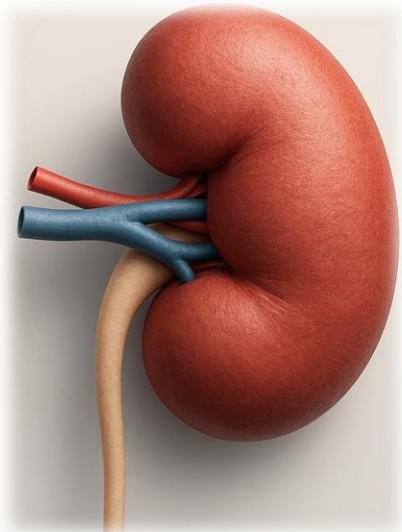


Comparing the efficacy of self-management interventions for chronic kidney disease

A systematic review and component network meta-analysis

Journal Club

16th January, 2026



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Research question



Population

Patients with CKD not receiving renal replacement therapies.



Intervention

Self-management interventions (SMIs).



Comparators

Usual care or other SMIs.



Study design

Systematic review and component network meta-analysis.

Outcomes



❖ Renal function

- eGFR

❖ Modifiable risk factors

- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Body mass index (BMI)

❖ Patient-reported outcomes

- Quality of life
- Self-management score
- Self-efficacy score

❖ Long-term clinical outcomes

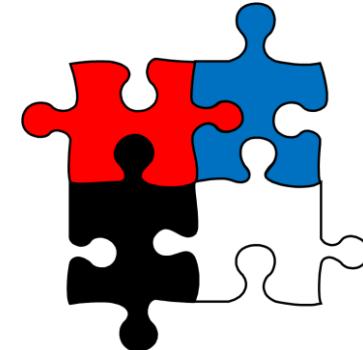
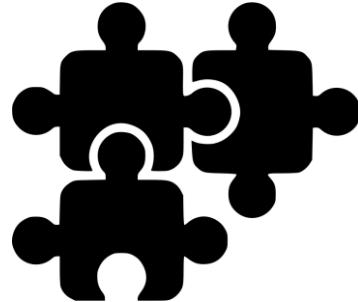
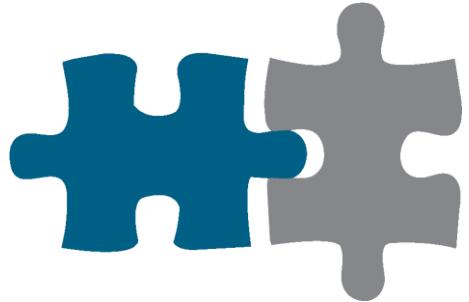
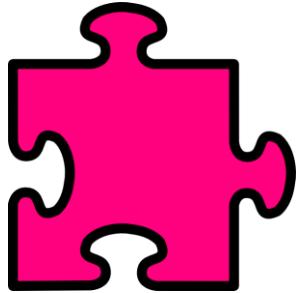
- Risk of death
- Risk of developing ESKD
- Risk of hospitalization
- Risk of initiating renal replacement therapies

Definition of components

SMI components	Definition*
Edu	<u>Education</u> : Providing information and/or skills related to the nature of the disease, CKD self-management behaviors (specifically action plan), and the positive and negative of not adopting health recommendation
Diet	<u>Dietary</u> : Apply the concept of cognitive-behavioral psychology to help patients build the skills necessary to adhere to the treatment and use techniques such as reminders, memory aids, synchronizing therapeutic activities with routine life events, goal-setting, self-monitoring, contracting, skill-building, and rewards to change their dietary behaviors.
PA	<u>Physical activity</u> : Apply the concept of cognitive-behavioral psychology to help patients build the skills necessary to adhere to the treatment and use techniques such as reminders, memory aids, synchronizing therapeutic activities with routine life events, goal-setting, self-monitoring, contracting, skill-building, and rewards to improve the level of physical activity.
Psycho	<u>Psychosocial</u> : Providing support to promote positive beliefs and attitudes toward the treatment such as rapport building through frequent telephone contact, home visits, family-based approaches, and intervention to enhance self-efficacy.

* The definition of SMI components was adapted from Dhippayom et al (2022) (10.1016/j.jaip.2021.09.049). A network meta-analysis of self-management interventions for asthma patients.

Possible SMIs



Mono-component SMIs

- Education (Edu)
- Dietary (Diet)
- Physical activity (PA)
- Psychosocial (Psycho)

Two-component SMIs

- Edu + Diet
- Edu + PA
- Edu + Psycho
- Diet + PA
- Diet + Psycho
- PA + Psycho

Three-component SMIs

- Edu + Diet + PA
- Edu + Diet + Psycho
- Edu + PA + Psycho
- Diet + PA + Psycho

Four-component SMIs

- Edu + Diet + PA + Psycho

15 self-management interventions

Why CNMA rather than SNMA?

Why CNMA rather than SNMA?

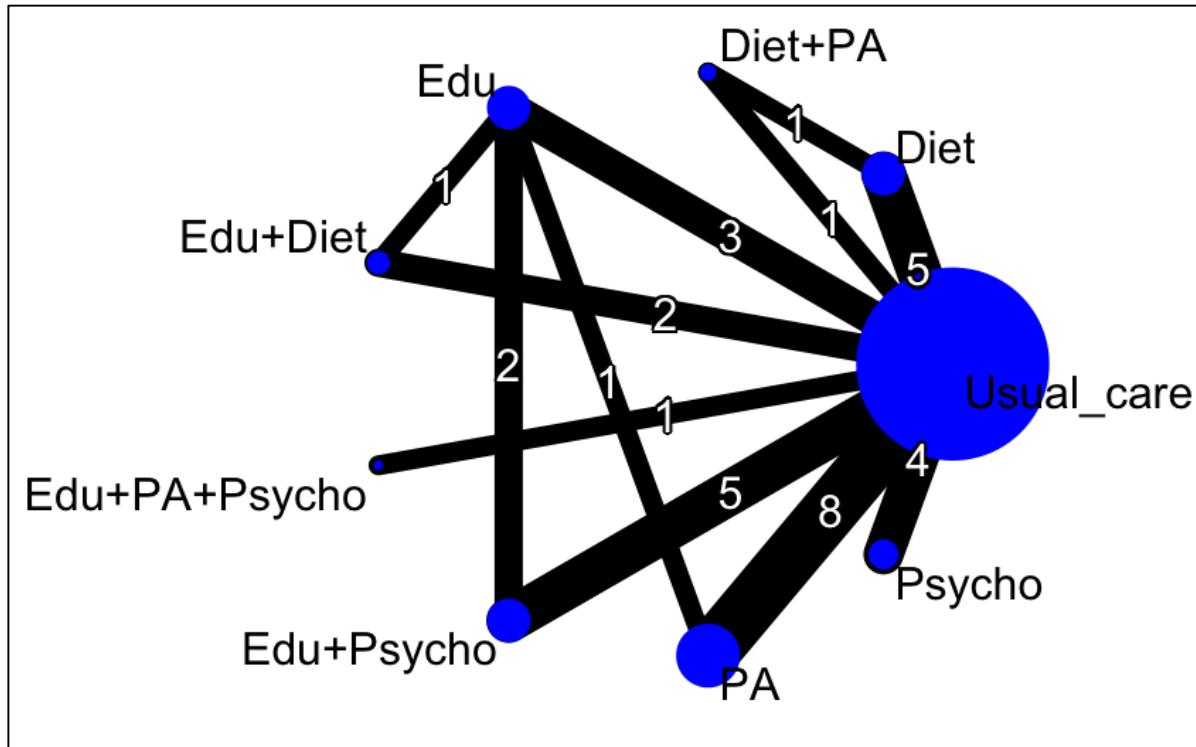


Figure: Network map for eGFR outcome

This network map:

- Sparse network.
- **8 interventions** + usual care.
- 12 direct comparisons.
- PA vs Usual care was the most common.

(Standard) network meta-analysis (SNMA)

Which type of intervention has the greatest probability of being most effective?

Why CNMA rather than SNMA?

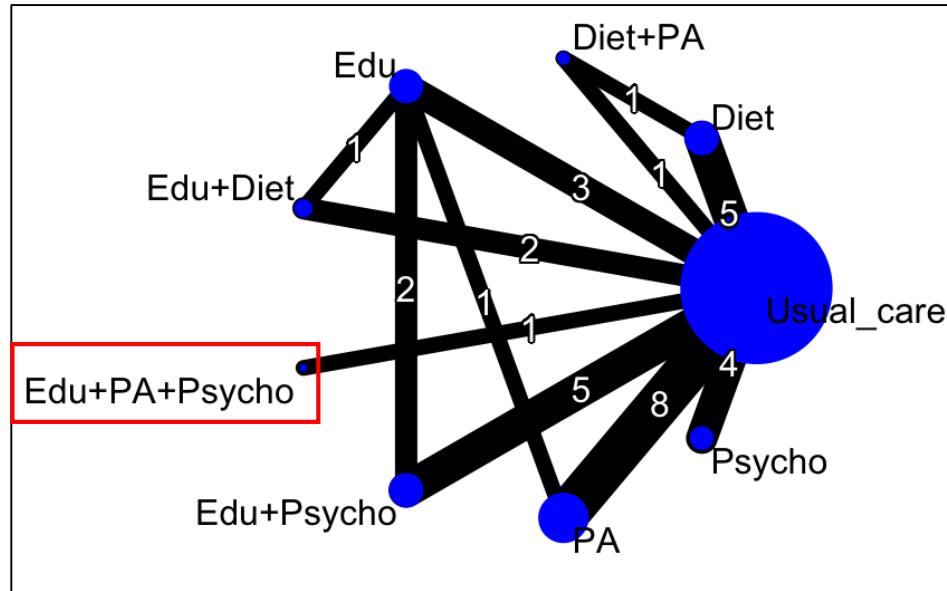


Figure: Network map for eGFR outcome

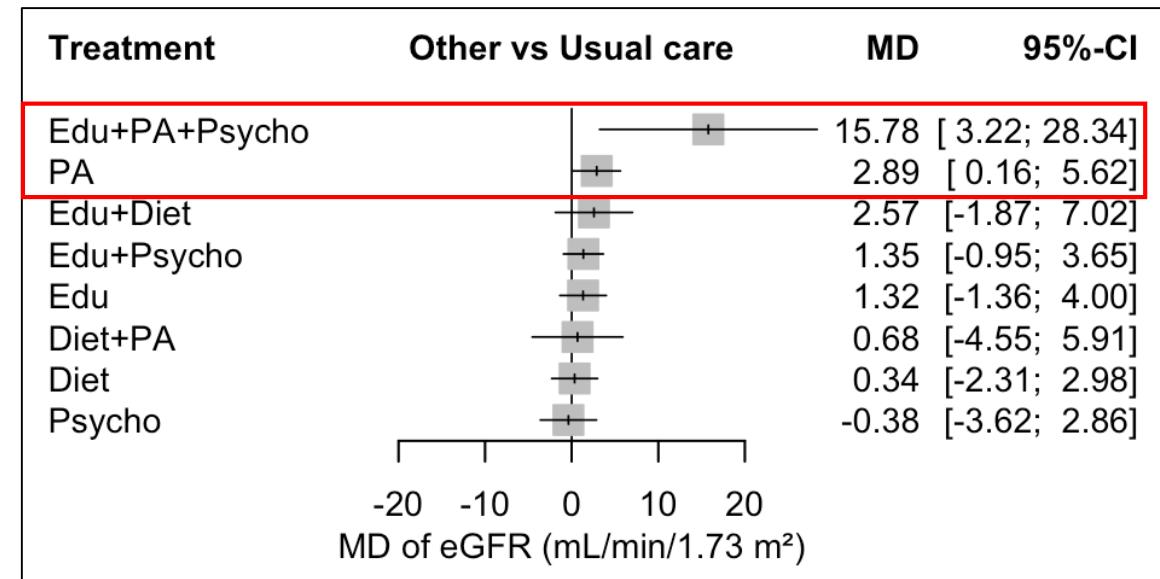


Figure: Forest plot for eGFR outcome (SNMA)

The results of SNMA showed:

- Only **Edu+PA+Psycho** and **PA** significantly improved eGFR compared to **Usual care**.
- Other interventions had no effect on eGFR.
- However, the treatment effect (TE) of **Edu+PA+Psycho** was based on only **one trial** with a very **high TE and wide CI**.

Difficult to interpret and explain the results (even after 2 – 3 team meetings)

Why CNMA rather than SNMA?

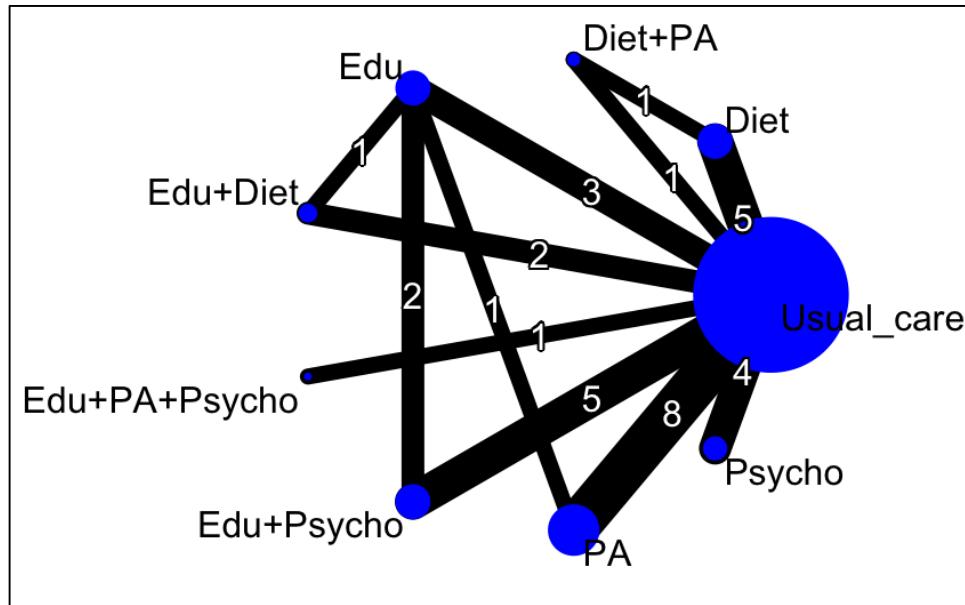


Figure: Network map for eGFR outcome

Component network meta-analysis

1. Which components work?
2. Does adding more components increase the treatment effect?

In addition, this network map also has:

- 8 interventions + usual care.

- 4 single interventions:

- Education (Edu)
 - Dietary (Diet)
 - Physical activity (PA)
 - Psychosocial (Psycho)

- 4 combination interventions:

- Edu+Diet
 - Diet+PA
 - Edu+Psycho
 - Edu+PA+Psycho

Complex,
multicomponent
interventions

They shared the **common components**.

Why CNMA rather than SNMA?

Issues	SNMA	CNMA
Sparse network	<ul style="list-style-type: none">- Each node is considered a unique intervention.- Results may reflect those of single studies in which the intervention's effect is very strong.	<ul style="list-style-type: none">- Unit of analysis: component.- Provides more precise estimates of intervention effects by using evidence from all studies that share the same components.
Unobserved combinations	<ul style="list-style-type: none">- Cannot estimate the TE of unobserved combinations.	<ul style="list-style-type: none">- Can estimate the TE of unobserved combinations.
→ CNMA is a suitable analytical approach for complex interventions such as SMIs.		

How was the data analysis done in R?
(eGFR outcome)

Model and assumption

- **Model used:** Additive model
- **Assumption:** $d_{SMI \text{ (combination)}} = d_{\text{component 1}} + d_{\text{component 2}} (+ \dots + d_{\text{component 4}})$

Components	Treatment effect
Edu	d_{Edu}
Diet	d_{Diet}
PA	d_{PA}
Psycho	d_{Psycho}

Combinations	Treatment effect
Edu+Diet	$= d_{Edu} + d_{Diet}$
Edu+PA	$= d_{Edu} + d_{PA}$
Edu+Psycho	$= d_{Edu} + d_{Psycho}$
Diet+PA	$= d_{Diet} + d_{PA}$
Diet+Psycho	$= d_{Diet} + d_{Psycho}$
PA+Psycho	$= d_{PA} + d_{Psycho}$
Edu+Diet+PA	$= d_{Edu} + d_{Diet} + d_{PA}$
Edu+Diet+Psycho	$= d_{Edu} + d_{Diet} + d_{Psycho}$
Diet+PA+Psycho	$= d_{Diet} + d_{PA} + d_{Psycho}$
Edu+PA+Psycho	$= d_{Edu} + d_{PA} + d_{Psycho}$
Edu+Diet+PA+Psycho	$= d_{Edu} + d_{Diet} + d_{PA} + d_{Psycho}$

d: Treatment effect

Prepare data

- Data can be prepared in long or wide format:
 - **Long format:** One row = one intervention (one study \geq two rows).
 - Wide format: One row = one study.

study_id	author	year	intervention	n	end_mean	end_sd	mean change	sd change
SMI_039	Hotu	2010	Edu+Psycho	30	33	17	-3	11.47
SMI_039	Hotu	2010	Edu	32	41	18	2	11.92
SMI_018	Chen	2011	Edu+Diet	27	29.11	20.61	1.98	13.65
SMI_018	Chen	2011	Usual_care	27	15.7	10.67	-7.93	8.68
SMI_085	Zuilen	2011	Psycho	395	36.2	16.4	-2.2	11.23
SMI_085	Zuilen	2011	Usual_care	393	35	16.2	-2.7	10.87
SMI_066	Paes-Barreto	2013	Edu+Diet	56	33.7	15.6	1.7	10.43
SMI_066	Paes-Barreto	2013	Usual_care	56	34.1	13.5	0	9.07
SMI_075	Haan	2013	Psycho	99	48.6	8.7	-0.5	5.92
SMI_075	Haan	2013	Usual_care	76	49.4	8	-0.6	5.34
SMI_008	Baria	2014	PA	19	30.16	10.44	2.65	7.25
SMI_008	Baria	2014	Usual_care	10	25.9	14.4	-1.8	10.41
SMI_005	Aoike_2	2015	PA	14	31.9	13.7	3.5	9.16
SMI_005	Aoike_2	2015	Usual_care	14	23.9	12.2	-1.4	9.12
SMI_084	Van Craenenbroeck	2015	PA	25	38.6	14.2	0.74	5.11
SMI_084	Van Craenenbroeck	2015	Usual_care	23	39.2	15.2	-0.33	4.16
SMI_053	Leehey	2016	Diet+PA	18	39.6	19.9	-1.9	13.72
SMI_053	Leehey	2016	Diet	18	35.8	20.2	-3.1	14.32

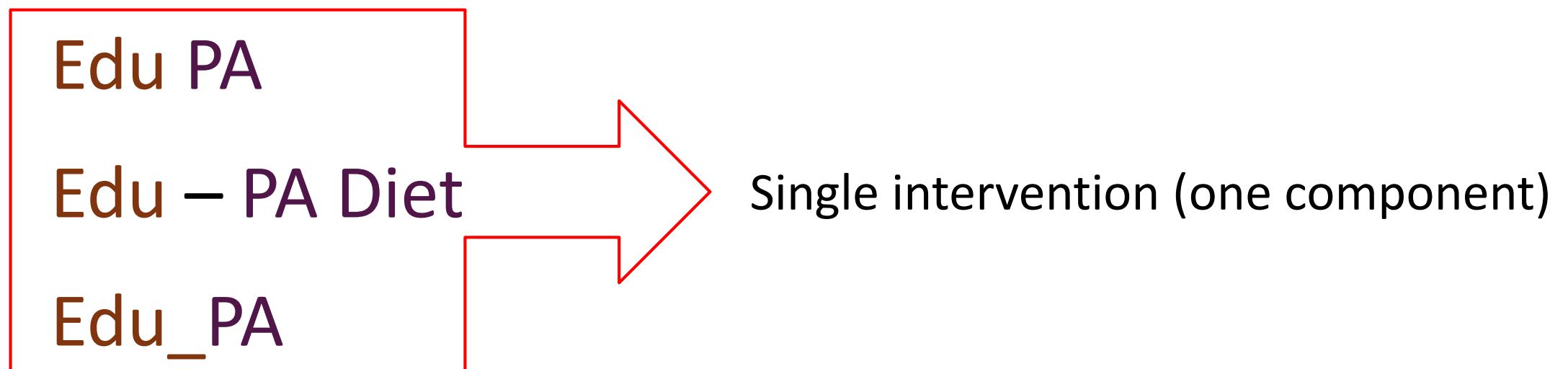
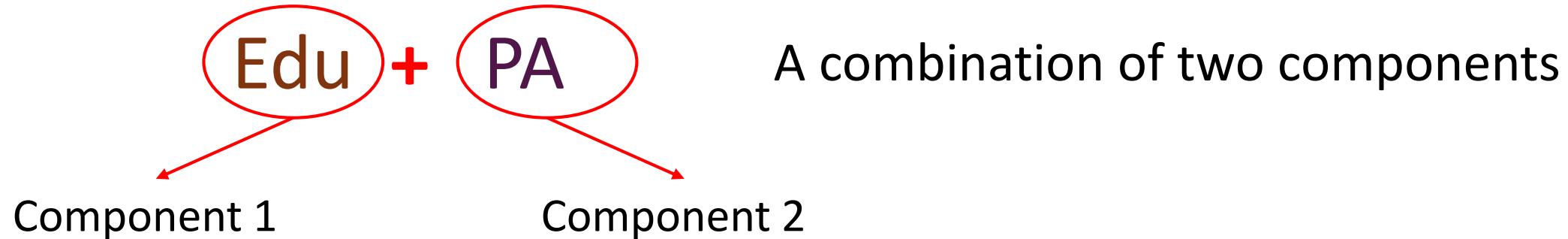
Require information:

- Study ID/author, year
- Intervention/treatment name
- n
- Mean
- SD

Data can be imported into RStudio from various formats, including Excel, Stata, SAS, SPSS, and text.

Prepare data

Make sure that the components within an intervention are connected by “+”!



Packages required

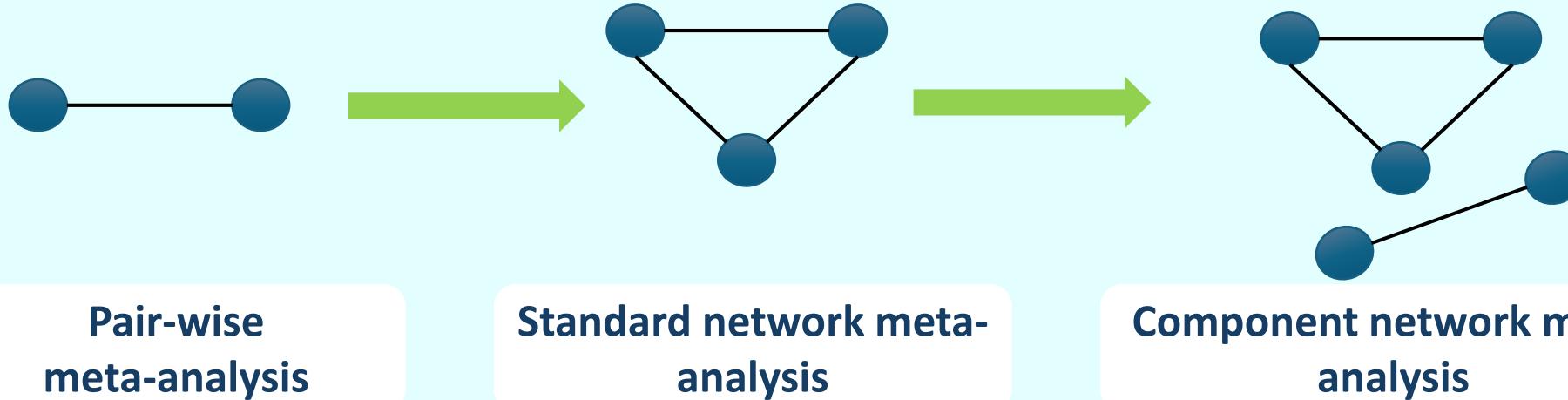
- For the **import dataset**:
 - `haven` (for Stata, SPSS, SAS files)
 - `readxl` (for Excel files)
- For **data analysis**:
 - `meta` (draw forest plots from NMA)
 - `netmeta` (for CNMA)
- For **data visualization**:
 - `ggplot2`
 - `grid`
- **Others**: `dplyr` (data manipulation), `stringr`.

Steps of analysis



Version: 2025.09.2+418

netmeta



Steps of analysis

1. Pair-wise meta-analysis

```
pw_eGFR <- pairwise(studlab = study_id, treat = intervention, n =  
n, mean = end_mean, sd = end_sd, data = SMIs_for_CKD_eGFR_End, sm =  
"MD", common = FALSE)
```

=> Prepare data for SNMA.

2. Standard network meta-analysis

```
netSMI_eGFR <- netmeta(pw_eGFR, ref = "Usual_care", common = FALSE)
```

Steps of analysis

2. Standard network meta-analysis

```
Treatment estimate (sm = 'MD', comparison: other treatments vs 'Usual_care'):  
MD      95%-CI      z p-value  
Diet    0.3376 [-2.3056; 2.9808] 0.25 0.8023  
Diet+PA 0.6766 [-4.5522; 5.9054] 0.25 0.7998  
Edu     1.3164 [-1.3632; 3.9960] 0.96 0.3356  
Edu+Diet 2.5730 [-1.8709; 7.0168] 1.13 0.2565  
Edu+PA+Psycho 15.7800 [ 3.2202; 28.3398] 2.46 0.0138  
Edu+Psycho 1.3499 [-0.9519; 3.6517] 1.15 0.2504  
PA      2.8916 [ 0.1600; 5.6233] 2.07 0.0380  
Psycho  -0.3766 [-3.6154; 2.8623] -0.23 0.8197  
Usual_care .          .          .          .
```

Quantifying heterogeneity / inconsistency:

$\tau^2 = 4.9121$; $\tau = 2.2163$; $I^2 = 52.8\% [26.2\%; 69.8\%]$

Tests of heterogeneity (within designs) and inconsistency (between designs):

Q d.f. p-value

Total 52.98 25 0.0009

Within designs 40.14 19 0.0031

Between designs 12.84 6 0.0457

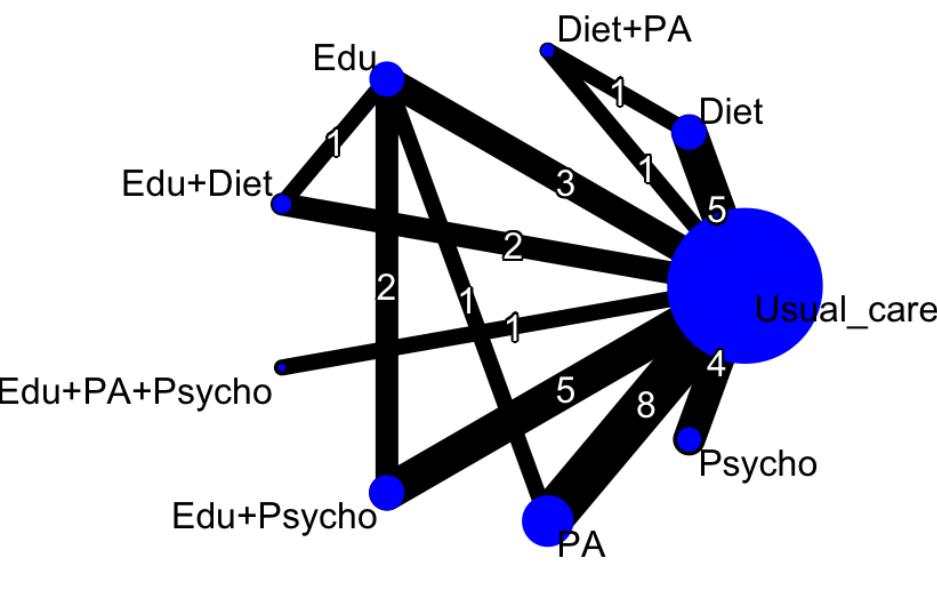


Figure: Network map for eGFR outcome

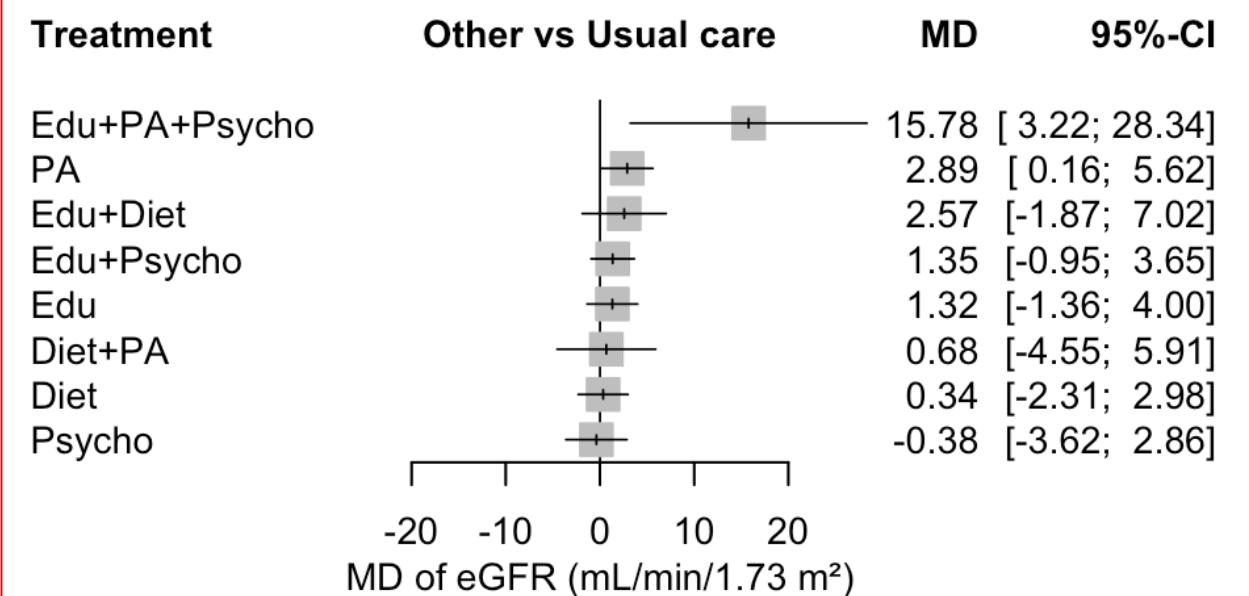


Figure: Forest plot for eGFR outcome (SNMA)

Steps of analysis

3. Component network meta-analysis

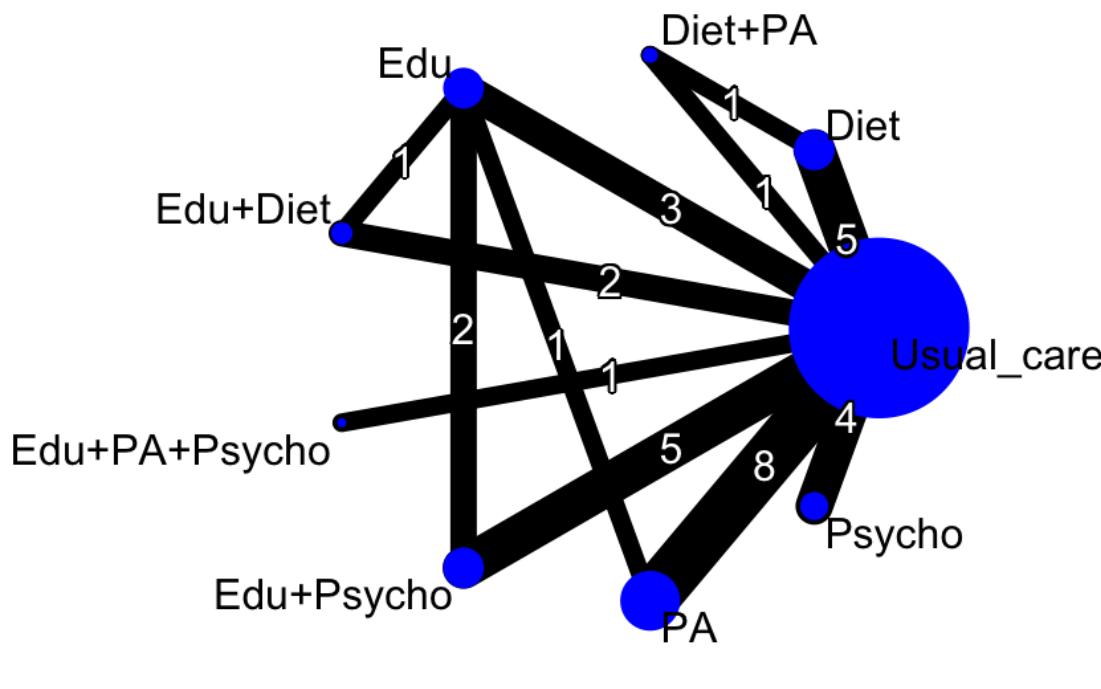


Figure: Network map for eGFR outcome

- Connected network => netcomb

```
cnma_eGFR <- netcomb(netSMI_eGFR, inactive =  
"Usual_care", component = TRUE, add=FALSE)
```

Incremental effect for existing combinations:

	iMD	95%-CI	z	p-value
Diet+PA	2.9919	[0.1424; 5.8414]	2.06	0.0396
Edu+Diet	1.8422	[-0.9229; 4.6073]	1.31	0.1916
Edu+PA+Psycho	4.4365	[1.2748; 7.5982]	2.75	0.0060
Edu+Psycho	1.6308	[-0.3732; 3.6348]	1.59	0.1107

Incremental effect for components:

	iMD	95%-CI	z	p-value
Diet	0.1862	[-1.9064; 2.2788]	0.17	0.8616
Edu	1.6560	[-0.5288; 3.8408]	1.49	0.1374
PA	2.8057	[0.4608; 5.1506]	2.35	0.0190
Psycho	-0.0252	[-2.1351; 2.0847]	-0.02	0.9813

Quantifying heterogeneity / inconsistency:

$\tau^2 = 4.3121$; $\tau = 2.0766$; $I^2 = 51.9\% [26.9\%; 68.3\%]$

Heterogeneity statistics:

	Q	df	p-value
Additive model	60.27	29	0.0006
Standard model	52.98	25	0.0009
Difference	7.29	4	0.1214

Steps of analysis

3. Component network meta-analysis

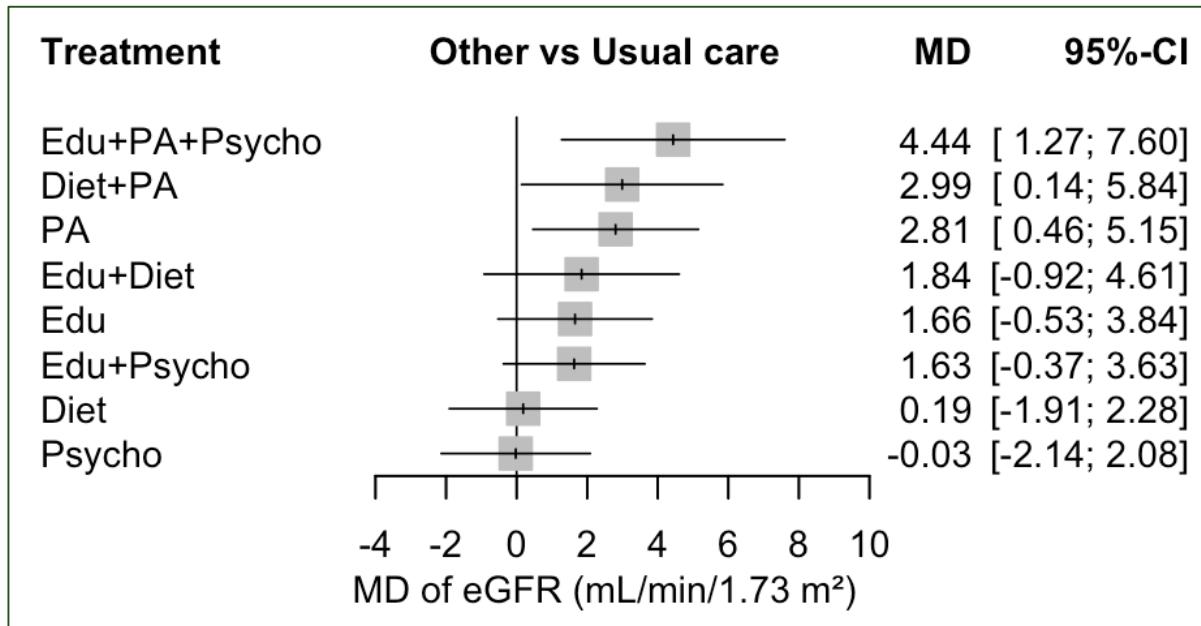


Figure: Forest plot for eGFR outcome (CNMA)

Results of **observed** monocomponents and combinations (8 out of 15 interventions).

3. Component network meta-analysis

Interventions	Observed from trials?
Edu	✓
Diet	✓
PA	✓
Psycho	✓
Edu+Diet	✓
Edu+PA	✗
Edu+Psycho	✓
Diet+PA	✓
Diet+Psycho	✗
PA+Psycho	✗
Edu+Diet+PA	✗
Edu+Diet+Psycho	✗
Diet+PA+Psycho	✗
Edu+PA+Psycho	✓
Edu+Diet+PA+Psycho	✗

Identify unobserved combinations

```
unobserved_comb_name <- c("Diet+Psycho",  
"Edu+PA", "PA+Psycho", "Edu+Diet+PA",  
"Edu+Diet+Psycho", "Diet+PA+Psycho",  
"Edu+Diet+PA+Psycho")
```

Estimate TEs of unobserved combinations

```
cnma_unobserved_eGFRend <-  
netcomplex(cnma_eGFR, unobserved_comb_name)
```

Combine the results of observed and unobserved interventions.

Steps of analysis

3. Component network meta-analysis

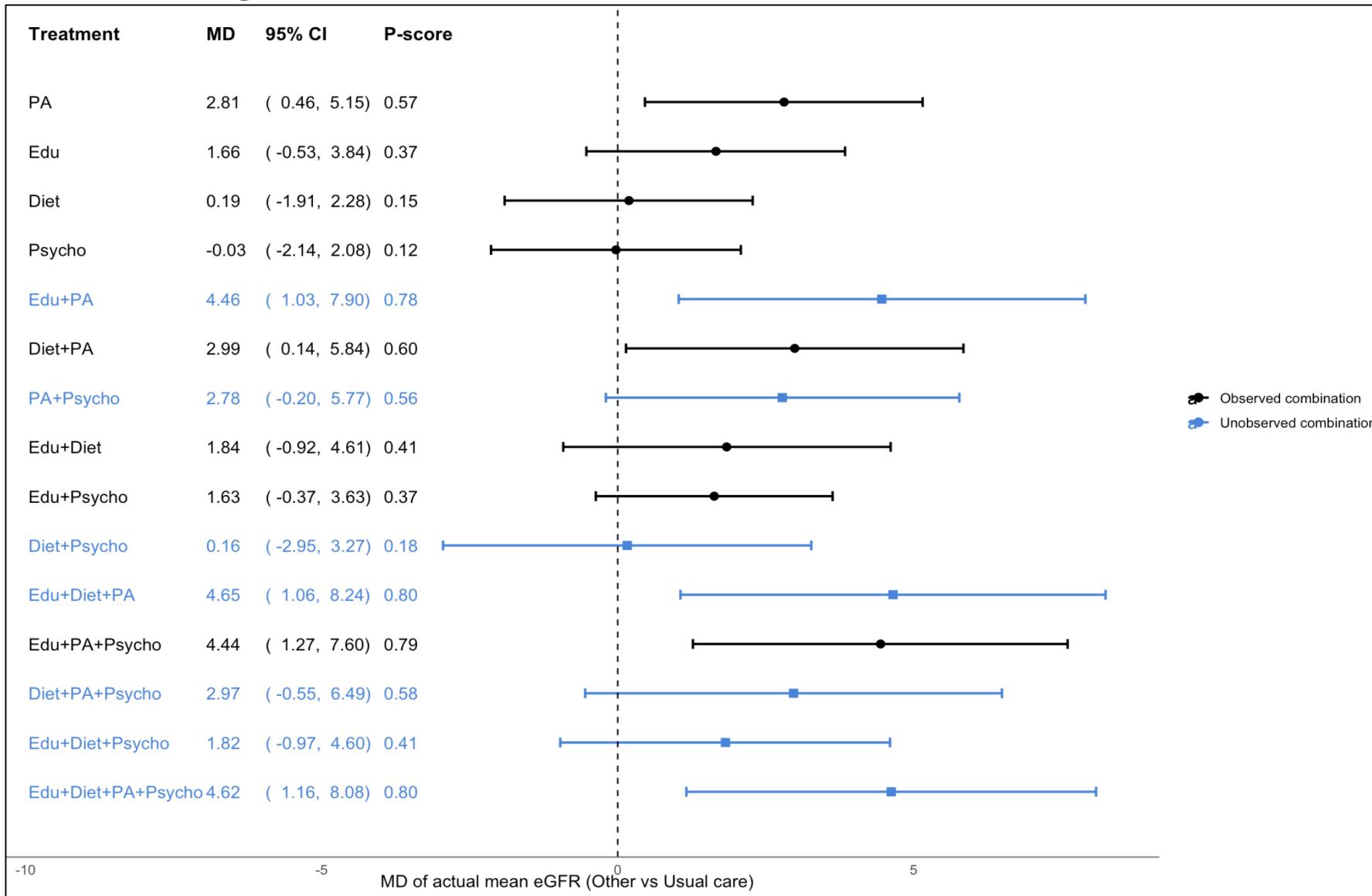


Figure: Forest plot of all interventions for eGFR outcome (CNMA)

How to interpret the results?

Interpret the results

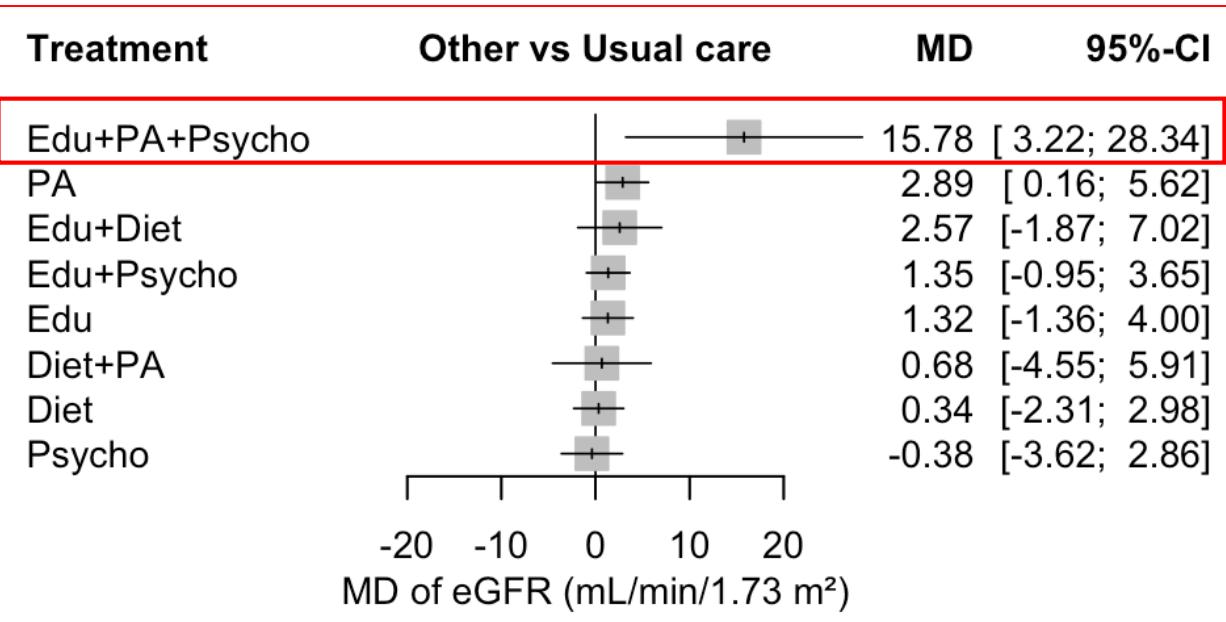


Figure: Forest plot for eGFR outcome (SNMA)

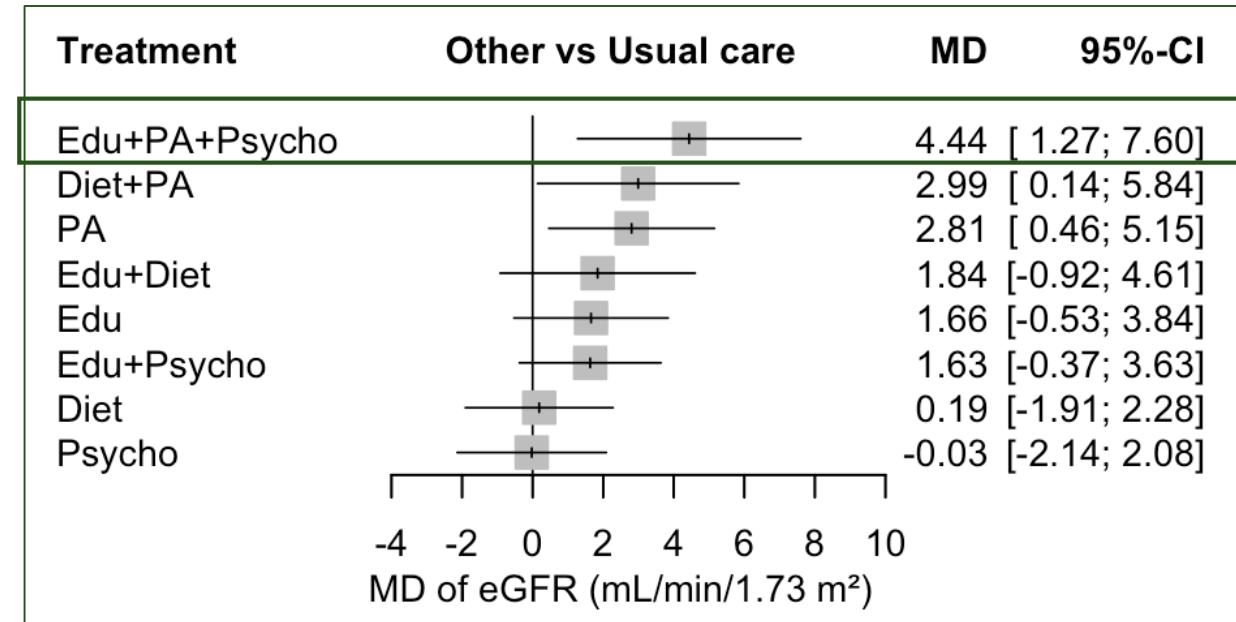


Figure: Forest plot for eGFR outcome (CNMA)

- TE of Edu+PA+Psycho **reduced** from 15.78 (SNMA) to 4.44 (CNMA) with a **narrower 95% CI** (1.27; 7.60).
- The CIs from CNMA were narrower than those from SNMA.
- In addition to Edu+PA+Psycho and PA, CNMA showed that Diet+PA significantly improved eGFR compared with Usual care.

→ CNMA provided **more precise and explainable** results

Interpret the results

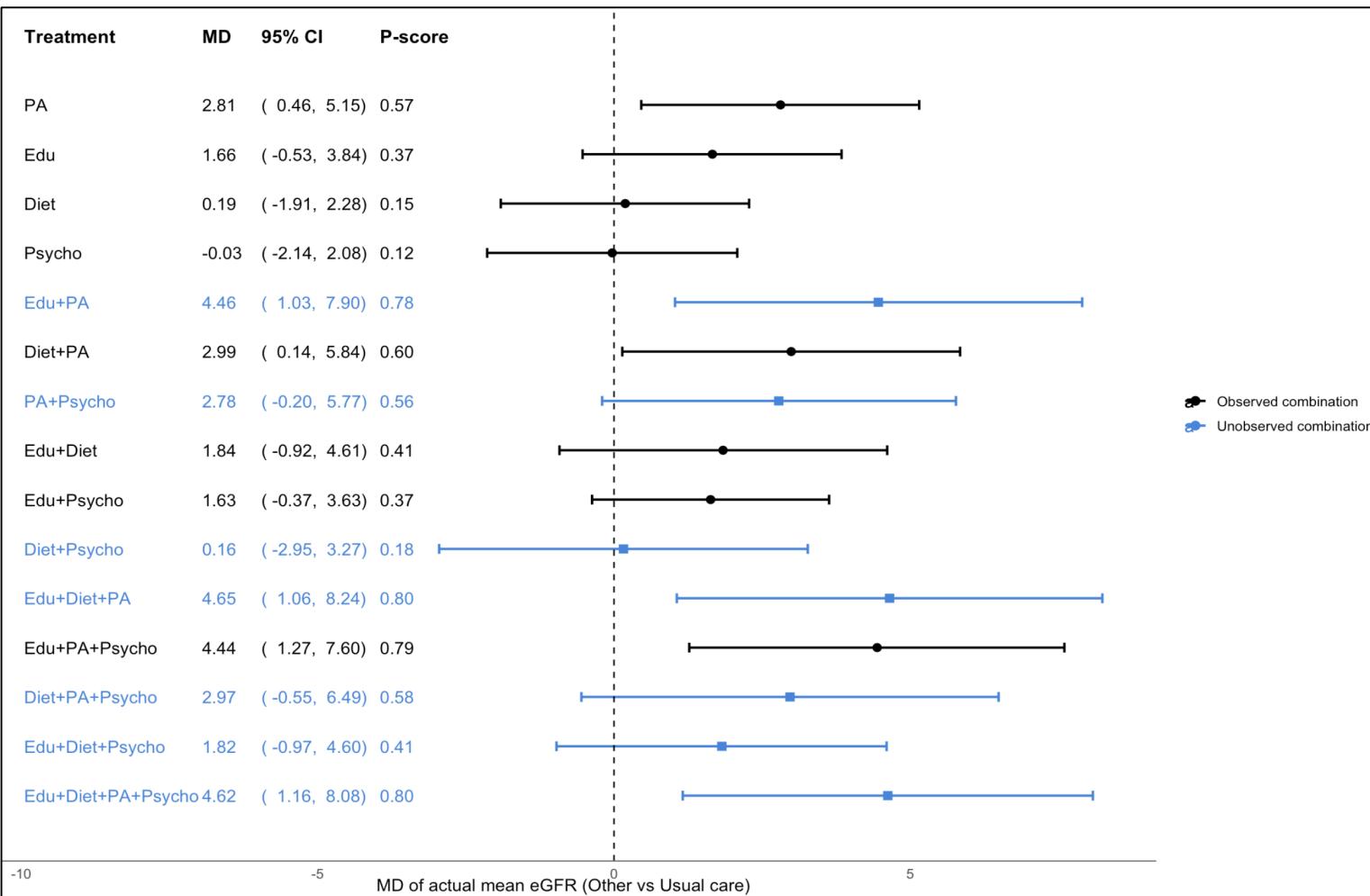


Figure: Forest plot of all SMIs for eGFR outcome (CNMA)

- PA was the only mono-component SMI that significantly improved eGFR.
- Among two-component SMIs:
 - Adding Edu and Diet to PA increased the TE compared with Edu+PA alone.
- Among three-component SMIs:
 - Adding Diet to Edu+PA also increased the TE compared with Edu+PA alone.
 - Adding Psycho to Edu+PA and Edu+Diet+PA did not yield any additional effect.

Additional outcomes

Systolic blood pressure (SBP)

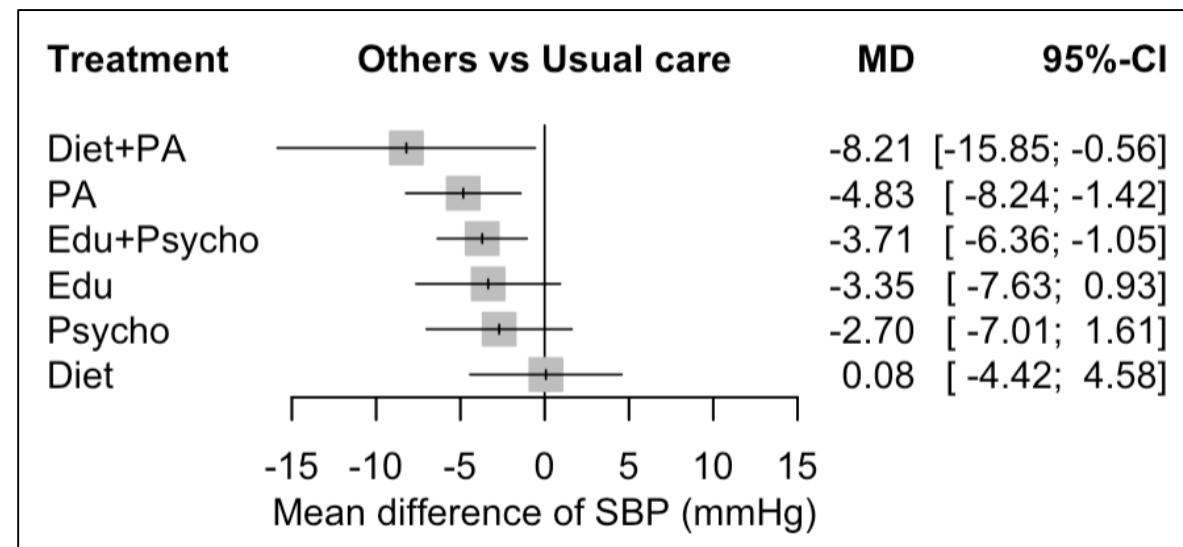
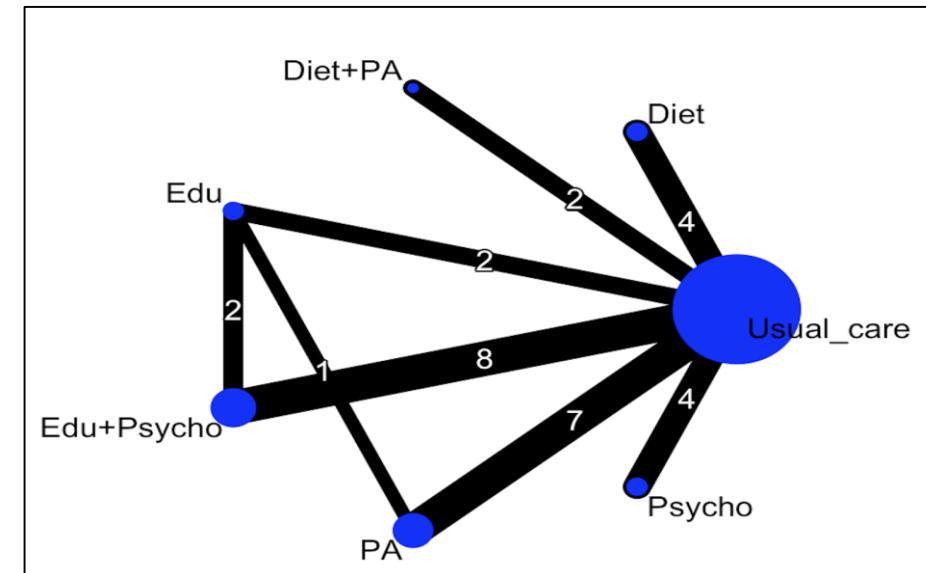


Figure: Forest plot for SBP outcome (SNMA)

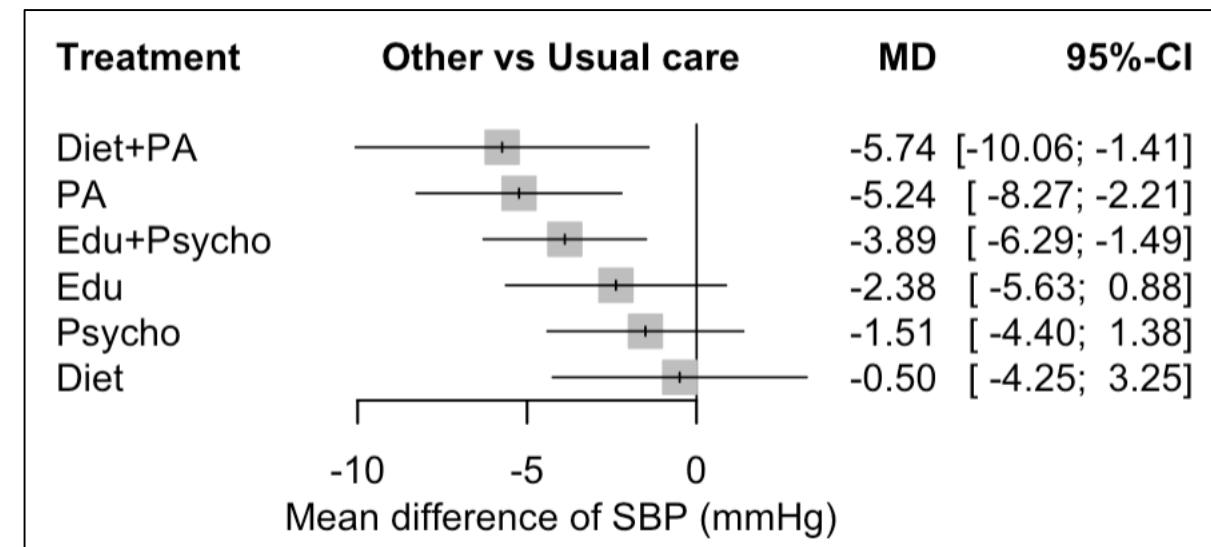


Figure: Forest plot for SBP outcome (CNMA)

Systolic blood pressure (SBP)

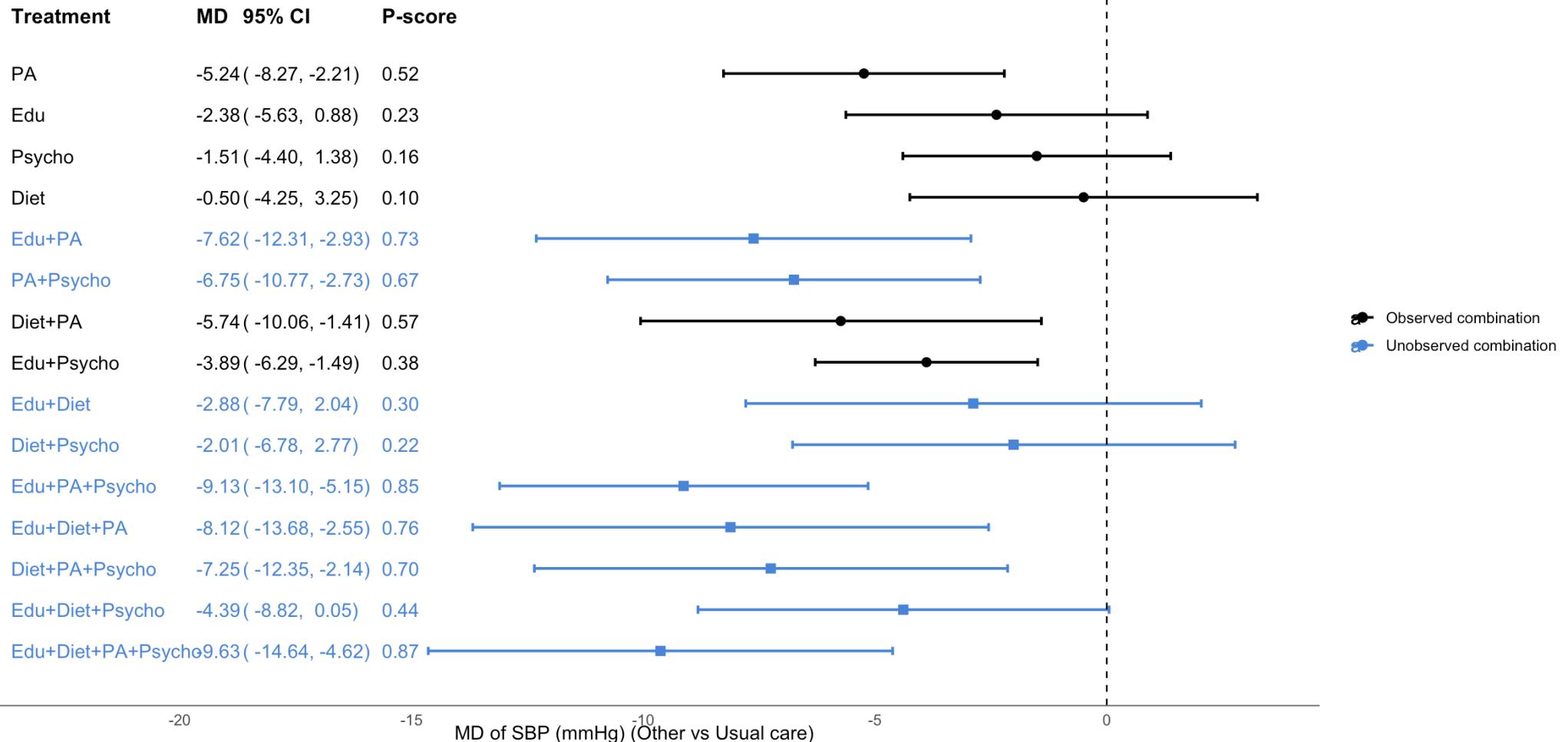


Figure: Forest plot of all SMIs for SBP outcome (CNMA)

Diastolic blood pressure (DBP)

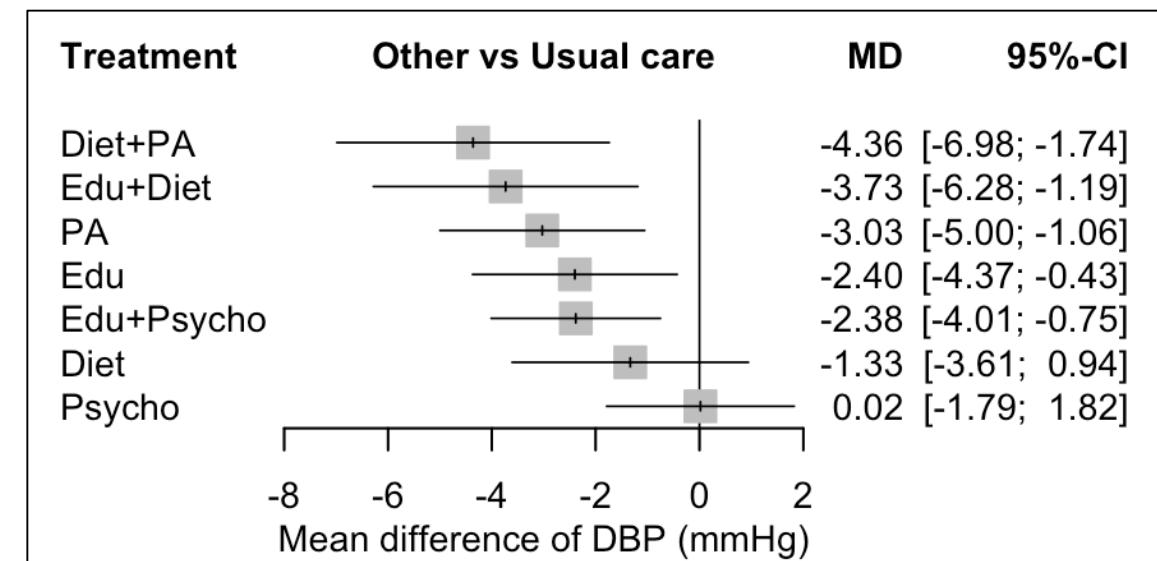
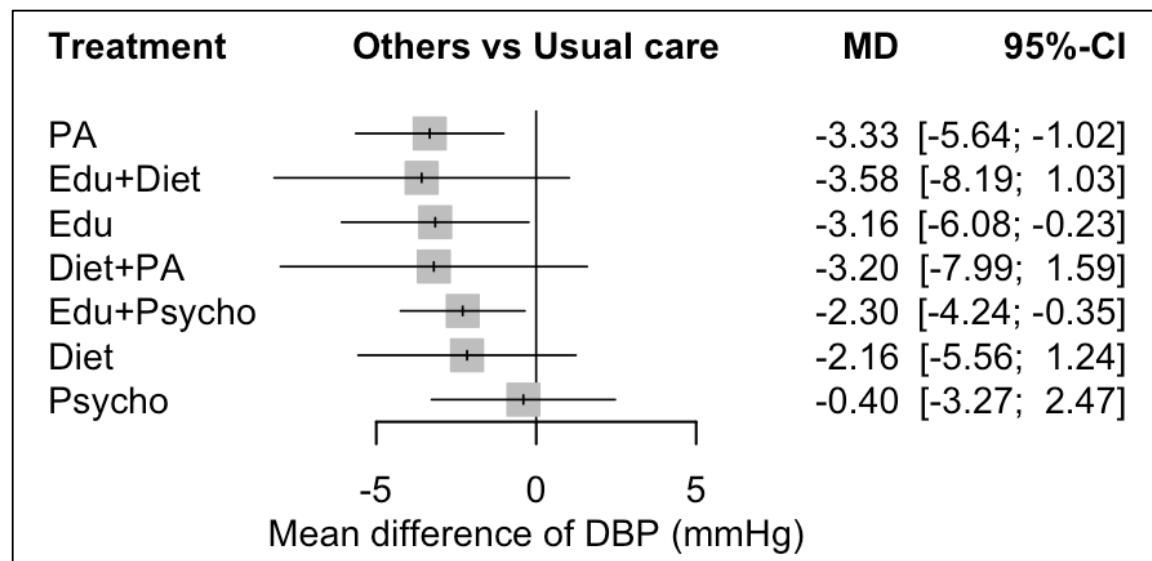
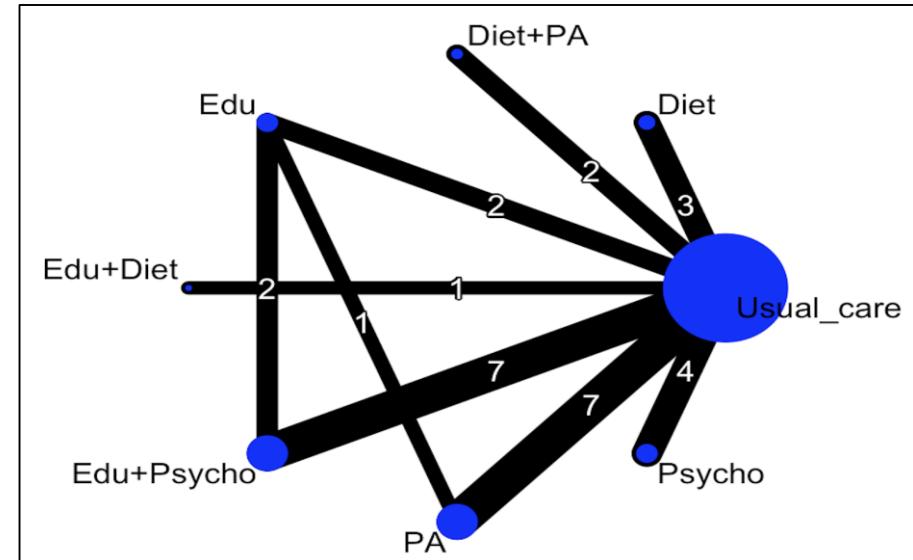


Figure: Forest plot for DBP outcome (SNMA)

Figure: Forest plot for DBP outcome (CNMA)

Diastolic blood pressure (DBP)

Treatment	MD	95% CI	P-score
PA	-3.03	(-5.00, -1.06)	0.42
Edu	-2.40	(-4.37, -0.43)	0.32
Diet	-1.33	(-3.61, 0.94)	0.17
Psycho	0.02	(-1.79, 1.82)	0.04
Edu+PA	-5.43	(-8.46, -2.39)	0.76
Diet+PA	-4.36	(-6.98, -1.74)	0.63
Edu+Diet	-3.73	(-6.28, -1.19)	0.53
PA+Psycho	-3.01	(-5.52, -0.50)	0.42
Edu+Psycho	-2.38	(-4.01, -0.75)	0.31
Diet+Psycho	-1.31	(-4.47, 1.84)	0.19
Edu+Diet+PA	-6.76	(-9.87, -3.66)	0.89
Edu+PA+Psycho	-5.41	(-8.08, -2.74)	0.77
Diet+PA+Psycho	-4.34	(-7.63, -1.06)	0.62
Edu+Diet+Psycho	-3.72	(-6.31, -1.12)	0.53
Edu+Diet+PA+Psycho	-6.74	(-9.75, -3.73)	0.89

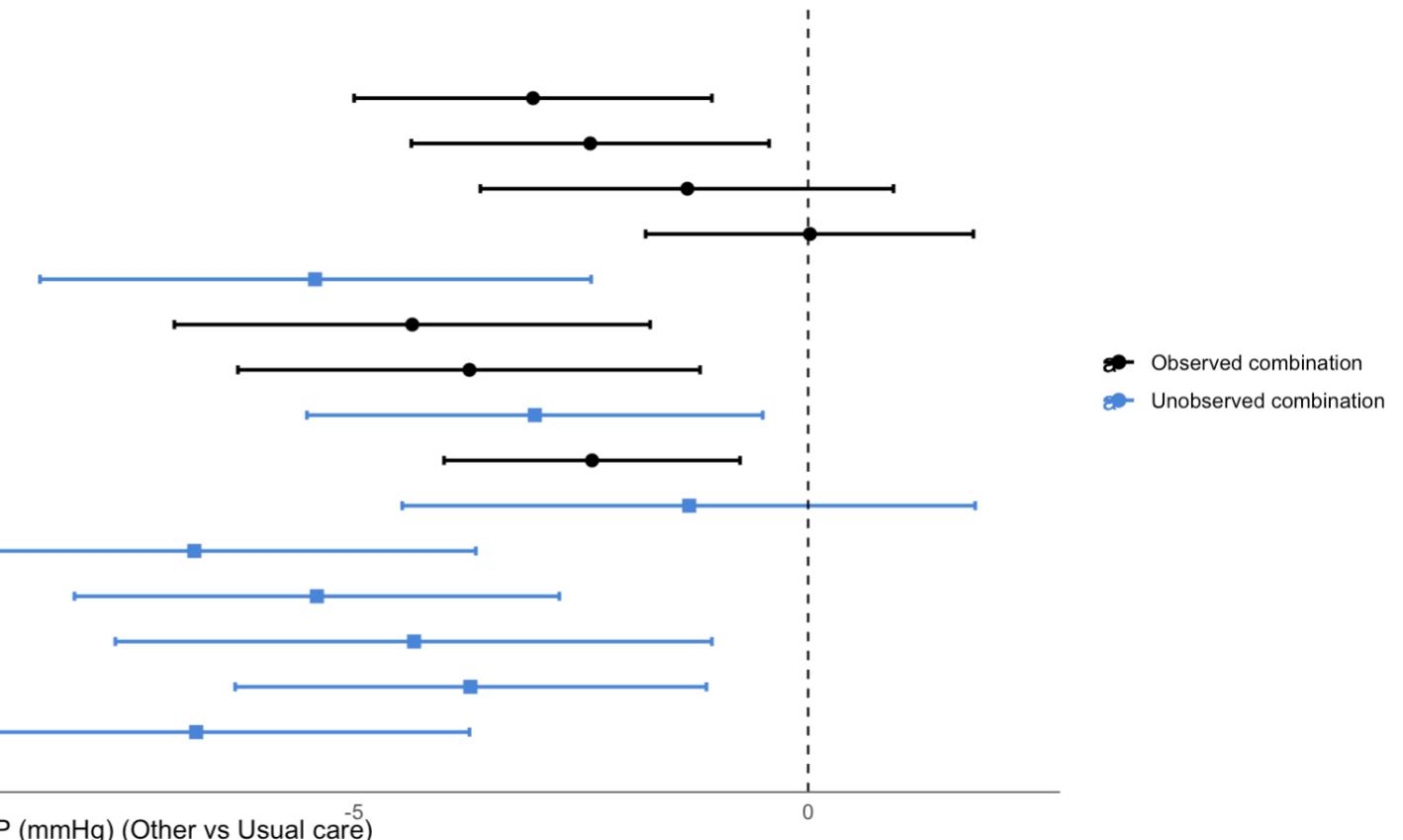


Figure: Forest plot of all SMIs for DBP outcome (CNMA)

Checking addictive assumption

Outcomes	Q (df) (Heterogeneity statistics)		
	CNMA (Additive model)	SNMA (Standard model)	Difference
eGFR	60.27 (29)	52.98 (25)	7.29 (4) p = 0.1214
SBP	58.54 (25)	55.99 (23)	2.56 (2) p = 0.2783
DBP	70.68 (24)	62.20 (21)	8.47 (3) p = 0.0372

For more information

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3. Rücker G, Schwarzer G. Reduce dimension or reduce weights? Comparing two approaches to multi-arm studies in network meta-analysis. *Stat Med.* 2014 Nov 10;33(25):4353-69. doi: 10.1002/sim.6236. Epub 2014 Jun 18. PMID: 24942211.
4. Rücker G, Petropoulou M, Schwarzer G. Network meta-analysis of multicomponent interventions. *Biom J.* 2020 May;62(3):808-821. doi: 10.1002/bimj.201800167. Epub 2019 Apr 25. PMID: 31021449; PMCID: PMC7217213.
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Thank you for your attention!

Discussion