

Visual Exploration of Pairwise Meta-Analysis Results in Real Time

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Introduction

Cancer is a significant health problem. A comprehensive summary of the treatment plan's benefit and harm outcomes will not only help researchers improve drug development but also help clinicians make clinical decisions.

To summarize the findings and synthesize evidence, pairwise metaanalyses (PWMAs) are used to get precise estimates of treatment effects. However, presenting the PWMA results from many trials and across many patient-important outcomes can be challenging.

To address the challenges, we developed a web-based visual analytics system based on a customized JavaScript PWMA module to facilitate real-time exploration of massive PWMA results. Clinicians and researchers can analyze the PWMA results data for guideline development and clinical decision-making.

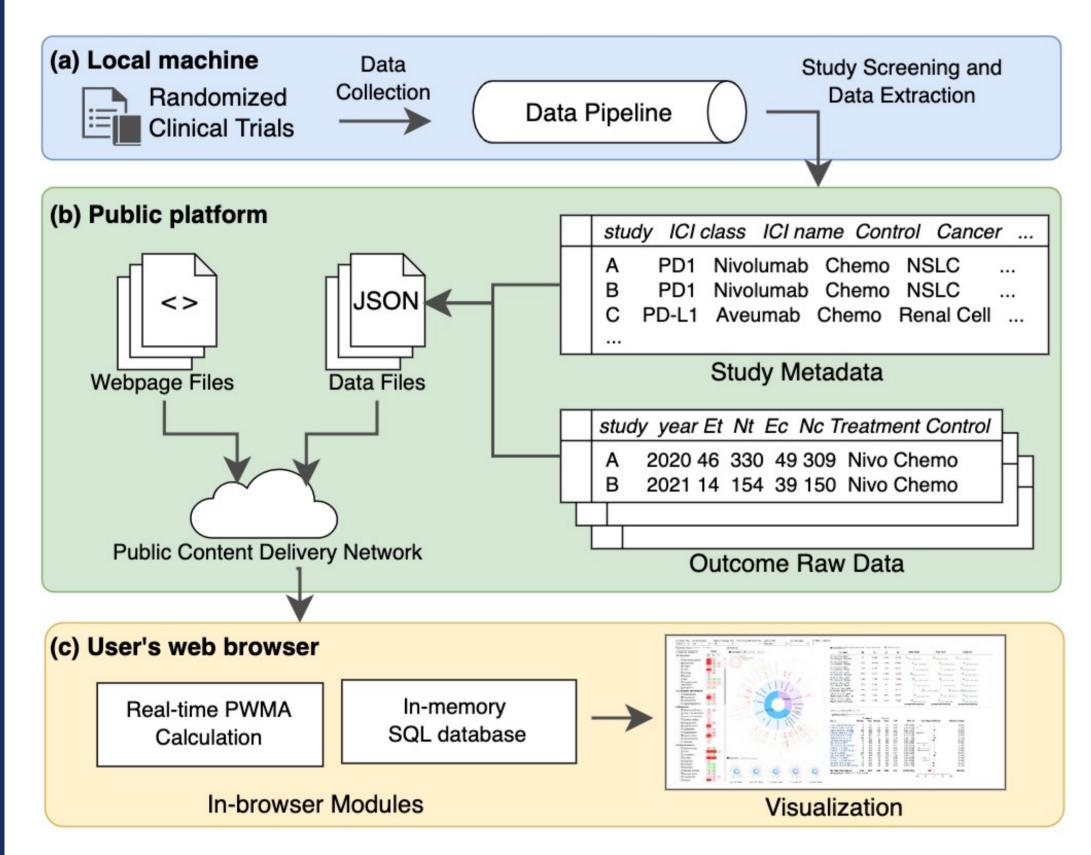
Visualization and Interactivity

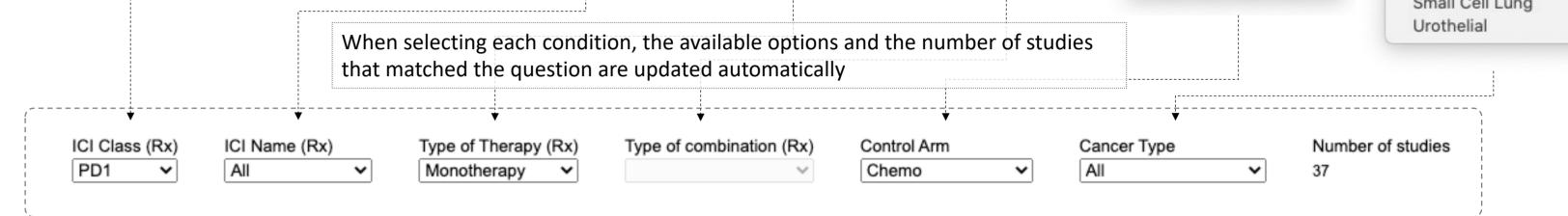
Clinical Question: What is the risk of *all-grade* rash, pruritus, nausea, and vomiting with **PD1** inhibitor **monotherapy** as compared to **chemotherapy** in patients with **cancer (type not specified)**?

Customize the analysis	ICI Class (Rx)	ICI Name (Rx)	Type of Therapy (Rx)	Type of combination (Rx)	Control Arm	Cancer Type
Customize the analysis scenario according to the clinical questions - PD1 inhibitor - Monotherapy - Compared with Chemotherapy	ICI Class (Rx)	ICI Name (Rx) ICI Name (Rx) All Atezolizumab Avelumab Cemiplimab Durvalumab Ipilimumab Nivolumab Pembrolizumab Tremelimumab	Type of Therapy (Rx)	Type of combination (Rx)	Control Arm All Chemo TKI Interferon Multikinase inhibitor mTOR inhibitor Radiation Vaccine Placebo Chemo/Anti-EGFR	Cancer Type All All Bladder Breast Colorectal Esophageal/GEJ Gastric/GEJ Hepatocellular Melanoma Mesothelioma Multiple Myeloma
- All cancers					Chemo+Anti-VEGF Chemo/TKI BRAFi+MEKi Best supportive care	Non-Small Cell Lung Pancreatic Prostate Renal cell
					Best supportive care	Renal cell Small Cell Lung

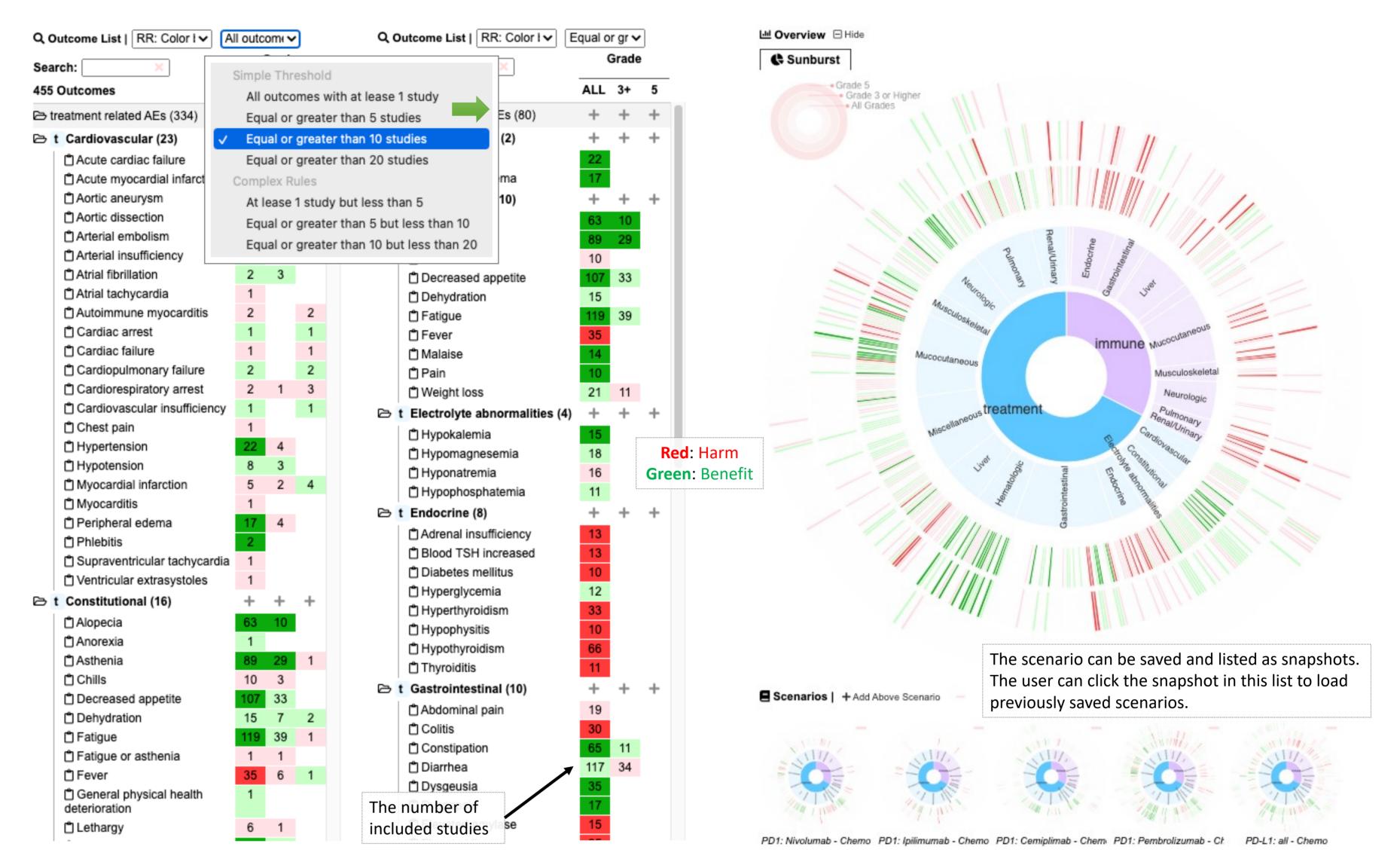
System Architecture

We applied a serverless architecture to design our system, which consists of three major components: a data pipeline that runs on a local machine, a public platform that hosts webpage and data files, and a visualization frontend that runs in the user's web browser:





Check the filtered available outcomes. The user can further specify the number to screen those outcomes with 2 more studies. The PWMA of these outcomes is processed in real-time and the results are visualized.

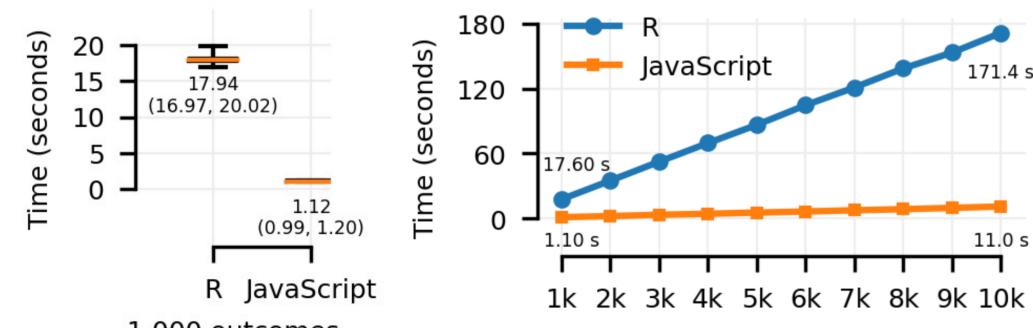


Real-time PWMA

To facilitate real-time exploration and reduce the time spent on computation and transmission, we developed **Meta.js**, a JavaScript PWMA module based on Math.js and implemented the commonly used PWMA indicators such as the DerSimonian-Laird estimator, the Cochran's Q, and the Higgins & Thompson's I2 statistic.

The source code and online demo of Meta.js are available at: https://github.com/OHNLP/Meta.js.

To evaluate the performance, we conducted two experiments: 1) Fixed effects of PWMA on randomly selected 1,000 outcomes; 2) Fixed effects of PWMA of a different number of outcomes. The results are as follows:



By selecting the outcome in the outcome list or the overview, the user can compare those selected outcomes in the comparison view and check the visualized PWMA results to address the clinical question.

G Category	Outcome	Grade	Treatment	Control	Cancer	Studies	Et	Nt	Ec	Nc	Odds Ratio	Risk Ratio	Incidence %	
t Mucocutaneous	Rash	ALL	PD1.ALL (MONO)	Chemo	ALL	33	1,018	9,167	621	9,057	= 2.15 (1.48; 3	.11) 2.05 (1.47; 2.86)	10.75 (9.51; 12.07)	-
Mucocutaneous	Pruritus	ALL	PD1.ALL (MONO)	Chemo	ALL	30	1,039	8,211	187	8,108	5 .59 (4.26	a; 7.32)	2) 12.66 (10.50; 14.98)	
Gastrointestinal	Vomiting	ALL	PD1.ALL (MONO)	Chemo	ALL	31	462	8,615	1,300	8,832	- 0.27 (0.20; 0.38)	.31 (0.22; 0.41)	4.79 (3.40; 6.38)	
Gastrointestinal	Nausea	ALL	PD1.ALL (MONO)	Chemo	ALL	35	1,072	9,748	3,165	9,797	0.23 (0.17; 0.31)	.30 (0.23; 0.40)	10.38 (7.66; 13.45)	
Constitutional	Alopecia	ALL	PD1.ALL (MONO)	Chemo	ALL	25	65	6,443	1,303	5,718	0.04 (0.02: 0.08)	0.05 (0.02; 0.10)	0.76 (0.37: 1.25)	c
Constitutional	Asthenia	ALL	PD1.ALL (MONO)	Chemo	ALL	30	593	8,669	1,070	8,911		of rash and pruritus asso		
	Addionia		FDT.ALL (MONO)	Chemo		00	000	0,000	.,	,	PD1 inhibitor	monotherapy when comp	pared to chemoth	nerap
Constitutional	Decreased appetite	ALL	PD1.ALL (MONO)	Chemo	ALL	37	970	10,055	1,909	10,042	Decreased ris	k of nausea and vomiting	with the use of P l	D1
Constitutional Constitutional											Decreased ris		with the use of P I d to chemotherap	D1 Dy.
	Decreased appetite	ALL	PD1.ALL (MONO)	Chemo	ALL	37	970	10,055	1,909	10,042 10,153	Decreased ris inhibitor mon	k of nausea and vomiting otherapy when compared	with the use of P I d to chemotherap	D1 Dy.
Constitutional Hematologic	Decreased appetite Fatigue	ALL	PD1.ALL (MONO) PD1.ALL (MONO)	Chemo Chemo	ALL ALL	37 38	970 1,593	10,055 10,291	1,909 2,377	10,042 10,153	Decreased ris inhibitor mon	k of nausea and vomiting otherapy when compared Based on evidence from >3	with the use of Pl d to chemotherap 0 trials with >15000	D1 Dy.
Constitutional Hematologic	Decreased appetite Fatigue Neutropenia	ALL ALL ALL	PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO)	Chemo Chemo Chemo	ALL ALL ALL	37 38 35	970 1,593 259	10,055 10,291 9,709	1,909 2,377 1,806	10,042 10,153 9,716	Decreased ris inhibitor mon	k of nausea and vomiting otherapy when compared Based on evidence from >3 0.04 (0.02; 0.08)	with the use of Pl d to chemotherap O trials with >15000 1.06 (0.23; 2.34)	D1 Dy.
Constitutional Hematologic Hematologic	Decreased appetite Fatigue Neutropenia Anemia	ALL ALL ALL ALL	PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO)	Chemo Chemo Chemo Chemo	ALL ALL ALL	37 38 35 38	970 1,593 259 683	10,055 10,291 9,709 10,291	1,909 2,377 1,806 2,946	10,042 10,153 9,716 10,153	Decreased ris inhibitor mon 0.03 (0.01; 0.07) 0.15 (0.10; 0.23)	k of nausea and vomiting otherapy when compared <i>Based on evidence from >3</i> 0.04 (0.02; 0.08) 0.20 (0.14; 0.30) 0.76 (0.63; 0.91)	with the use of Pl d to chemotherap 0 trials with >15000 1.06 (0.23; 2.34) 5.75 (3.91; 7.91)	D1 Dy.
Constitutional Hematologic Hematologic Gastrointestinal Gastrointestinal	Decreased appetite Fatigue Neutropenia Anemia Diarrhea	ALL ALL ALL ALL	PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO)	Chemo Chemo Chemo Chemo	ALL ALL ALL ALL	37 38 35 38 38	970 1,593 259 683 1,145	10,055 10,291 9,709 10,291 10,267	1,909 2,377 1,806 2,946 1,428	10,042 10,153 9,716 10,153 10,104	Decreased ris inhibitor mon 0.03 (0.01; 0.07) 0.15 (0.10; 0.23) 0.72 (0.58; 0.90)	k of nausea and vomiting otherapy when compared <i>Based on evidence from >3</i> 	with the use of Pl d to chemotherap 0 trials with >15000 1.06 (0.23; 2.34) 5.75 (3.91; 7.91) 10.99 (9.24; 12.87)	D1 Dy.
t Constitutional t Hematologic t Hematologic t Gastrointestinal	Decreased appetite Fatigue Neutropenia Anemia Diarrhea Colitis	ALL ALL ALL ALL ALL	PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO) PD1.ALL (MONO)	Chemo Chemo Chemo Chemo Chemo	ALL ALL ALL ALL ALL	37 38 35 38 38	970 1,593 259 683 1,145 67	10,055 10,291 9,709 10,291 10,267 3,322	1,909 2,377 1,806 2,946 1,428	10,042 10,153 9,716 10,153 10,104 3,193	Decreased ris inhibitor mon 0.03 (0.01; 0.07) 0.15 (0.10; 0.23) 0.72 (0.58; 0.90) 4.27 (2.32; 3.60 (1.56;	k of nausea and vomiting otherapy when compared <i>Based on evidence from >3</i> 	with the use of Pl d to chemotherap 0 trials with >15000 1.06 (0.23; 2.34) 5.75 (3.91; 7.91) 10.99 (9.24; 12.87) 1.97 (1.29; 2.77)	D1 Dy.

1,000 outcomes

Number of outcomes

Test machine: Intel Core i5-10400 and 16G RAM, running Ubuntu 20.04 LTS. Google Chrome is Version 99.0.4844.51 (Official 64-bit). The R environment is 3.6.3 with meta library 4.18-0 and RStudio 1.4.1106. In both R and JavaScript versions, the test dataset is pre-loaded to reduce I/O cost.

The results show significant performance improvements, which can enable users to check multiple effects (e.g., odds ratio, risk ratio, etc.) at the same time and compare the results between different cohorts, clinical scenarios, and treatment plans.

Future Work

As the next step, we will keep developing the PWMA module and the visual design for further exploration of large-scale PWMA results and apply the results in shared decision-making.

For each outcome, the user can check the detailed analysis information from each study (i.e., forest plot) to 4 validate the certainty of evidence and track the original source of each study.

Le Outcome Detail | Export CSV

I~ Forest Plot

3

	Tre	atment		Control				
Study	Events	Total	Events	Total	OR	95% CI	Odds Ratio (95% CI)	Relative weight
Antoni Ribas et al 2015	2	178	1	171	1.93	[0.17; 21.50]	+ •	6.42%
Antoni Ribas et al 2015 Comp	2 3	179	1	171	2.90	[0.30; 28.13]		- 7.22%
Martin Reck et al 2016	3	154	0	150	6.95	[0.36; 135.79]		4.22%
Joaquim Bellmunt et al 2017	6	266	1	255	5.86	[0.70; 49.03]		8.27%
Omid Hamid et al 2017	1	178	1	171	0.96	[0.06; 15.48]		4.83%
Omid Hamid et al 2017 Comp	2 5	179	1	171	4.89	[0.56; 42.25]	_	- 8.01%
Martin Reck et al 2019	6	154	0	150	13.18	[0.74; 235.98]		4.48%
Mok TSK et al 2019	7	636	2	615	3.41	[0.71; 16.48]	_	15.03%
Shitara K et al 2020	7	254	1	244	6.89	[0.84; 56.40]		8.44%
Shitara K et al 2020 Comp 2	9	250	1	244	9.07	[1.14; 72.18]	-	8.67%
Popat S et al 2020	2	72	0	70	5.00	[0.24; 106.03]		4.00%
Kojima T et al 2020	3	314	2	296	1.42	[0.24; 8.55]	_	11.56%
Andre T et al 2020	10	153	0	143	21.00	[1.22; 361.78]		4.60%
Sezer A et al 2021	3	355	0	342	6.80	[0.35; 132.17]		4.24%
Random effects model	67	3322	11	3193	4.27	[2.32; 7.87]		100.00%
Heterogeneity: I ² =0%, T ² =0.00	00, <i>p</i> =0.9	4						
							0.01 0.1 1 10	100

Advanced Save Email Send to Clinical Trial > Lancet Oncol. 2015 Aug;16(8):908-18. doi: 10.1016/S1470-2045(15)00083-2. FULL TI	Se
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chemotherapy for ipilimumab-refractory melanoma (KEYNOTE-002): a randomised, controlled, phase 2	IS
(KEYNOTE-002): a randomised, controlled, phase 2 trial "	Cite
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Forest Plot of the selected outcome

The study name is linked to the PubMed for details