

Towards Real-time Visual Exploration of Network Meta-analysis Results

Making Sense of Data with Visualizations
S37

Huan He, PhD and Irbaz Bin Riaz, MD, MS, PhD

Mayo Clinic
Twitter: #IS23



Disclosure



I and my spouse/partner have no relevant relationships with commercial interests to disclose.

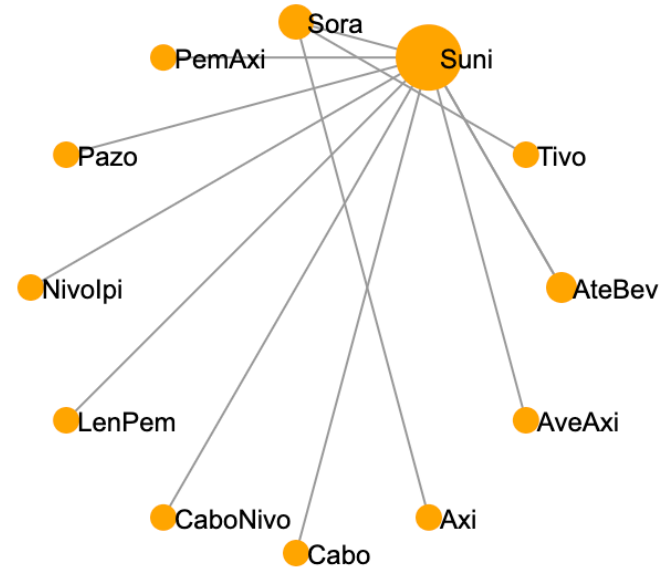
Outline

1. Background - Network meta-analysis
2. Methods - Hybrid framework and interactive data visualization
3. Prototype and demo

Background - Network Meta-analysis

Network meta-analysis (NMA) is a technique for comparing three or more interventions simultaneously in a single analysis by combining both direct and indirect evidence across a network of studies.

For example, NMA can be a useful tool for comparing the effectiveness of different treatments, even if those treatments have not been directly compared in a clinical trial. It can help to identify sources of treatment heterogeneity and assess the strength of evidence for different treatments.



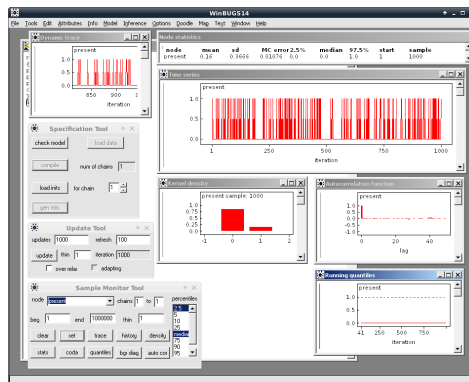
<https://rcc.network-meta-analysis.com/RCC.html>

The comparison network for the outcome of overall survival in metastatic renal cell cancer

Background - NMA Tools & Libraries

- Statistics tools

- WinBUGS
- OpenBUGS
- NetMetaXL



WinBUGS¹

- R and libraries:

- meta
- netmeta
- gemtc
- BUGSnet
- dmetar

The screenshot shows the NetMetaXL interface with a data table. The table has columns for Study, Treatment, Events, and Patients. The data is organized into rows for different studies and treatments.

Study	Treatment	Events	Patients
1	1	100	1000
1	2	100	1000
2	1	100	1000
2	2	100	1000
3	1	100	1000
3	2	100	1000
4	1	100	1000
4	2	100	1000
5	1	100	1000
5	2	100	1000
6	1	100	1000
6	2	100	1000
7	1	100	1000
7	2	100	1000
8	1	100	1000
8	2	100	1000
9	1	100	1000
9	2	100	1000
10	1	100	1000
10	2	100	1000
11	1	100	1000
11	2	100	1000
12	1	100	1000
12	2	100	1000
13	1	100	1000
13	2	100	1000
14	1	100	1000
14	2	100	1000
15	1	100	1000
15	2	100	1000
16	1	100	1000
16	2	100	1000
17	1	100	1000
17	2	100	1000
18	1	100	1000
18	2	100	1000
19	1	100	1000
19	2	100	1000
20	1	100	1000
20	2	100	1000

NetMetaXL²

```
nma-sample.R
rst_meta

21
22   sigma <- sqrt(1/tau)
23 }
24
25 # Compile the JAGS model and define the data and initial values
26 jags.model <- jags.model(textConnection(model), data=list(y=data$effect_size, x=data$covariate),
27                       n.chains=4, n.adapt=1000)
28 jags.data <- list(y=data$effect_size, x=data$covariate, N=nrow(data))
29 jags.inits <- function() {
30   list(beta0=rnorm(1), beta1=rnorm(1), tau=rgamma(1, 0.01, 0.01))
31 }
32
33 # Run the JAGS model using the coda package
34 jags.samples <- coda.samples(jags.model, variable.names=c("beta0", "beta1", "sigma"),
35                             n.iter=10000, thin=10, init=jags.inits)
36
37 # Check the convergence of the chains
38 gelman.diag(jags.samples)
39
40 # Summarize the posterior distributions
41 summary(jags.samples)
42
43 # Plot the posterior distributions
44
2:3 (Top Level) | R Script
```

R is a collaborative project with many contributors. Type 'contributors()' for more information and 'citation()' on how to cite R or R packages in publications.

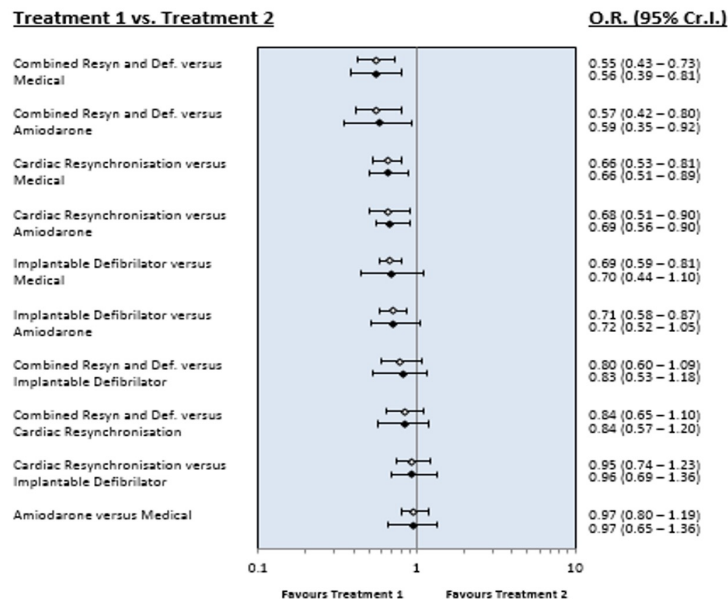
Type 'demo()' for some demos, 'help()' for on-line help, or 'help.start()' for an HTML browser interface to help. Type 'q()' to quit R.

RStudio and meta-analysis in R

Background - Challenges

1. Presentation of the results.

The presentation of NMA results to clinicians for shared-decision making, policymakers, and guideline developers is limited by static tabulations and visualizations that often omit critically important details necessary for clinical decision making



Screenshot of NetMetaXL output

Background - Challenges

2. Efficiency.

The NMA process requires technical expertise and manual effort. Hence, researchers need to learn the workflow of the tools or how to write the correct R scripts with correct parameters.

Moreover, as the network expands with the evolving evidence, not only does the number of primary studies and outcomes increase, but also the time spent on computation and manual configuration increases.

```
network<-mtc.network(data.re = data)
model<-mtc.model(network, link="log", likelihood="poisson", linearModel="{{ fixed_or_random }}")
mcmc1<-mtc.run(model, n.adapt = 50, n.iter = 1000, thin = 1)
mtc.run(model) -> results
summary(results)

# RANKOGRAM
rank.probability <- rank.probability(mcmc1)
rank.probsmat = as.matrix(rank.probability)
rank.rownames = rownames(rank.probsmat)
rank.sucra<-sucra(rank.probability, lower.is.better = {{ sucra_lower_is_better }})
# rank.sucra<-sucra(rank.probability)

# plot(sucra)

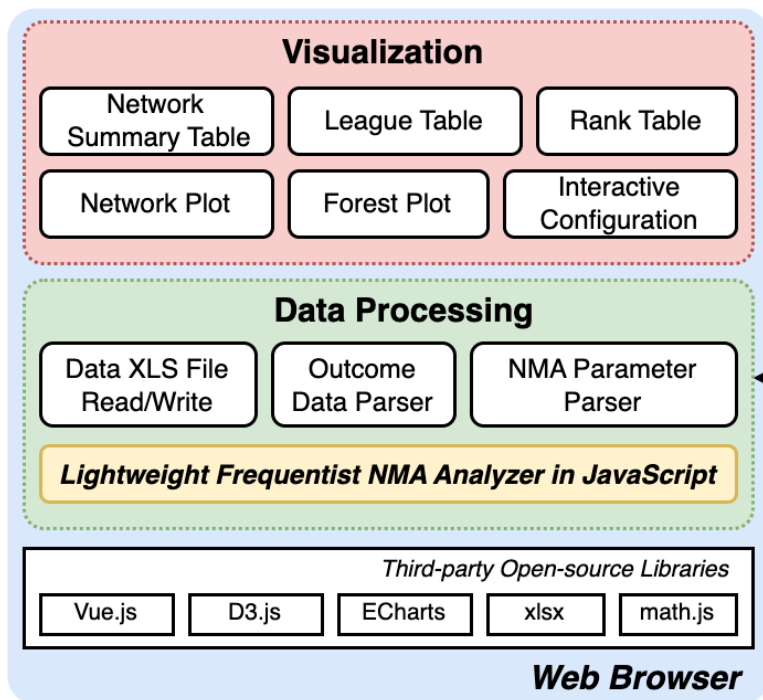
# FORET PLOT
myforest <- forest(relative.effect(results, t1="{{ reference_treatment }}"), digits=2)

# LEAGUE TABLE (for back transforming and exporting)
league<-relative.effect.table(results)
expleague<-data.frame(exp(league))
#write.csv(expleague, file = "name.csv")

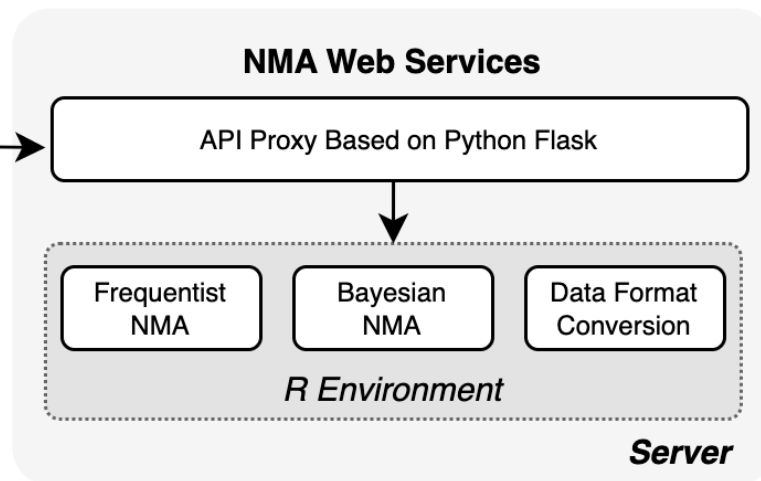
all_ret <- list(
  model = model,
  expleague = expleague,
  sucraplot = list(
    probs = rank.probability,
    rows = rank.rownames
  ),
  sucra = rank.sucra,
  version = list(
    jsonlite = packageVersion('jsonlite'),
    gemtc = packageVersion('gemtc')
  )
)
```

Conducting Bayesian NMA with R and gemtc

Methods - Hybrid framework (JS + R + Py)



We propose a **hybrid framework** to accommodate comprehensive statistics associated with visually exploring NMA results in real time.



Demo - Input data (.xlsx file)

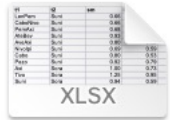
	A	B	C	D	E	F	
1	t1	t2	sm	lowerci	upperci	study	
2	LenPem	Suni	0.66	0.49	0.88	Motzer RJ et al (3)	
3	CaboNivo	Suni	0.66	0.50	0.87	Motzer RJ et al (4)	
4	PemAxi	Suni	0.68	0.55	0.85	Powles T et al	
5	AteBev	Suni	0.93	0.76	1.14	Rini BI et al	
6	AveAxi	Suni	0.80	0.62	1.03	Choueiri TK et al (2)	
7	Nivolpi	Suni	0.69	0.59	0.81	Albiges L et al	
8	Cabo	Suni	0.80	0.53	1.21	Choueiri TK et al (3)	
9	Pazo	Suni	0.92	0.79	1.06	Motzer RJ et al (1)	
10	Axi	Sora	1.00	0.73	1.36	Hutson TE et al	
11	Tivo	Sora	1.25	0.95	1.62	Motzer RJ et al (2)	
12	Suni	Sora	0.94	0.59	1.49	Tomita Y et al	

Pre-calculated values

	A	B	C	D
1	study	treat	event	total
2	Motzer RJ et al (3)	LenPem	57	355
3	Motzer RJ et al (3)	Suni	15	357
4	Motzer RJ et al (4)	CaboNivo	30	323
5	Motzer RJ et al (4)	Suni	14	328
6	Powles T et al	PemAxi	38	432
7	Powles T et al	Suni	13	429
8	Rini BI et al	AteBev	49	454
9	Rini BI et al	Suni	32	461
10	Albiges et al	Nivolpi	59	550
11	Albiges et al	Suni	14	546
12	Atkins MB et al	AteBev	7	101
13	Atkins MB et al	Suni	5	101
14	Motzer RJ et al (1)	Pazo	1	557
15	Motzer RJ et al (1)	Suni	3	553

Raw values

Demo - Load data file



NMA-pre-smlu.xlsx

drag and drop file



DATASET

Select Data File

Choose File No file chosen

Upload & Read Data File

SETTINGS

Input Format: HR, Lower, U

Analysis Method: Frequentist I

Measure of Effect: Relative Risk

Ref. Treatment:

Fixed / Random: Fixed Effect I

Which is Better: Lower is Bett

Analyze

parse the data file



DATASET

Select Data File

Choose File NMA-pre-smlu.xlsx

Upload & Read Data File

Input Data Summary

NMA-pre-smlu.xlsx

HRLU format

12 treats: Suni, Sora, Cabo, AteBev, Axi, PemAxi, AveAxi, Tivo, LenPem, Nivolpi, Pazo, CaboNivo

11 studies of 11 lines

SETTINGS

Input Format: HR, Lower, U

Analysis Method: Frequentist I

Measure of Effect: Relative Risk

Ref. Treatment: Suni

Fixed / Random: Fixed Effect I

Which is Better: Lower is Bett

Analyze

Demo - Customize parameters

DATASET

Select Data File

Choose File NMA-pre-smlu.xlsx

Upload & Read Data File

Input Data Summary

NMA-pre-smlu.xlsx

HRLU format

12 treats: Suni, Sora, Cabo, AteBev, Axi, PemAxi, AveAxi, Tivo, LenPem, Nivolpi, Pazo, CaboNivo

11 studies of 11 lines

SETTINGS

Input Format: HR, Lower, U

Analysis Method: Frequentist

Measure of Effect: Relative Risk

Ref. Treatment: Suni

Fixed / Random: Fixed Effect

Which is Better: Lower is Better

Analyze

✓ HR, Lower, Upper
Event Total
Follow-up Time, Event, Total

✓ Frequentist NMA
Bayesian NMA

✓ Hazard Ratio
Odds Ratio
Relative Risk
Risk Difference

✓ Fixed Effect Model
Random Effect Model

	A	B	C	D	E	F
1	t1	t2	sm	lowerci	upperci	study
2	LenPem	Suni	0.66	0.49	0.88	Motzer RJ et al (3)
3	CaboNivo	Suni	0.66	0.50	0.87	Motzer RJ et al (4)
4	PemAxi	Suni	0.68	0.55	0.85	Powles T et al
5	AteBev	Suni	0.93	0.76	1.14	Rini BI et al
6	AveAxi	Suni	0.80	0.62	1.03	Choueiri TK et al (2)
7	Nivolpi	Suni	0.69	0.59	0.81	Albiges L et al
8	Cabo	Suni	0.80	0.53	1.21	Choueiri TK et al (3)
9	Pazo	Suni	0.92	0.79	1.06	Motzer RJ et al (1)
10	Axi	Sora	1.00	0.73	1.36	Hutson TE et al
11	Tivo	Sora	1.25	0.95	1.62	Motzer RJ et al (2)
12	Suni	Sora	0.94	0.59	1.49	Tomita Y et al

Outcome data

```
1 {  
2   "analyze_type": "nma",  
3   "study_list": [],  
4   "input_format": "HRLU",  
5   "reference_treatment": "Suni",  
6   "analysis_method": "freq",  
7   "measure_of_effect": "HR",  
8   "fixed_or_random": "fixed",  
9   "which_is_better": "small"  
10 }
```

Parameters

NMA Web Services

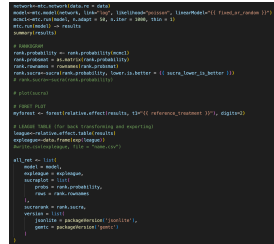
R Env

Demo - Convert NMA results to JSON

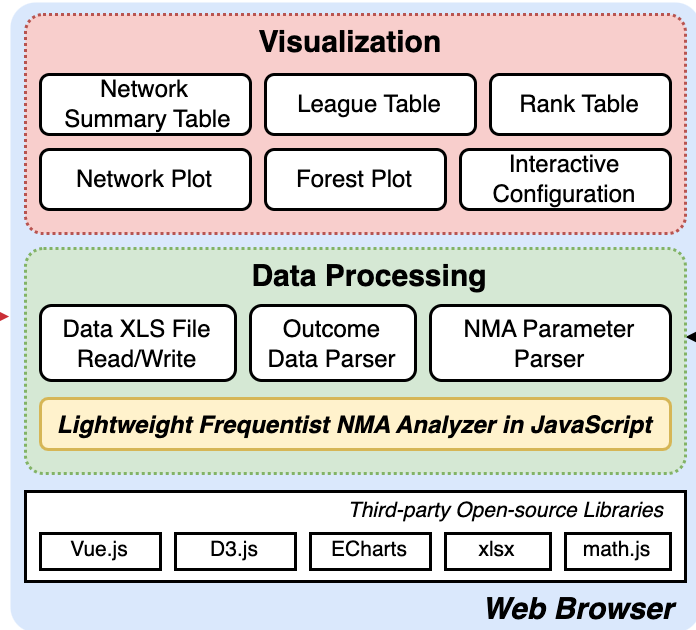
Run R scripts to get the NMA results and convert the R objects to JSON



```
▼ data: {forest: {backend: "netmeta", glb_max: 2.269346716532471, glt
  ▼ forest: {backend: "netmeta", glb_max: 2.269346716532471, glb_min:
    backend: "netmeta"
    glb_max: 2.269346716532471
    glb_min: 0.492468884030211
    sm: "HR"
    subtitle: "Fixed Effect Model"
    title: "Comparison vs 'Suni'"
    val_max: 1.3297620281214737
    val_min: 0.6600101930934101
    ▶ vals: [,...]
  }
  ▼ league: {backend: "netmeta",...}
    backend: "netmeta"
    ▶ cols: ["AteBev", "AveAxi", "Axi", "Cabo", "CaboNivo", "LenPen",
      n: 12
      ▶ tabledata: [{lci: [1, 0.6211180124223602, 0.6289308176100629, 0
        ▶ netcha: [{cha: "Number of Interventions", val: 12}, {cha: "Number
        ▶ netplt: {backend: "netmeta",...}
        ▶ psrank: {backend: "netmeta", col: "pscore",...}
```



A screenshot of a terminal window showing R code and output. The code includes library calls for netmeta, netmeta.js, and netmeta.js. The output shows the results of the netmeta function, including forest and league objects.



Demo - Data Visualization

☰ NMA Analyzer

DATASET

Select Data File

Choose File NMA-pre-smlu.xlsx
 Upload & Read Data File

Input Data Summary

NMA-pre-smlu.xlsx
 HRLU format
 12 treats: Suni, Sora, Cabo, AteBev, Axi, PemAxi, AveAxi, Tivo, LenPem, Nivolpi, Pazo, CaboNivo
 11 studies of 11 lines

SETTINGS

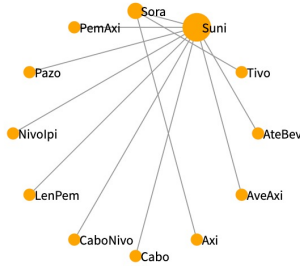
Input Format: HR, Lower, U
 Analysis Method: Frequentist I
 Measure of Effect: Relative Risk
 Ref. Treatment: Suni
 Fixed / Random: Fixed Effect I
 Which is Better: Lower is Better

Analyze

NETWORK CHARACTERISTICS

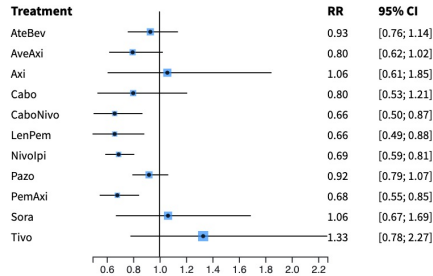
Number of Interventions: 12
 Number of Studies: 11
 Total Number of Patients in Network: -
 Total Possible Pairwise Comparisons: 72
 Total Number of Pairwise Comparisons...: 11
 Is the network connected? TRUE
 Number of Two-arm Studies: 11
 Number of Multi-Arms Studies: 0
 Number of Studies With No Zero Events: 11
 Number of Studies With At Least One Z...: 0
 Number of Studies with All Zero Events: 0

NETWORK PLOT Save PNG



FOREST PLOT Save PNG

Comparison vs 'Suni'
Fixed Effect Model



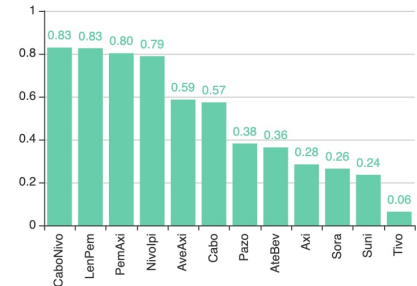
RANK TABLE Save CSV

Treatment	P-Score	Rank
CaboNivo	0.829	1
LenPem	0.826	2
PemAxi	0.8026	3
Nivolpi	0.7887	4
AveAxi	0.5865	5
Cabo	0.5735	6
Pazo	0.3817	7
AteBev	0.3635	8
Axi	0.2843	9
Sora	0.2644	10
Suni	0.236	11
Tivo	0.0638	12

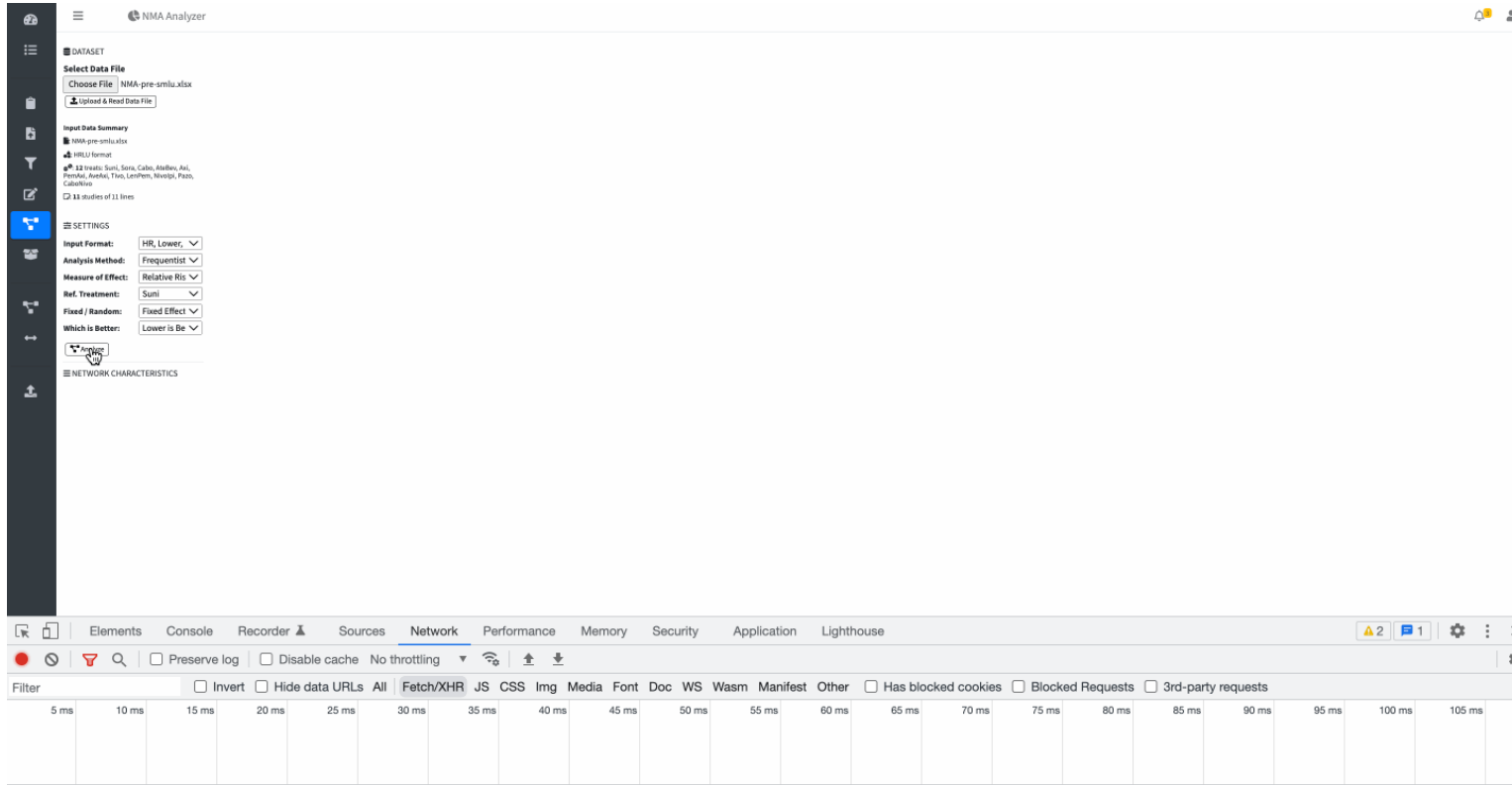
LEAGUE TABLE Save PNG

Comparator	Treatments											
	AteBev	AveAxi	Axi	Cabo	CaboNivo	LenPem	Nivolpi	Pazo	PemAxi	Sora	Suni	Tivo
AteBev		0.85 (0.62, 1.18)	1.14 (0.63, 2.04)	0.86 (0.54, 1.37)	0.71 (0.50, 1.00)	0.71 (0.50, 1.01)	0.74 (0.57, 0.96)	0.99 (0.77, 1.27)	0.73 (0.54, 0.98)	1.15 (0.69, 1.89)	1.08 (0.88, 1.32)	1.43 (0.81, 2.56)
AveAxi	1.17 (0.85, 1.61)		1.33 (0.72, 2.44)	1.00 (0.62, 1.64)	0.83 (0.57, 1.20)	0.83 (0.56, 1.22)	0.87 (0.65, 1.16)	1.15 (0.86, 1.54)	0.85 (0.61, 1.19)	1.33 (0.79, 2.27)	1.25 (0.92, 1.61)	1.67 (0.93, 3.03)
Axi	0.88 (0.49, 1.59)	0.75 (0.41, 1.39)		0.76 (0.38, 1.52)	0.63 (0.33, 1.16)	0.63 (0.33, 1.16)	0.65 (0.36, 1.16)	0.87 (0.49, 1.54)	0.64 (0.35, 1.16)	1.01 (0.74, 1.37)	0.94 (0.54, 1.64)	1.25 (0.83, 1.89)
Cabo	1.16 (0.73, 1.84)	1.00 (0.61, 1.61)	1.32 (0.66, 2.65)		0.83 (0.50, 1.35)	0.83 (0.50, 1.37)	0.86 (0.56, 1.33)	1.15 (0.74, 1.79)	0.85 (0.53, 1.35)	1.33 (0.71, 2.50)	1.25 (0.83, 1.89)	1.67 (0.85, 3.23)
CaboNivo	1.41 (1.00, 1.99)	1.21 (0.83, 1.75)	1.60 (0.86, 2.99)	1.21 (0.74, 1.99)		1.00 (0.67, 1.49)	1.04 (0.76, 1.43)	1.39 (1.02, 1.92)	1.03 (0.72, 1.47)	1.61 (0.94, 2.50)	1.52 (1.15, 2.00)	2.00 (1.10, 3.70)
LenPem	1.41 (0.99, 2.01)	1.21 (0.82, 1.78)	1.60 (0.86, 3.01)	1.21 (0.73, 2.01)	1.00 (0.67, 1.50)		1.04 (0.75, 1.45)	1.39 (1.00, 1.92)	1.39 (0.71, 1.49)	1.61 (0.93, 2.78)	1.52 (1.14, 2.04)	2.00 (1.10, 3.70)
Nivolpi	1.35 (1.04, 1.74)	1.15 (0.86, 1.55)	1.53 (0.86, 2.74)	1.16 (0.75, 1.80)	0.96 (0.70, 1.32)	0.96 (0.69, 1.33)		1.33 (1.08, 1.67)	0.99 (0.75, 1.28)	1.54 (0.94, 2.50)	1.45 (1.23, 1.69)	1.92 (1.10, 3.33)
Pazo	1.01 (0.79, 1.30)	0.87 (0.65, 1.16)	1.15 (0.65, 2.05)	0.87 (0.56, 1.35)	0.72 (0.52, 0.98)	0.97 (0.52, 1.00)	0.75 (0.60, 0.93)		0.74 (0.57, 0.96)	1.16 (0.71, 1.89)	1.09 (0.93, 1.27)	1.45 (0.83, 2.50)
PemAxi	1.37 (1.02, 1.84)	1.17 (0.84, 1.63)	1.56 (0.86, 2.83)	1.18 (0.74, 1.88)	0.97 (0.68, 1.38)	0.97 (0.67, 1.40)	1.01 (0.78, 1.33)	1.35 (1.04, 1.76)		1.56 (0.93, 2.63)	1.47 (1.18, 1.82)	1.96 (1.10, 3.45)
Sora	0.87 (0.53, 1.45)	0.75 (0.44, 1.27)	1.06 (0.73, 1.36)	0.99 (0.40, 1.40)	0.62 (0.36, 1.06)	0.65 (0.36, 1.07)	0.65 (0.40, 1.06)	0.86 (0.53, 1.41)	0.64 (0.38, 1.07)		0.94 (0.59, 1.49)	1.25 (0.96, 1.64)
Suni	0.93 (0.76, 1.14)	0.80 (0.62, 1.02)	1.06 (0.61, 1.85)	0.80 (0.53, 1.21)	0.66 (0.50, 0.87)	0.66 (0.49, 0.88)	0.69 (0.59, 0.81)	0.92 (0.79, 1.07)	0.68 (0.55, 0.85)	1.06 (0.67, 1.69)		1.33 (0.78, 2.27)
Tivo	0.70 (0.39, 1.24)	0.60 (0.33, 1.08)	0.60 (0.53, 1.20)	0.60 (0.31, 1.18)	0.50 (0.27, 0.91)	0.50 (0.27, 0.91)	0.52 (0.30, 0.91)	0.69 (0.40, 1.20)	0.51 (0.29, 0.91)	0.80 (0.61, 1.04)	0.75 (0.44, 1.28)	

P-Score PLOT Save PNG



Demo - Data Visualization



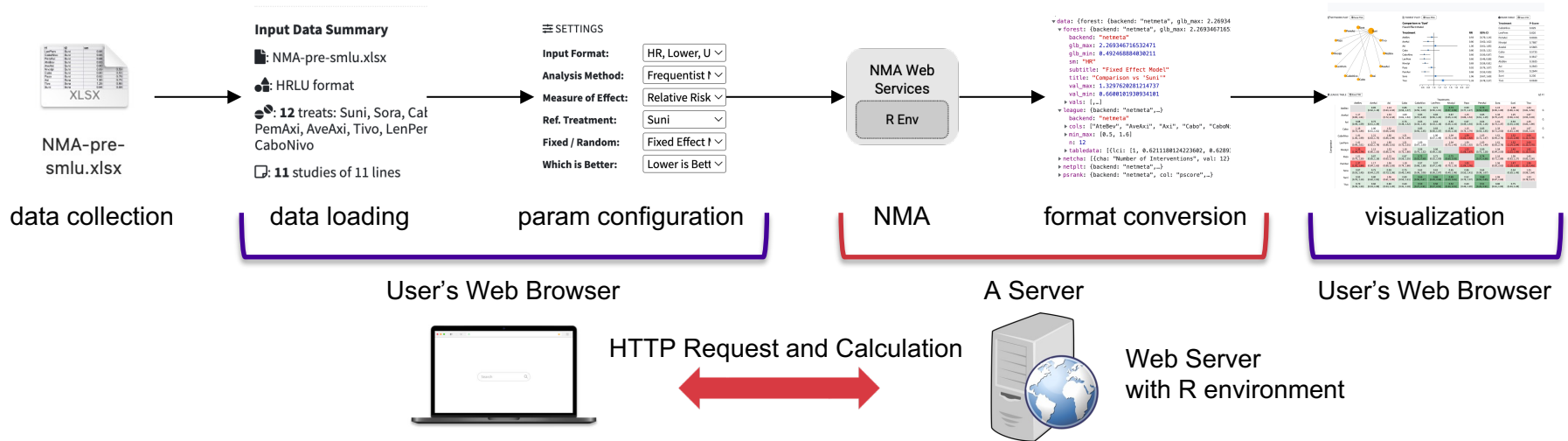
The screenshot shows the NMA Analyzer web application interface. The top navigation bar includes a hamburger menu, the text "NMA Analyzer", and a user profile icon. The main content area is divided into three sections: DATASET, SETTINGS, and NETWORK CHARACTERISTICS. The DATASET section includes a "Select Data File" button, a "Choose File" button with the file "NMA-pre-smlu.xlsx" selected, and an "Upload & Read Data File" button. Below this is an "Input Data Summary" section showing "NMA-pre-smlu.xlsx" in HRU format, with 13 studies from 11 lines. The SETTINGS section includes dropdown menus for "Input Format" (HR, Lower), "Analysis Method" (Frequentist), "Measure of Effect" (Relative Ris), "Ref. Treatment" (Sun), "Fixed / Random" (Fixed Effect), and "Which is Better" (Lower is Be). The NETWORK CHARACTERISTICS section is currently empty. At the bottom of the screenshot, a browser's developer tools window is open, showing the "Network" tab with a timeline of network activity. The timeline is currently empty, with a message "Recording network activity..." and instructions to "Perform a request or hit ⌘ R to record the reload." A "Learn more" link is provided below the instructions.

Recording network activity...

Perform a request or hit ⌘ R to record the reload.

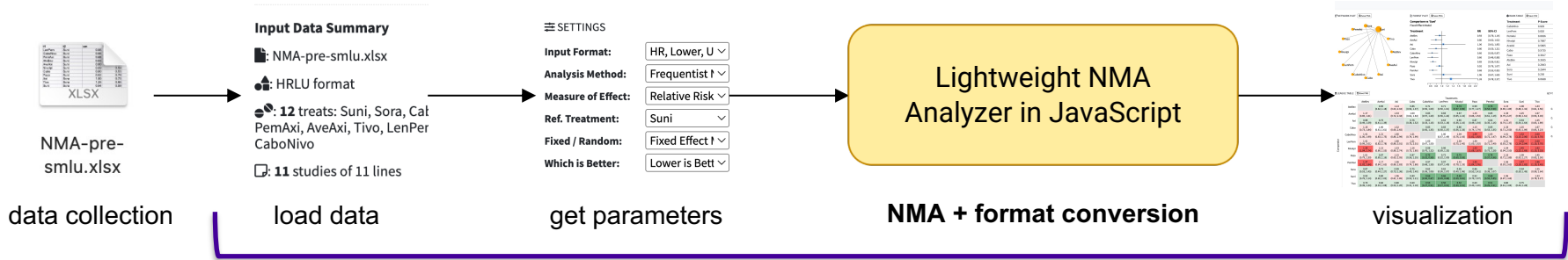
[Learn more](#)

It works! but it takes 4s for a single NMA



1. An always-on server is required
2. Data must be sent out for calculation
3. It takes a little while to get the results

An in-browser NMA module

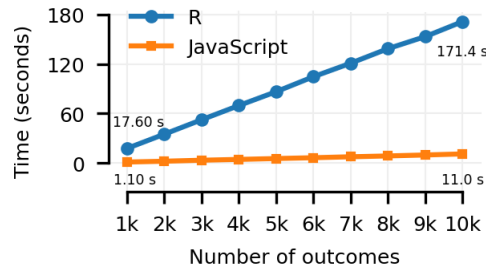
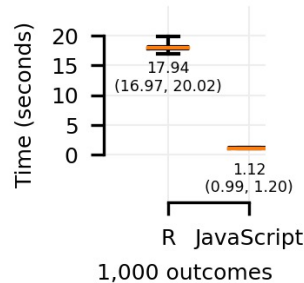


1. The server is not required anymore
2. Data won't be sent out.
3. Faster!

User's Web Browser



All run in the user's web browser
(in-memory object exchange)
0 cost on network transfer



Demo - In-browser NMA

Network Meta-analysis

Load Sample Data

Download Sample Data

Drop .xlsx / .csv File Here

Input Format:
Analysis Engine:
Analysis Method:
Measure of Effect:
Fixed / Random:
Which is Better:

Analyze

LEAGUE TABLE

The values in each cell represent the relative treatment effect (and 95% CI) of the treatment on the top, compared to the treatment on the left. Green color suggests relative treatment benefit. Light green suggests non-significant benefit and dark green suggests significant benefit. Red color suggests relative treatment harm. Light red suggests non-significant harm and dark red suggests significant harm.

Network Plot

Forest Plot

Demo - In-browser NMA takes less than 1s



Network Meta-analysis

Load Sample Data [Download Sample Data](#)

RCC-pre-smfu.xlsx
Load 11 Records

Columns:
t1, t2, sm, lower, upper, study

Records:
11

Input Format:

Analysis Engine:

Analysis Method:

Measure of Effect:

Fixed / Random:

Which is Better:

LEAGUE TABLE

The values in each cell represent the relative treatment effect (and 95% CI) of the treatment on the top, compared to the treatment on the left. Green color suggests relative treatment benefit. Light green suggests non-significant benefit and dark green suggests significant benefit. Red color suggests relative treatment harm. Light red suggests non-significant harm and dark red suggests significant harm.

Network Plot

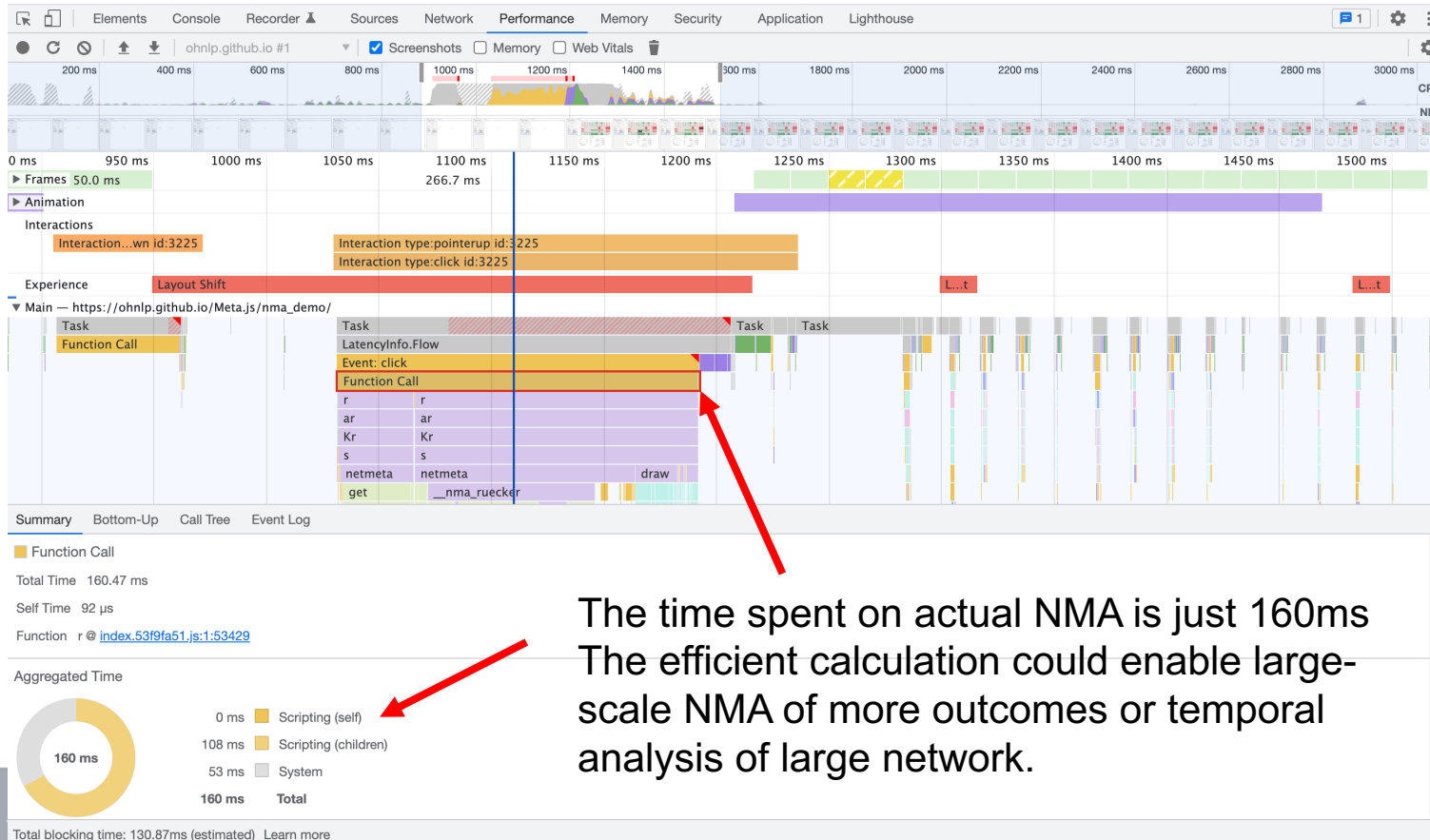
Forest Plot

Click the record button or hit **⌘ E** to start a new recording.

Click the reload button or hit **⌘ ⇧ E** to record the page load.

After recording, select an area of interest in the overview by dragging. Then, zoom and pan the timeline with the mousewheel or **WASD** keys. [Learn more](#)

Demo - In-browser NMA takes less than 1s



The time spent on actual NMA is just 160ms
The efficient calculation could enable large-scale NMA of more outcomes or temporal analysis of large network.

Demo - Example Usage

The visualized NMA results can be used to generate living evidence for public access.

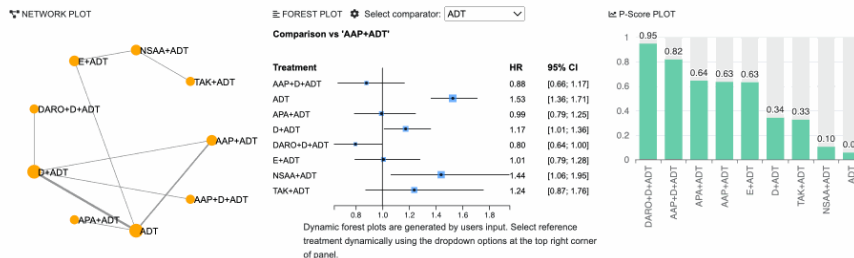
First-line Treatment of Metastatic Renal Cell Carcinoma: A Living, Interactive Systematic Review and Network Meta-Analysis
 European Urology, PMID: [33824031](https://pubmed.ncbi.nlm.nih.gov/33824031/)
<https://rcc.network-meta-analysis.com/RCC.html>

A Living Interactive Systematic Review and Network Meta-Analysis on First-Line Treatment Options in Metastatic Castration Sensitive Prostate Cancer
 JAMA Oncology, PMID: [36862387](https://pubmed.ncbi.nlm.nih.gov/36862387/)
<https://mcspc.living-evidence.com/>

Primary Analysis



The values in each cell represent the relative treatment effect (and 95% CI) of the treatment on the top, compared to the treatment on the left. Green color suggests relative treatment benefit. Light green suggests non-significant benefit and dark green suggests significant benefit. Red color suggests relative treatment harm. Light red suggests non-significant harm and dark red suggests significant harm.



<https://mcspc.living-evidence.com/>

Takeaways

1. Use web-based data visualization techniques for exploration of the network meta-analysis results
2. Provide in-depth meta-analysis as a web service for better integration
3. Leverage JavaScript-based frontend techniques to distribute the computation abilities to users without extra server cost

Source code and online demo: <https://github.com/OHNLP/Meta.js>

Example usages: <https://living-evidence.com/>

Acknowledgments



Iterative improvement based on community feedback from AMIA



Oct. 30 - Nov. 3, 2021

San Diego, CA



Informatics Summit

**March 21-24, 2022 |
Chicago, IL**



November 5-9, 2022

Washington, DC

Acknowledgments - Co-authors



Irbaz Bin Riaz



Syed Arsalan
Ahmed Naqvi



Rabbia Siddiqi



Noureen Asghar



Mahnoor Islam



M. Hassan Murad



Hongfang Liu

Thank you!

Emails: liu.hongfang@mayo.edu
riaz.dr@mayo.edu, he.huan@mayo.edu

