and the 95% credible interval on the y-axis and the covariate value on the x-axis. One plot page will be generated per pair of treatments.

#### Usage

```
plotCovariateEffect(result, t1, t2, xlim=NULL, ylim=NULL,
                    ask=dev.interactive(orNone=TRUE))
```
# Arguments



#### Details

Default x-axis limits will be set to three standard deviations above and below the centering value of the covariate. The y-axis limits will be set based on the minimum and maximum 95% CrI limits among the set of effects computed.

# Value

None.

<span id="page-29-0"></span>

# <span id="page-30-0"></span>rank.probability 31

# Author(s)

Gert van Valkenhoef

#### See Also

[relative.effect](#page-31-1), [mtc.run](#page-26-1)

<span id="page-30-1"></span>rank.probability *Calculating rank-probabilities*

# Description

Rank probabilities indicate the probability for each treatment to be best, second best, etc.

#### Usage

```
rank.probability(result, preferredDirection=1, covariate=NA)
```

```
## S3 method for class 'mtc.rank.probability'
print(x, \ldots)## S3 method for class 'mtc.rank.probability'
plot(x, ...)
```

```
sucra(ranks)
rank.quantiles(ranks, probs=c("2.5%"=0.025, "50%"=0.5, "97.5%"=0.975))
```
# Arguments



# Details

For each MCMC iteration, the treatments are ranked by their effect relative to an arbitrary baseline. A frequency table is constructed from these rankings and normalized by the number of iterations to give the rank probabilities.

#### <span id="page-31-0"></span>Value

rank.probability: A matrix (with class mtc.rank.probability) with the treatments as rows and the ranks as columns. sucra: A vector of SUCRA values. rank.quantiles: A matrix with treatments as rows and quantiles as columns, giving the quantile ranks (by default, the median and 2.5% and 97.5% ranks).

# Author(s)

Gert van Valkenhoef, Joël Kuiper

# See Also

[relative.effect](#page-31-1)

# Examples

```
model <- mtc.model(smoking)
# To save computation time we load the samples instead of running the model
## Not run: results <- mtc.run(model)
results <- readRDS(system.file("extdata/luades-smoking-samples.rds", package="gemtc"))
ranks <- rank.probability(results)
print(ranks)
## Rank probability; preferred direction = 1
## [,1] [,2] [,3] [,4]
## A 0.000000 0.003000 0.105125 0.891875
## B 0.057875 0.175875 0.661500 0.104750
## C 0.228250 0.600500 0.170875 0.000375
## D 0.713875 0.220625 0.062500 0.003000
print(sucra(ranks))
## A B C D
## 0.03670833 0.39591667 0.68562500 0.88175000
print(rank.quantiles(ranks))
## 2.5% 50% 97.5%
## A 3 4 4
## B 1 3 4
## C 1 2 3
## D 1 1 3
plot(ranks) # plot a cumulative rank plot
plot(ranks, beside=TRUE) # plot a 'rankogram'
```
<span id="page-31-1"></span>relative.effect *Calculating relative effects*

# Description

Calculates the relative effects of pairs of treatments.

# <span id="page-32-0"></span>relative.effect 33

# Usage

```
relative.effect(result, t1, t2 = c(), preserve.extra = TRUE, covariate = NA)
```
#### Arguments



# Value

Returns an mtc.results object containing the calculated relative effects.

Note that this method stores the raw samples, which may result in excessive memory usage. You may want to consider using [relative.effect.table](#page-33-1) instead.

#### Author(s)

Gert van Valkenhoef, Joël Kuiper

#### See Also

[rank.probability](#page-30-1), [relative.effect.table](#page-33-1)

# Examples

```
model <- mtc.model(smoking)
# To save computation time we load the samples instead of running the model
## Not run: results <- mtc.run(model)
results <- readRDS(system.file("extdata/luades-smoking-samples.rds", package="gemtc"))
# Creates a forest plot of the relative effects
forest(relative.effect(results, "A"))
summary(relative.effect(results, "B", c("A", "C", "D")))
## Iterations = 5010:25000
## Thinning interval = 10
## Number of chains = 4
## Sample size per chain = 2000
##
## 1. Empirical mean and standard deviation for each variable,
## plus standard error of the mean:
##
## Mean SD Naive SE Time-series SE
```

```
## d.B.A -0.4965 0.4081 0.004563 0.004989
## d.B.C 0.3394 0.4144 0.004634 0.004859
## d.B.D 0.6123 0.4789 0.005354 0.005297
## sd.d 0.8465 0.1913 0.002139 0.002965
##
## 2. Quantiles for each variable:
##
## 2.5% 25% 50% 75% 97.5%
## d.B.A -1.3407 -0.7530 -0.4910 -0.2312 0.2985
## d.B.C -0.4809 0.0744 0.3411 0.5977 1.1702
## d.B.D -0.3083 0.3005 0.6044 0.9152 1.5790
## sd.d 0.5509 0.7119 0.8180 0.9542 1.2827
```
<span id="page-33-1"></span>relative.effect.table *Table of relative effects*

#### Description

Generates a table of the relative effects of all pairs of treatments. Unlike [relative.effect](#page-31-1), this method stores summaries only, not raw samples.

# Usage

relative.effect.table(result, covariate=NA)

```
## S3 method for class 'mtc.relative.effect.table'
print(x, \ldots)## S3 method for class 'mtc.relative.effect.table'
forest(x, t1, use.description=FALSE, ...)
## S3 method for class 'mtc.relative.effect.table'
as.data.frame(x, ...)
```
# Arguments



#### <span id="page-34-0"></span>smoking 35

### Value

Returns an mtc.relative.effect.table object containing the quantiles of the calculated relative effects of all pair-wise comparisons among the treatments.

The result will be pretty printed as an n-by-n table of relative treatment effects. It can also be used to produce Forest plots against any arbitrary baseline. Finally, the as.data.frame generic method makes it possible to export the table for use in Excel or other spreadsheet software, using the core R methods write.csv or write.csv2.

# Author(s)

Gert van Valkenhoef

# See Also

[relative.effect](#page-31-1)

## Examples

```
model <- mtc.model(smoking)
# To save computation time we load the samples instead of running the model
## Not run: results <- mtc.run(model)
results <- readRDS(system.file("extdata/luades-smoking-samples.rds", package="gemtc"))
# Creates a forest plot of the relative effects
tbl <- relative.effect.table(results)
# Print the n*n table
print(tbl)
# Plot effect relative to treatment "C"
forest(tbl, "C")
# Write to CSV (e.g. to import to Excel, then use in a Word table)
## Not run: write.csv(tbl, "smoking-effects.csv")
# Note: use write.csv2 for Western European locales
```
smoking *Psychological treatments to aid smoking cessation*

#### Description

A dataset of 24 trials investigating four psychological treatments and no treatment for smoking cessation. The outcome is the number of people who stopped smoking.

#### Format

A network meta-analysis dataset containing 50 rows of arm-based data (responders and sample size).

#### <span id="page-35-0"></span>Source

Lu and Ades (2006), *Assessing Evidence Inconsistency in Mixed Treatment Comparisons*, Journal of the American Statistical Society, 101(474):447-459. [\[doi:10.1198/016214505000001302\]](https://doi.org/10.1198/016214505000001302)

Hasselblad (1998), *Meta-analysis of multitreatment studies*, Medical Decision Making 18(1):37-43. [\[doi:10.1177/0272989X9801800110\]](https://doi.org/10.1177/0272989X9801800110)

thrombolytic *Thrombolytic treatment after acute myocardial infarction*

#### Description

A dataset of 28 trials investigating eight thrombolytic treatments administered after a myocardial infarction. The outcome is mortality after 30-35 days.

# Format

A network meta-analysis dataset containing 58 rows of arm-based data (responders and sample size).

#### Source

Lu and Ades (2006), *Assessing Evidence Inconsistency in Mixed Treatment Comparisons*, Journal of the American Statistical Society, 101(474):447-459. [\[doi:10.1198/016214505000001302\]](https://doi.org/10.1198/016214505000001302)

Boland et al. (2003), *Early thrombolysis for the treatment of acute myocardial infarction: a systematic review and economic evaluation*, Health Technology Assessment 7(15):1-136. [\[doi:10.3310/](https://doi.org/10.3310/hta7150) [hta7150\]](https://doi.org/10.3310/hta7150)

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