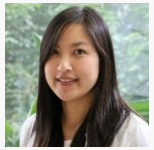
Automated NMA Results Slide Generation with multiNMA in R: Streamlining Evidence Synthesis

6 JUNE 2025

Introductions



Mei Sum Chan DPhil FIA CStat

Senior Statistician

Mei is a statistician, epidemiologist and actuary with extensive experience in biostatistics, RWE and HEOR projects across multiple chronic disease areas.

Emma Hawe

Evidence Synthesis, Statistics and EU-HTAR Lead

Emma is a statistician with 25 years of experience in consulting, academia, and regulatory settings. She has led numerous literature reviews and statistical analysis projects, including network meta-analyses. Emma is interested in health technology assessment (HTA) and joint clinical assessment (JCA) strategies.

Alexandra Boskovic

Analyst

Alexandra is an analyst with a background in biomedical and population health sciences. She has a strong background in programming and database management in R and geospatial analysis in ArcGIS.

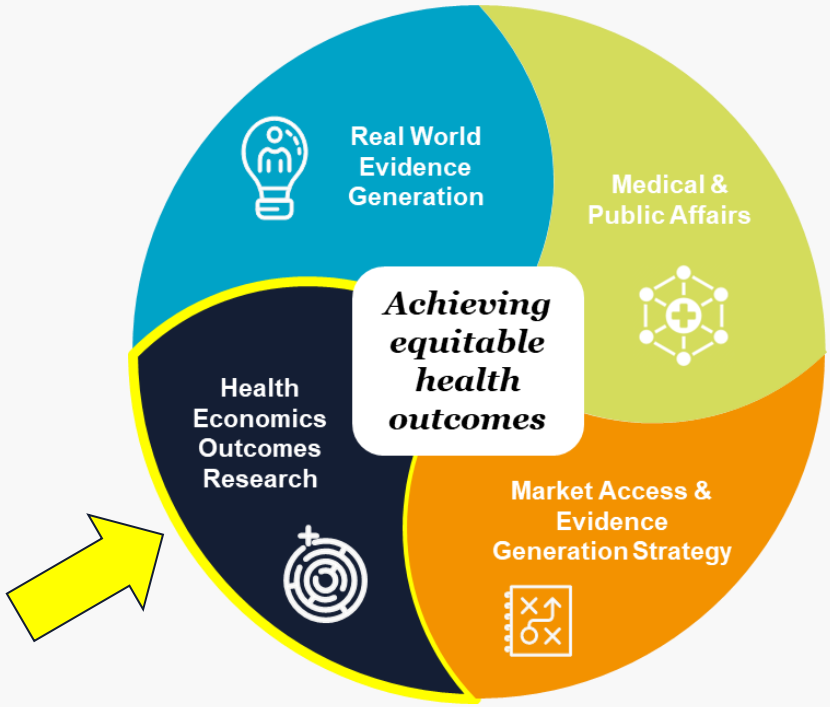
With thanks to Catrin Treharne, Niraj Shah and Zheyuan Yang

Who are LCP Health Analytics?

LCP is a consultancy and technology firm with >1,000 people working across financial services and health and energy analytics.

Our Health Analytics team contains clinicians, epidemiologists, data scientists, health economists and actuaries. We leverage real world datasets and applied analytics to analyse the health and economic value of medicines and other healthcare sector interventions.

LCP Health Analytics website



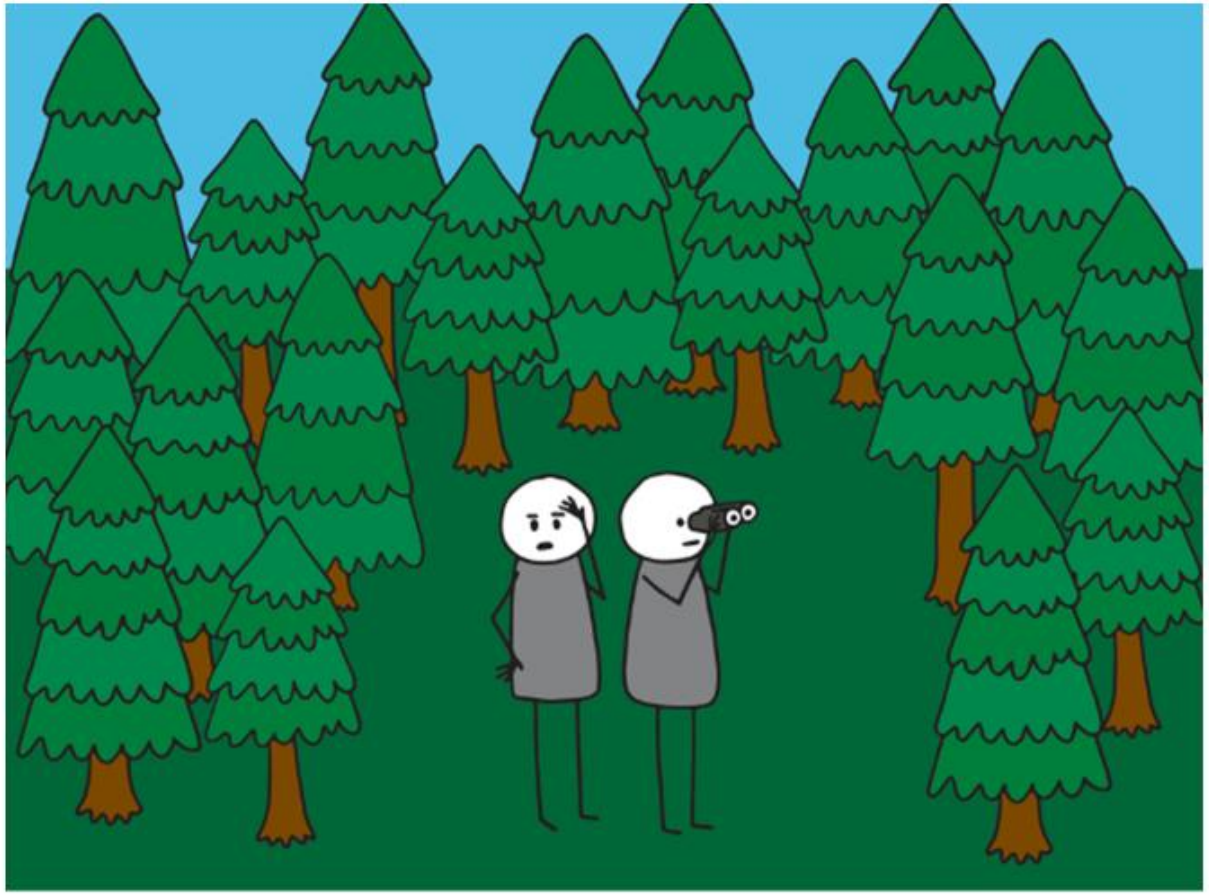
Contents

- Background and motivations
- Approach
- Demo
- Conclusions and next steps

Background and motivations

Bayesian network meta-analysis (NMA) – the big picture

- NMAs help us to see the bigger picture.
- Many treatment options for the same indication.
- Randomised controlled trials (RCTs) of all treatments of interest almost never exist.
- Instead, RCTs tend to compare with placebo or a subset of comparators.
- How do we determine which treatment is “best”?



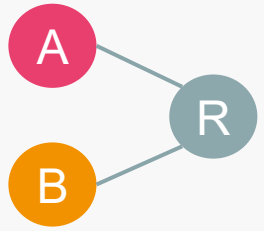
ISPOR Introduction to NMA webinar by Emma Hawe

https://www.ispor.org/education-training/webinars/webinar/an-introduction-to-network-meta-analysis

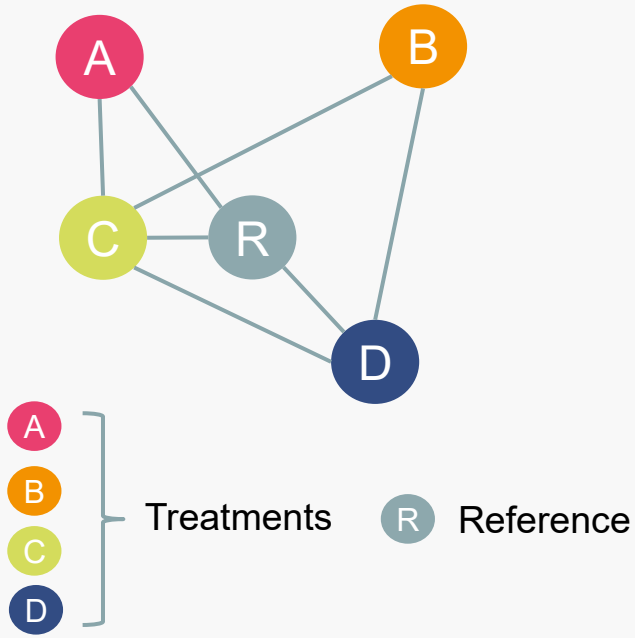
What is Bayesian network meta-analysis (NMA)?

- Understanding the **comparative efficacy and safety** of disease therapies, even in the absence of head-to-head trials, is crucial for clinicians and decision-makers.
- **Network meta-analysis (NMA)**, a type of indirect treatment comparison (ITC), estimates this relative efficacy and safety.
- NMA extends standard pairwise meta-analysis by relating the relative differences in the efficacy of multiple treatments, accounting for **all available evidence** from a network of studies.
- When performing NMA, one must choose between a **frequentist or Bayesian** model. For Bayesian models, prior distributions are typically non-informative.

Standard pairwise meta-analysis



Network meta-analysis



HTA requirements for NMA

- For HTA submissions, it is necessary to generate efficacy estimates relative to all comparators of interest. When there is a connected network of evidence, NMA is typically performed, with HTA agencies generally preferring the **Bayesian approach** over the frequentist one.
- The Bayesian NMA approach used in this tool aligns with **NICE DSU guidelines** and utilizes NICE DSU examples.
- However, conducting systematic literature reviews for data extraction and manually reporting results can be **time-consuming**, posing challenges for meeting HTA submission timelines.
- Specifically, the EU Health Technology Assessment Regulation (EU-HTAR) for Joint Clinical Assessments (JCA) from 2025 will likely require multiple analyses to be performed within 100 days of the PICO scoping. This currently applies to oncology drugs and Advanced Therapy Medicinal Products (ATMPs) from January 2025, will apply to orphan products from January 2028, and will extend to all new medicines from January 2030.

*Automated results outputs improve **efficiency** and **quality control***

Approach

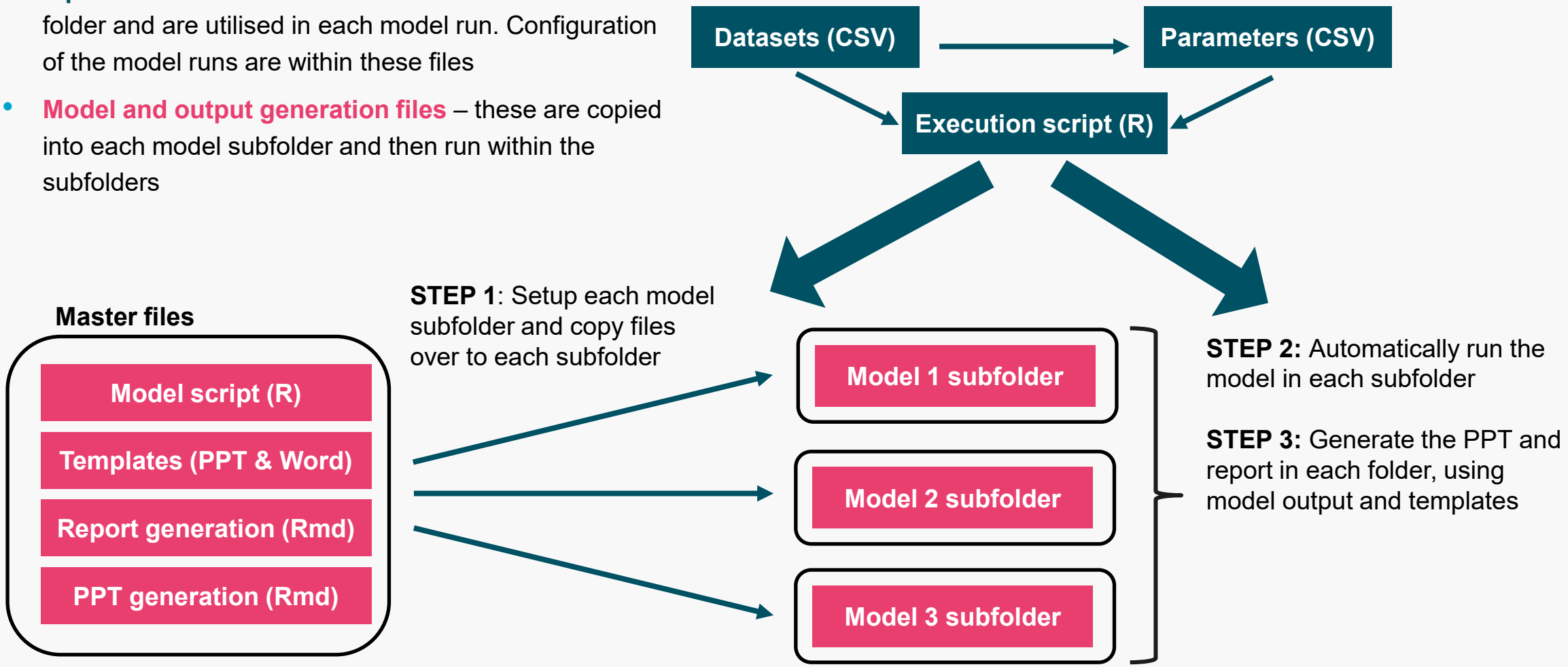
Building blocks

- We developed a R code workflow around these three key components :
  - R multinma package for NMA modelling[1]
  - R Markdown for PowerPoint slides and Word document automation
  - LCP templates for PowerPoint slide packs and Word reports
- The workflow integrates: automated model specification, batch processing with parallelisation of NMA models, diagnostic tests, results and diagnostics plotting and results extraction
- The outputs are client-ready slides and reports with consistent styling, in addition to the underlying plots and results tables
- The tool is scalable, accommodating in the same framework:
  - Multiple outcome types – binary, rates, continuous
  - Random and fixed effects NMA
  - Sensitivity analyses – unrelated mean effects and nodesplit (for checking the consistency assumption)
  - Custom configurations for: run settings, prior distributions and names of headings

Source: 1. Phillippo, D. M. (2025). *multinma: Bayesian Network Meta-Analysis of Individual and Aggregate Data*. R package version 0.8.0, doi: 10.5281/zenodo.3904454.

Tool architecture

- Two sets of files are used:
  - **Input and execution files** – these sit within the main folder and are utilised in each model run. Configuration of the model runs are within these files
  - **Model and output generation files** – these are copied into each model subfolder and then run within the subfolders



Demo

Conclusions and next steps

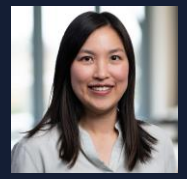
The NMA automation tool has accelerated and simplified the process for conducting multiple NMAs

- It minimises user input and variability in the analytical approach and in how findings are presented.
- For reporting, visuals include forest plots, pairwise grids, rank plots and summary tables, with reproducible code ensuring transparency and reliability.
- For straightforward NMA analyses, users only need to specify characteristics of the data and of the analysis (allowing for flexibility in characteristics and prior distributions) in a table of metadata, and do not need to generate any code in R.
- By streamlining the process of converting NMA outputs into ready-to-use slides and reports, our tool addresses an urgent need for greater speed and reliability in reporting analysis results for HTAs, particularly under strict EU-HTAR deadlines.

Next steps

- Integrating non-multinma NMA models into this tool
- Extension to multilevel network meta-regression (ML-NMR), which is in the multinma package
- Potentially adapting the tool based on client feedback *(the tool can already capture customised information within clients' templates, if desired)*

Contact us



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Our strategic mission:
We aim to lead the transition of health systems from importers of illness to exporters of health through realigning value between patients, manufacturers of medicines and payers.

Our mission is to help transition health systems from importers of illness to exporters of health

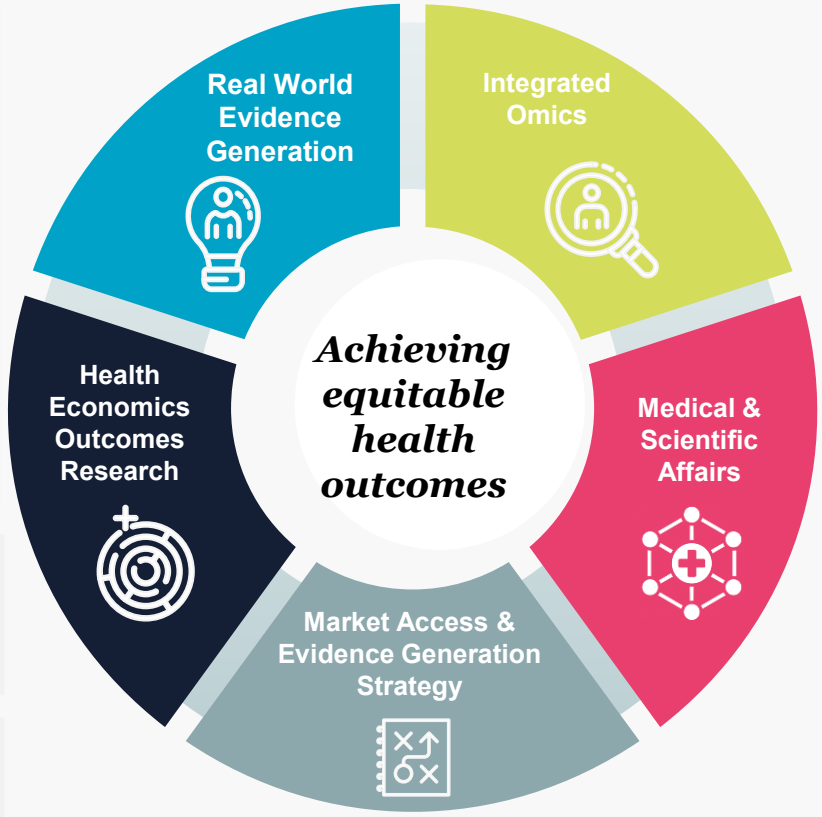
Addressing the two driving challenges for health systems:

- Increasingly complex multimorbid unmet patient needs
- A misalignment of how HTA bodies and governments value medicines and the value – healthcare and wider societal – of health to patients, populations and economies.

Underpinned by our approach to support clients to improve the population's health and reduce inequalities

Expertise in data science, medicine, research, health economics, epidemiology & statistics

State of the art expertise, methods and technology



Why LCP Health Analytics?

Visionary approach to our clients' challenges

- Leading the market in identifying solutions for tomorrow's challenges for patients, health systems and our clients
- Clear mission-based team and approach

Unique leadership team & sector experience

- Unique combination of leadership experience across science, medicine, pharmaceutical, consultancy and policy sectors
- Demonstrative partnerships and network with key decision makers across the sector

Delivering greater value to clients

- Thought partners who deliver value beyond core issues and leverage early access to emerging datasets and collaborations
- Continuity of team from pitch to delivery, with hands on project leadership by senior experts across service areas

We leverage real world datasets and applied analytics to enable clear articulation of health and economic value of medicines in an increasingly complex healthcare environment.

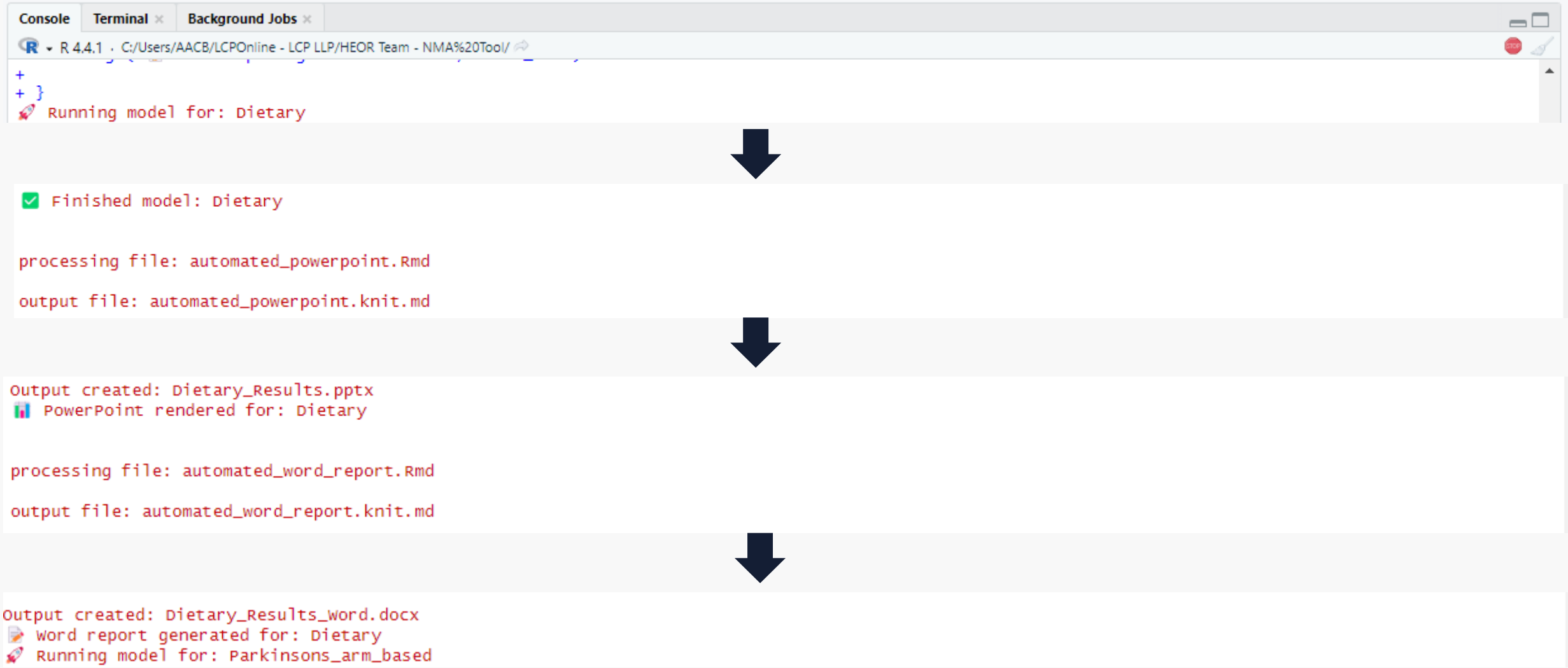
Parameters File

	A	B	C	D	E	F	G	H
1	**Variablenames**	**Dietary**	**Thrombolytics**	**Thrombolytics_ume**	**Thrombolytics_nodesplit**	**Parkinsons_arm_based**	**Diabetes**	**Myeloma**
2	Study data	X	X	X	X	X	X	X
3	dataname	dietary_fat	thrombolytics_example.csv	thrombolytics_example.csv	thrombolytics_example.csv	parkinsons_example.csv	diabetes_example.csv	ndmm_agd.csv
4	studyn	Study ID	Study ID	Study ID	Study ID	Study ID	Study ID	Study ID
5	studyc	Study	Study	Study	Study	Study	Study	Study
6	trtn	Arm ID	Arm ID	Arm ID	Arm ID	Arm ID	Arm ID	Arm ID
7	trtc	Arm	Arm	Arm	Arm	Arm	Arm	Arm
8	response	Mean rate	Mean rate	Mean rate	Mean rate	Mean rate	Mean rate	Mean rate
9	sample_size	Number rar	Number randomised	Number randomised	Number randomised	Number randomised	Number randomised	Number randomised
10	exposure	Person yea	Person years at risk	Person years at risk	Person years at risk	Person years at risk	Person years at risk	Person years at risk
11	studyc_col	studyc	studyn	studyn	studyn	studyn	studyc	studyf
12	trtc_col	trtc	trtc	trtc	trtc	trtn	trtc	trtf
13	response_col	r	r	r	r	y	r	status
14	exposure_col	E	NA	NA	NA	NA	time	eventtime
15	sample_size_col	n	n	n	n	n	n	NA
16	se_col	NA	NA	NA	NA	se	NA	NA
17	trt_ref	Control	SK	SK	SK	4	Placebo	Pbo
18	Analysis params	X	X	X	X	X	X	X
19	Comparisontype	bayesnma	bayesnma	bayesnma	bayesnma	bayesnma	bayesnma	bayesnma
20	outcometype	rate	binary	binary	binary	continuous	binary	time-to-event
21	effecttype	random	random	random	random	random	random	random
22	likelihood_dist	poisson	binomial	binomial	binomial	normal	binomial	mspline
23	link_function	log	logit	logit	logit	identity	cloglog	NA
24	consistency_setting	consistency	consistency	ume	nodesplit	consistency	consistency	consistency
25	niter	1000	2000	2000	2000	2000	2000	2000
26	prior_int_dist	normal	normal	normal	normal	normal	normal	normal
27	prior_int_location	0	0	0	0	0	0	0
28	prior_int_scale	10	10	10	10	10	10	10
29	prior_trt_dist	normal	normal	normal	normal	normal	normal	normal
30	prior_trt_location	0	0	0	0	0	0	0
31	prior_trt_scale	10	10	10	10	10	10	10
32	prior_het_dist	half_norma	half_normal	half_normal	half_normal	half_normal	half_normal	half_normal
33	prior_het_scale	5	5	5	5	5	5	5
34	baseline_dist	qnorm	qnorm	qnorm	qnorm	qnorm	qnorm	qnorm
35	baseline_location	0	0	0	0	0	0	0
36	baseline_scale	10	10	10	10	10	10	10
37	Report params	X	X	X	X	X	X	X
38	outcomename	outcome	outcome	outcome	outcome	outcome	outcome	outcome
39	comparisonname	Bayesian n	Bayesian network meta-analysis	Bayesian network meta-analysis	Bayesian network meta-analysis	Bayesian network meta-analysis	Bayesian network meta-analysis	Bayesian network meta-analysis
40								

Execution Script

```r
library(rmarkdown)
library(fs)
library(rstudioapi)
library(here)

# Define base path for models
base_path <- dirname(getActiveDocumentContext()$path)
working_dir <- here("working")
model_script <- here("Model code.r")    # Script to run models
#ppt_template <- here("automated_powerpoint.Rmd")
#word_template <- here("automated_word_report.Rmd")
params1 <- read.csv(here("Multinma_params.csv"), stringsAsFactors = FALSE)
modelnames <- colnames(params1)[-1]
modelnames_inconsistency <- grep("_nodesplit", modelnames, value = TRUE, invert = FALSE) # identify nodesplit runs
modelnames <- grep("_nodesplit|_ume", modelnames, value = TRUE, invert = TRUE) # exclude nodesplit and ume runs from the main set of runs
modelnames <- modelnames[which(modelnames %in% c("Dietary", "Parkinsons_arm_based"))]
############### COPYING OVER FILES INTO MODEL FOLDERS ##############

for (model_name in c(modelnames,modelnames_inconsistency)) {
  model_n <- which(modelnames == model_name) + 1
  model_path <- file.path(base_path, model_name)


  # 1. Copy Multinma_params.csv
  file.copy(from = file.path(base_path, "Multinma_params.csv"),
            to   = file.path(model_path, "Multinma_params.csv"),
            overwrite = TRUE)

  # 2. Copy automated PowerPoint Rmd
  file.copy(from = here("automated_powerpoint.Rmd"),
            to   = file.path(model_path, "automated_powerpoint.Rmd"),
            overwrite = TRUE)

  # 3. Copy automated Word Rmd
  file.copy(from = here("automated_word_report.Rmd"),
            to   = file.path(model_path, "automated_word_report.Rmd"),
            overwrite = TRUE)


  # 4. Copy Model code.r into each model folder
  file.copy(from = here("Model code.r"),
            to   = file.path(model_path, "Model code.r"),
            overwrite = TRUE)

  # 5. Copy Health Analytics Presentation Template NEW_RmdCOMPATIBLE.pptx into each model folder
  file.copy(from = here("Health Analytics Presentation Template NEW_RmdCOMPATIBLE.pptx"),
            to   = file.path(model_path, "Health Analytics Presentation Template NEW_RmdCOMPATIBLE.pptx"),
            overwrite = TRUE)

  # 6. Copy LCP Word Document Template.docx into each model folder
  file.copy(from = here("LCP Word Document Template.docx"),
            to   = file.path(model_path, "LCP Word Document Template.docx"),
            overwrite = TRUE)


############## RUNNING MODEL CODE FOR EACH MODEL ###############

  model_path <- file.path(base_path, model_name)
  message("🚀 Running model for: ", model_name)
  setwd(model_path)
  source("Model code.r", local = TRUE)
  message("✅ Finished model: ", model_name)

  # copy over nodesplit plots
  if (model_name %in% modelnames_inconsistency){
    file.copy(from = file.path(model_path, paste(model_name,"Direct indirect network estimates density plot.png")),
              to   = file.path(sub("_nodesplit","",model_path), paste(model_name,"Direct indirect network estimates density plot.png")),
              overwrite = TRUE)

    file.copy(from = file.path(model_path, paste(model_name,"Posterior dists inconsistency factors forest plot.png")),
              to   = file.path(sub("_nodesplit","",model_path), paste(model_name,"Posterior dists inconsistency factors forest plot.png")),
              overwrite = TRUE)
  }
################# CREATING POWERPOINT FOR EACH MODEL ##############

  rmarkdown::render(
    input = file.path(model_path, "automated_powerpoint.Rmd"),
    output_file = paste0(model_name, "_Results.pptx"),
    output_dir = model_path,
    envir = new.env()
  )
  message("📊 PowerPoint rendered for: ", model_name)

################# CREATING WORD REPORT FOR EACH MODEL ################

  rmarkdown::render(
    input = file.path(model_path, "automated_word_report.Rmd"),
    output_file = paste0(model_name, "_Results_Word.docx"),
    output_dir = model_path,
    envir = new.env()
  )
  message("📝 Word report generated for: ", model_name)

}
```

Running the execution script



Model folders before and after running the execution script

Parkinsons_arm_based

This folder is empty

Drag and drop files here to access them from any device.

Parkinsons_arm_based

Name

- Health Analytics Presentation Template NEW_RmdCOMPATIBLE.pptx
- LCP Word Document Template.docx
- Model code.r
- Multinma_params.csv
- nmafit_ranks.RData
- Parkinsons_arm_based Autocorrelation diagnostic histograms.pdf
- Parkinsons_arm_based Autocorrelation diagnostic histograms.png
- Parkinsons_arm_based Cumulative rank probabilities.pdf
- Parkinsons_arm_based Cumulative rank probabilities.png
- Parkinsons_arm_based Effective sample size histogram.pdf
- Parkinsons_arm_based Effective sample size histogram.png
- Parkinsons_arm_based Funnel plots of treatment effects.png
- Parkinsons_arm_based Gelman-Rubin statistic histogram.pdf
- Parkinsons_arm_based Gelman-Rubin statistic histogram.png
- Parkinsons_arm_based Gelman-Rubin statistic plots.pdf
- Parkinsons_arm_based Gelman-Rubin statistic plots.png
- Parkinsons_arm_based output.xlsx
- Parkinsons_arm_based_Results.pptx
- Parkinsons_arm_based_Results_Word.docx

PowerPoint and Word templates

Model code and parameters file

NMA plots

NMA results as csv

PowerPoint and Word report outputs

PowerPoint output

Network Meta-analysis (NMA) Results

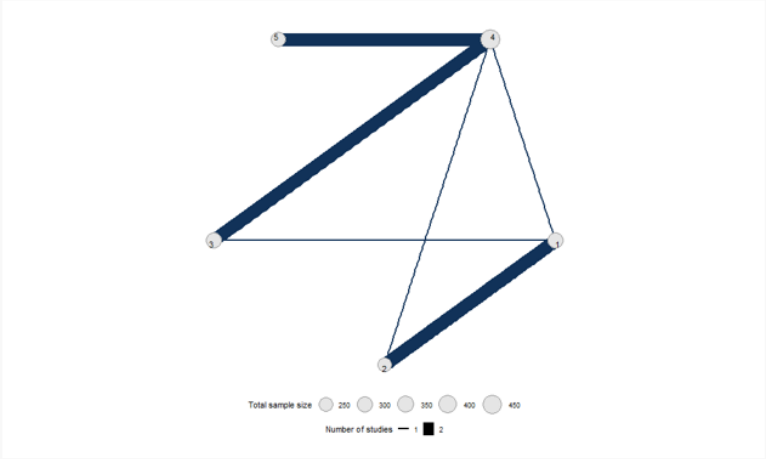
Prepared for: Client Name

Analysis performed

A Bayesian random effects model has been performed. - Treatment effect prior: A Normal distribution with mean 0 and standard deviation 10 - Intercept prior: A Normal distribution with mean 0 and standard deviation 10 - Heterogeneity prior: A half-Normal distribution with scale 5 - Number of iterations: 2000 (half of these iterations are burn in)

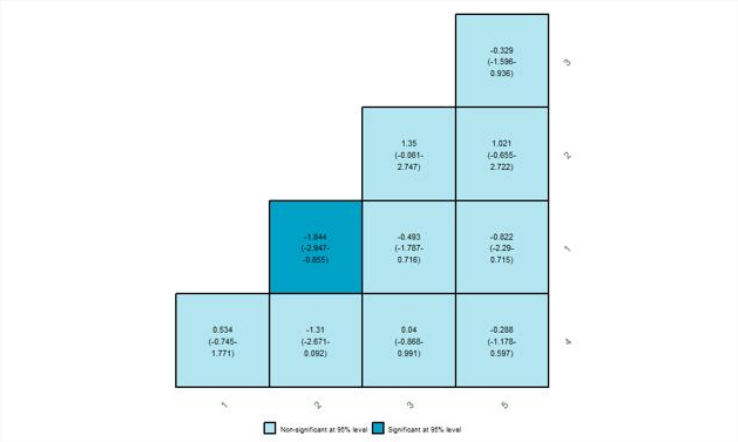
These priors have all been selected to be relatively non-informative, following NICE DSU guidance on choice of priors. List any additional analysis performed or sensitivity analysis proposed (e.g. exclusion of outliers, baseline risk, informative priors)

Study network diagram



Study network diagram

Pairwise grid



Posterior relative treatment effect pairwise grid

Results table

	Mean	Standard Deviation	Lower 95% credible interval	Upper 95% credible interval
1	0.534	0.657	-0.745	1.771
2	-1.310	0.696	-2.671	0.092
3	0.040	0.467	-0.868	0.991
5	-0.288	0.432	-1.178	0.597

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Cumulative rankogram

The cumulative rankogram visually summarises how treatments stack up against one another in terms of their probability of being the best, second-best, third-best, and so on in relation the endpoint of interest.

1 treatment has the highest probability of being the treatment with the greatest efficacy for outcome, with a probability of 71.6%.

Results from rankograms should be interpreted with caution, they may not present a clear picture of the evidence, particularly in sparse networks, further they do not consider whether differences in ordering are clinically meaningful.

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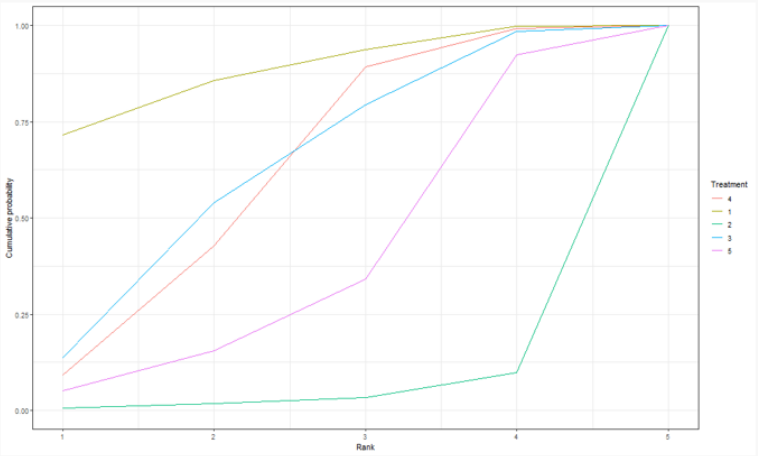
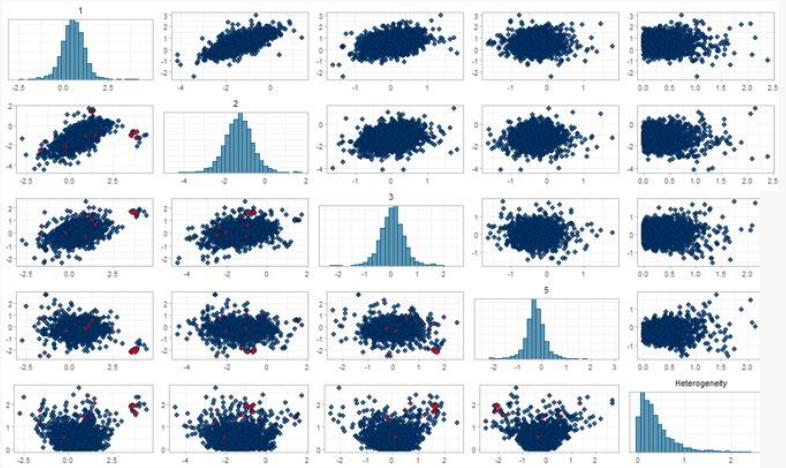


Cumulative rank probabilities

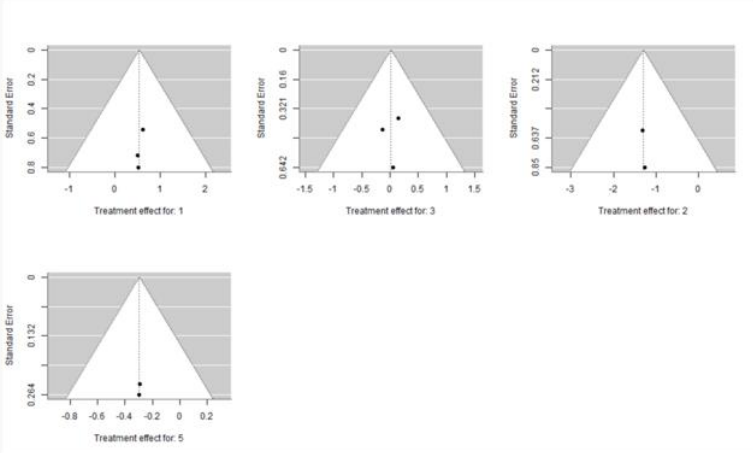
Model diagnostic tests - identifying patterns in divergent transitions

There were 16 divergent transitions.



Scatterplot matrix

Funnel plot



Funnel plots of treatment effects

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Contact us

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Our strategic mission:
We aim to lead the transition of health systems from importers of illness to exporters of health through realigning value between patients, manufacturers of medicines and payers.

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Word Report output

Network Meta-analysis (NMA) Results

Prepared for: Client Name

Prepared by: Lane Clark & Peacock LLP (LCP)

Contact details:

Version:

Date:

Contents

Overview of Network Meta-analysis

When synthesizing data collected from SLRs, standard pairwise meta-analysis allow the estimation of the mean effect of an intervention versus a single comparator (often placebo). When multiple comparisons are required or the evidence base consists of multiple comparators, a more extensive methodology is required. Network meta-analysis is an extension of standard pairwise meta-analysis. An NMA relates the relative difference in the efficacy of multiple treatments by accounting for all available evidence from a network of studies.

Statistical considerations

Frequentist vs Bayesian Methods

One selection required when performing NMA is whether to use frequentist, typically a general lineal mixed model with variance restricted to a standard distribution, or a Bayesian model, in which the exact distributions are estimated from the evidence base Frequentist methods tend

Results

Study network diagram

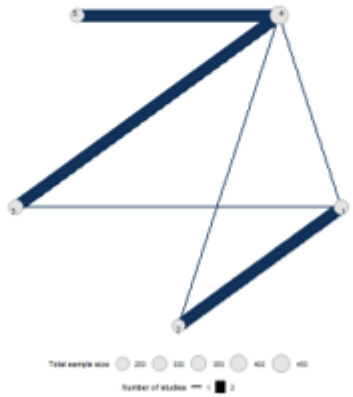

Fig 1. Study network map diagram

Table 1. Summary of studies by treatment

Treatment	Studies
1 vs 2	2, 3
1 vs 3	1
1 vs 4	3
2 vs 4	3
3 vs 4	4, 5
4 vs 5	6, 7

Table 2. Heterogeneity and model fit parameters

	Values
Deviance Information Criterion (DIC)	26.393
pD penalty	12.627
Residual deviance	13.766

The estimated heterogeneity is 0.385 (SD=0.37).

Table 3. NMA results

	Mean	Standard Deviation	Lower 95% credible interval	Upper 95% credible interval
1	0.534	0.657	-0.746	1.771
2	-1.310	0.696	-2.671	0.092
3	0.040	0.467	-0.868	0.991
5	-0.288	0.432	-1.178	0.597

Cumulative rankogram

The cumulative rankogram visually summarises how treatments stack up against one another in terms of their probability of being the best, second-best, third-best, and so on in relation the endpoint of interest. 1 treatment has the highest probability of being the treatment with the greatest efficacy for outcome, with a probability of 71.6%. Results from rankograms should be interpreted with caution, they may not present a clear picture of the evidence, particularly in sparse networks, further they do not consider whether differences in ordering are clinically meaningful.