

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

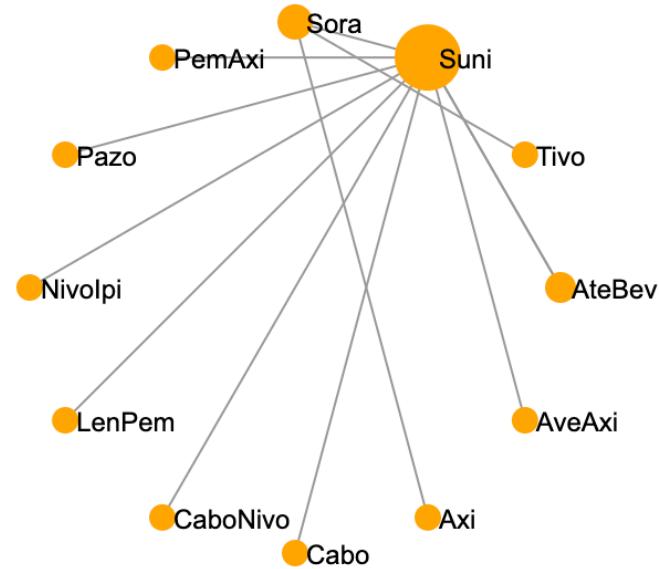


1. Background - Network meta-analysis
2. Methods - Hybrid framework and interactive data visualization
3. Prototype and demo

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.



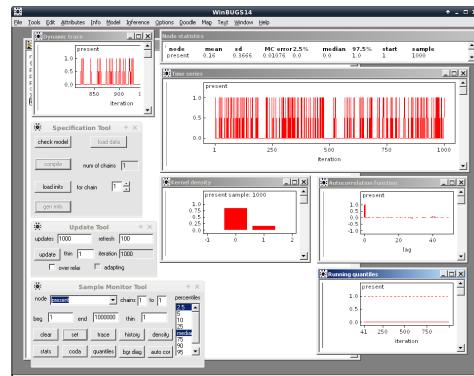
<https://rcc.network-meta-analysis.com/RCC.html>
The comparison network for the outcome of overall survival in metastatic renal cell cancer

Background - NMA Tools & Libraries



- Statistics tools

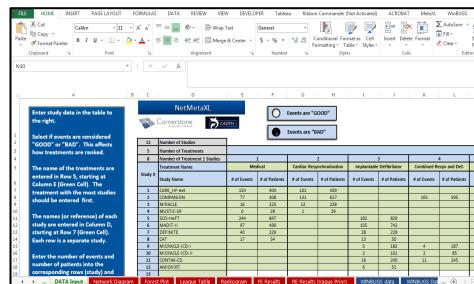
- WinBUGS
- OpenBUGS
- NetMetaXL



WinBUGS¹

- R and libraries:

- meta
- netmeta
- gemtc
- BUGSnet
- dmetar



NetMetaXL²

```
sigma <- sqrt(1/tau)

# Compile the JAGS model and define the data and initial values
jags.model <- jags.model(textConnection(model), data=list(y=data$effect_size, x=data$covariate),
n.chains=4, n.adapt=1000)
jags.data <- list(y=data$effect_size, x=data$covariate, N=nrow(data))
jags.inits <- function() {
  list(beta0=rnorm(1), beta1=rnorm(1), tau=rgamma(1, 0.01, 0.01))
}

# Run the JAGS model using the coda package
jags.samples <- coda.samples(jags.model, variable.names=c("beta0", "beta1", "sigma"),
n.iter=10000, thin=10, init=jags.inits)

# Check the convergence of the chains
gelman.diag(jags.samples)

# Summarize the posterior distributions
summary(jags.samples)

# Plot the posterior distributions

```

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

Treatment 1 vs. Treatment 2

Combined Resyn and Def. versus Medical

Combined Resyn and Def. versus Amiodarone

Cardiac Resynchronisation versus Medical

Cardiac Resynchronisation versus Amiodarone

Implantable Defibrillator versus Medical

Implantable Defibrillator versus Amiodarone

Combined Resyn and Def. versus Implantable Defibrillator

Combined Resyn and Def. versus Cardiac Resynchronisation

Cardiac Resynchronisation versus Implantable Defibrillator

Amiodarone versus Medical

O.R. (95% Cr.I.)

0.55 (0.43 – 0.73)
0.56 (0.39 – 0.81)

0.57 (0.42 – 0.80)
0.59 (0.35 – 0.92)

0.66 (0.53 – 0.81)
0.66 (0.51 – 0.89)

0.68 (0.51 – 0.90)
0.69 (0.56 – 0.90)

0.69 (0.59 – 0.81)
0.70 (0.44 – 1.10)

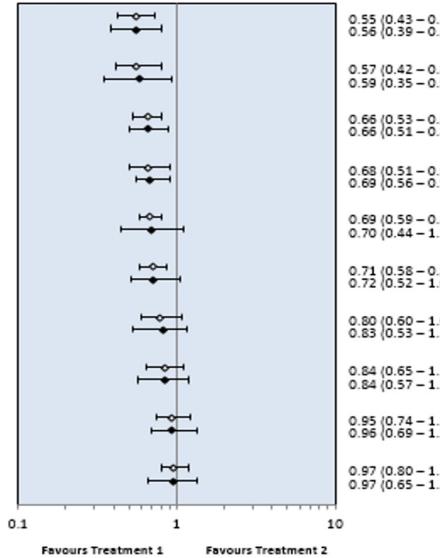
0.71 (0.58 – 0.87)
0.72 (0.52 – 1.05)

0.80 (0.60 – 1.09)
0.83 (0.53 – 1.18)

0.84 (0.65 – 1.10)
0.84 (0.57 – 1.20)

0.95 (0.74 – 1.23)
0.96 (0.69 – 1.36)

0.97 (0.80 – 1.19)
0.97 (0.65 – 1.36)



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)

# RANKGRAM
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)

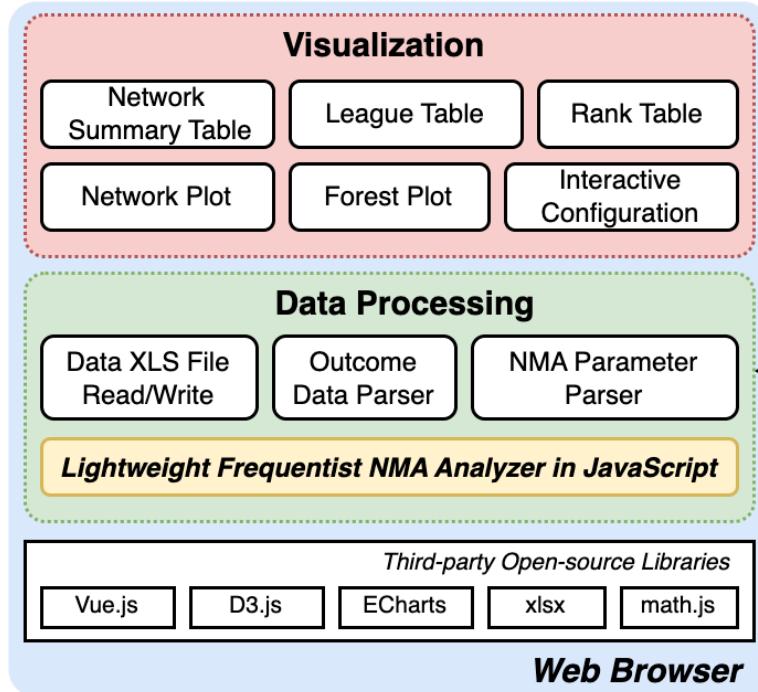
# FORET PLOT
myforest <- forest(relative.effect(results, t1="{{ reference_treatment }}"), digits=2)

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

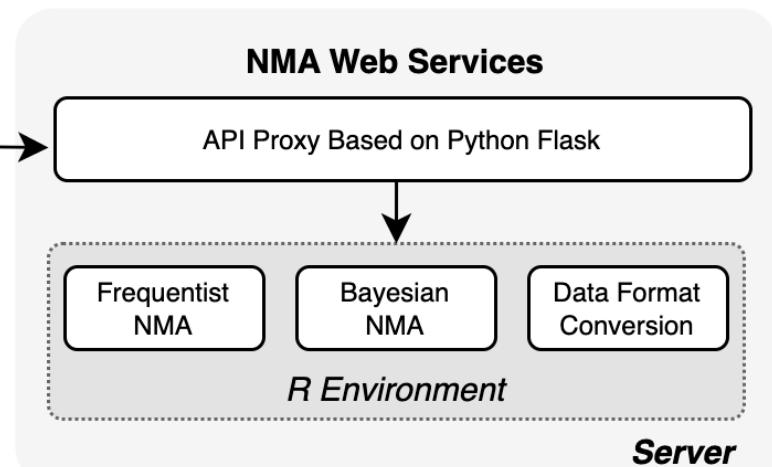
all_ret <- list(
  model = model,
  expleague = expleague,
  sucraplot = list(
    probs = rank.probability,
    rows = rank.rownames
  ),
  sucrarank = rank.sucra,
  version = list(
    jsonlite = packageVersion('jsonlite'),
    gemtc = packageVersion('gemtc')
  )
)
```

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

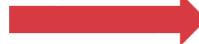
Raw values

Demo - Load data file



NMA-pre-
smlu.xlsx

drag and drop file



NMA Analyzer

Dataset

Select Data File

Choose File No file chosen
Upload & Read Data File

Settings

Input Format: HR, Lower, U ▾
Analysis Method: Frequentist ▾
Measure of Effect: Relative Risk ▾
Ref. Treatment: ▾
Fixed / Random: Fixed Effect ▾
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

File: NMA-pre-smlu.xlsx
Format: HR LU format
Treatments: 12 treats: Suni, Sora, Cabo, AteBev, Axi, PemAxi, AveAxi, Tivo, LenPem, Nivolpi, Pazo, CaboNivo
Studies: 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 Bett ▾

Analyze

Demo - Customize parameters

Dataset

Select Data File

Choose File NMA-pre-smu.xlsx

Input Data Summary

NMA-pre-smu.xlsx
HRLU format
12 treats: Suni, Sora, Cabo, AteBev, Axi, PemAxi, AveAxi, Tivo, LenPem, Nivolpi, Pazoo, 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 Bett

✓ 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
t1	t2	sm	lowerci	upperci	study
LenPem	Suni	0.66	0.49	0.88	Motzer RJ et al (3)
CaboNivo	Suni	0.66	0.50	0.87	Motzer RJ et al (4)
PemAxi	Suni	0.66	0.55	0.85	Powles T et al
AteBev	Suni	0.93	0.76	1.14	Rini BI et al
AveAxi	Suni	0.89	0.62	1.03	Choueiri TK et al (2)
Nivolpi	Suni	0.69	0.59	0.81	Abigay L et al
Cabo	Suni	0.80	0.53	1.21	Choueiri TK et al (3)
Pazo	Suni	0.92	0.79	1.06	Motzer RJ et al (1)
Axi	Sora	1.00	0.73	1.36	Hutson TE et al
Tivo	Sora	1.25	0.95	1.62	Motzer RJ et al (2)
Suni	Sora	0.94	0.59	1.49	Tomita Y et al

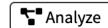
Outcome data

```
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

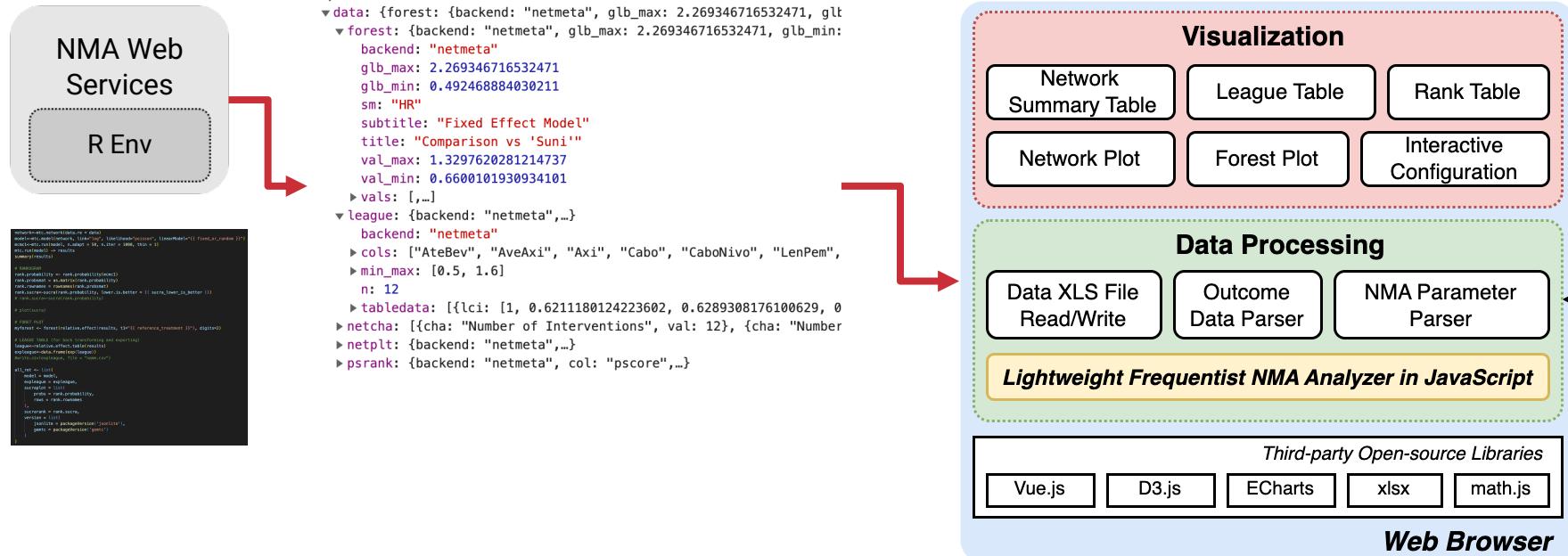
NMA Web Services

R Env



Demo - Convert NMA results to JSON

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



Demo - Data Visualization

NMA Analyzer

Dataset

Select Data File
Choose File: NMA-pre-smlu.xlsx

Input Data Summary
NMA-pre-smlu.xlsx
HRU format
12 treatments: 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 Comparison.: 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

LEAGUE TABLE

	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, 1.20)	1.33 (0.79, 2.27)	1.25 (0.98, 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)	1.15 (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, 2.78)	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)	1.03 (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 (0.69, 1.33)	0.96 (0.62, 0.98)	0.96 (0.52, 1.00)	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)	0.72 (0.52, 0.98)	0.72 (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)	0.97 (0.78, 1.33)	1.35 (1.04, 1.76)	0.64 (0.93, 2.63)	1.56 (1.18, 1.82)	1.47 (1.10, 3.45)	1.96 (1.10, 3.45)
Sora	0.87 (0.53, 1.45)	0.75 (0.44, 1.27)	0.99 (0.73, 1.36)	0.75 (0.40, 1.40)	0.62 (0.36, 1.06)	0.62 (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)	0.80 (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)	

Forest Plot

Comparison vs 'Suni'
Fixed Effect Model

Rank Table

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

P-Score Plot

Demo - Data Visualization



NMA Analyzer

DATASET

Select Data File
Choose File NMA-pre-smliu.xlsx
Upload & Read Data File

Input Data Summary
NMA-pre-smliu.xlsx
HRU format
g^P 12 studies, Suri, Sora, Cabe, Andleev, Ali,
Papadimitriou, Averill, Tien, Lempp, Novigli, Patti,
Calevitz
11 studies of 11 lines

SETTINGS

Input Format: HR, Lower, ✓
Analysis Method: Frequentist, ✓
Measure of Effect: Relative Ris, ✓
Ref. Treatment: Suri, ✓
Fixed / Random: Fixed Effect, ✓
Which is Better: Lower is Be, ✓

NETWORK CHARACTERISTICS

Elements Console Recorder Sources Network Performance Memory Security Application Lighthouse

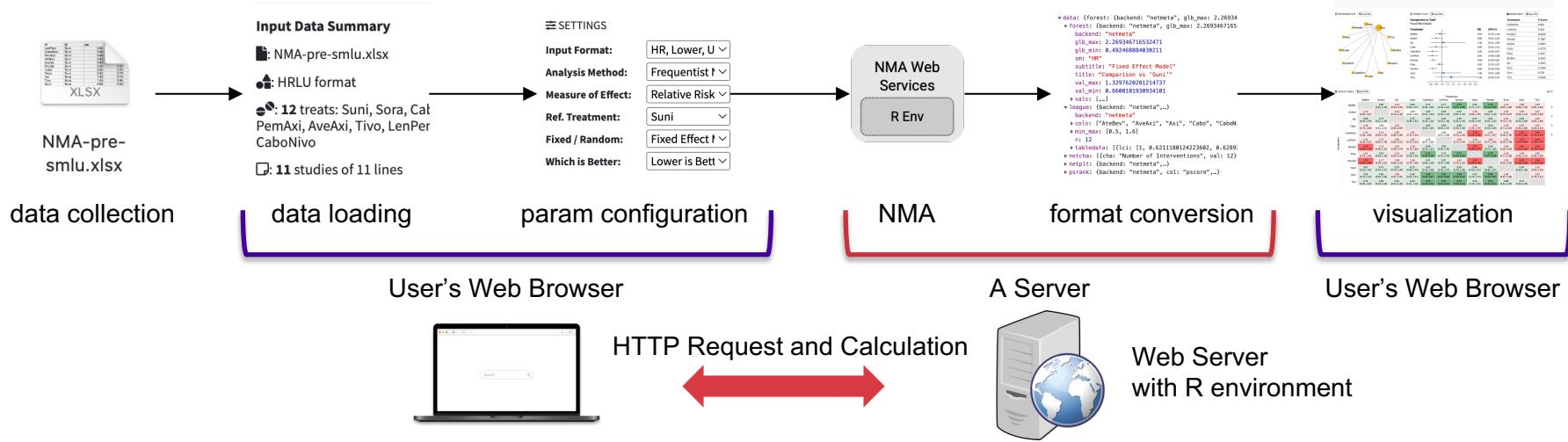
Preserve log Disable cache No throttling

FetchXHR JS CSS Img Media Font Doc WS Wasm Manifest Other Has blocked cookies Blocked Requests 3rd-party requests

5 ms 10 ms 15 ms 20 ms 25 ms 30 ms 35 ms 40 ms 45 ms 50 ms 55 ms 60 ms 65 ms 70 ms 75 ms 80 ms 85 ms 90 ms 95 ms 100 ms 105 ms 1

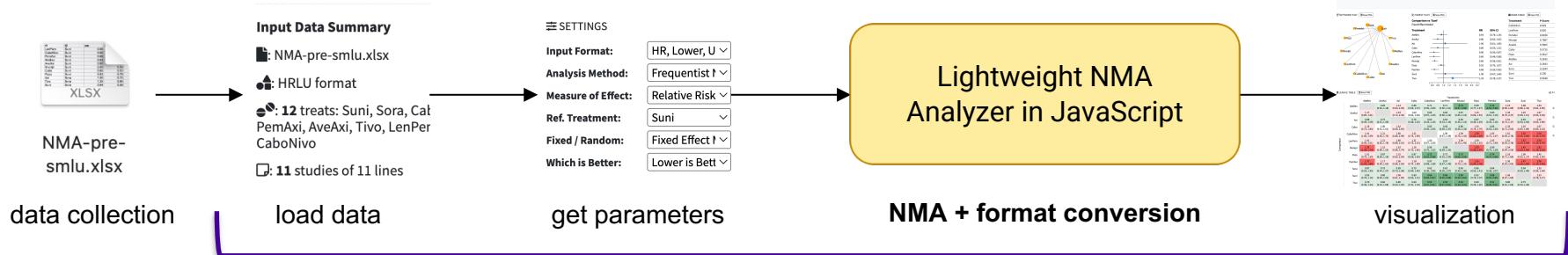
Recording network activity...
Perform a request or hit ⌘ R to record the reload.
[Learn more](#)

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

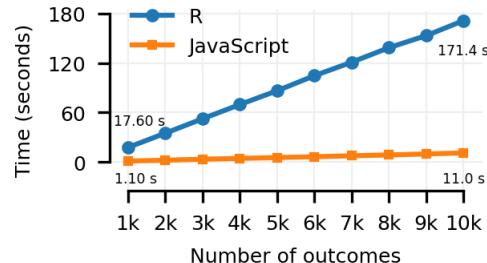
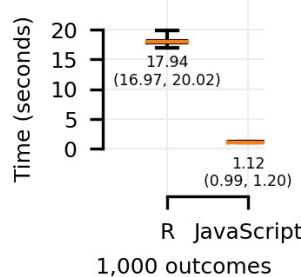


1. An always-on server is required
 2. Data must be sent out for calculation
 3. It takes a little while to get the results

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: Pre-calculated| SM, I

Analysis Engine: **Meta.js**

Frequentist NMA

Measure of Effect: Hazard Ratio

Fixed / Random: Fixed Effect Model

Which is Better: Lower 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

Demo - In-browser NMA takes less than 1s



Network Meta-analysis

[Load Sample Data](#) [Download Sample Data](#)

RCC-pre-smiu.xlsx
Load 11 Records

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

Records:
11

Input Format: Pre-calculated| SM, i ▾

Analysis Engine: Meta.js ▾

Analysis Method: Frequentist NMA ▾

Measure of Effect: Hazard Ratio ▾

Fixed / Random: Fixed Effect Model ▾

Which is Better: Lower 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

Elements Console Performance > 1 1

Recordings: (no recordings)

Screenshots Memory

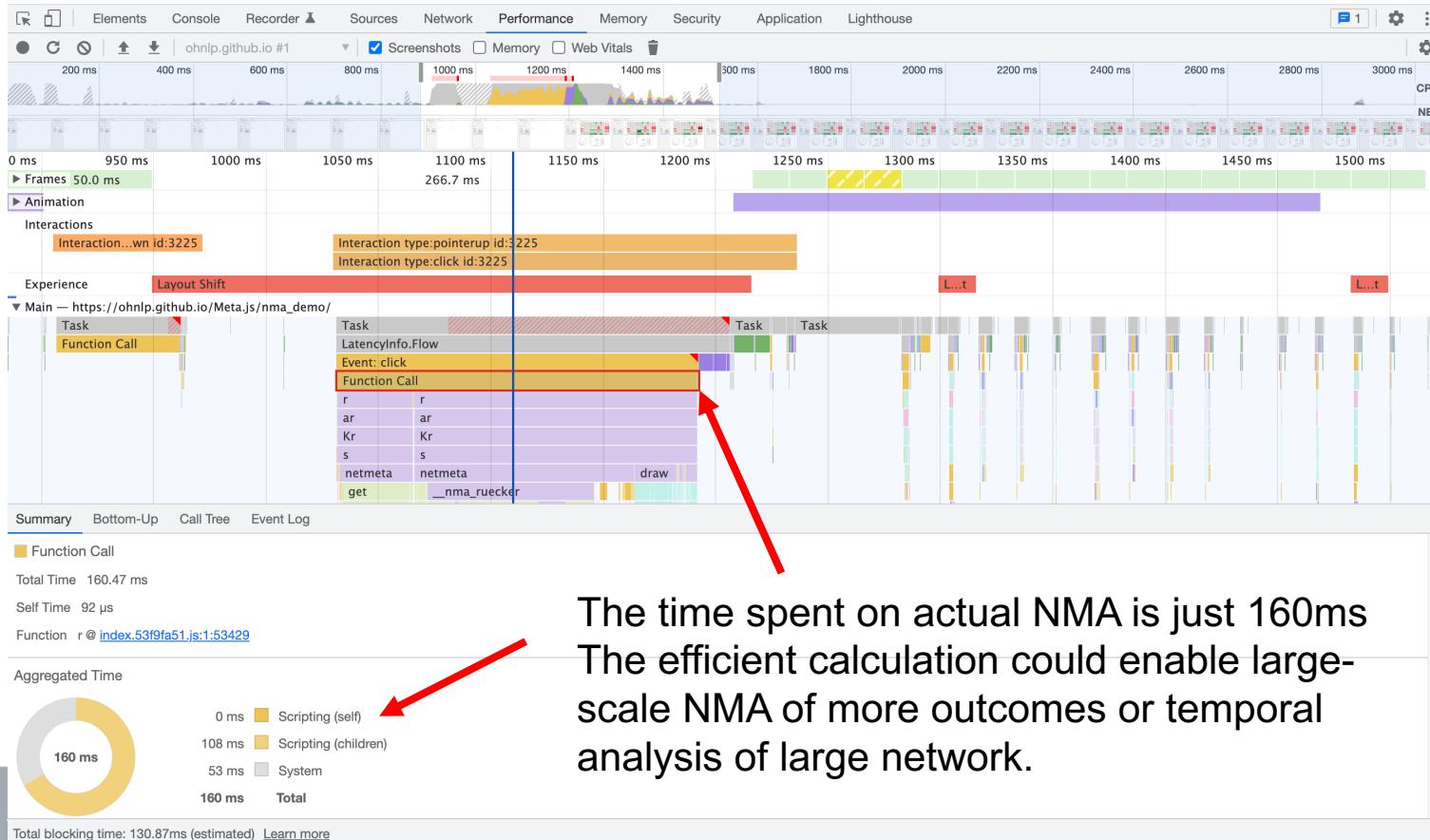
Web Vitals

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

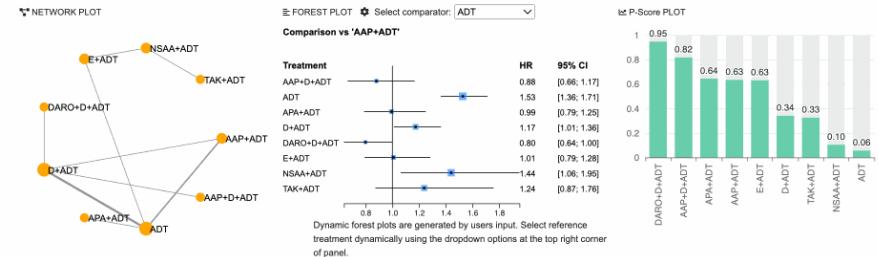
A Living Interactive Systematic Review and Network Meta-Analysis on First-Line Treatment Options in Metastatic Castration Sensitive Prostate Cancer

JAMA Oncology, PMID: [36862387](#)

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



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.



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