



BEST TREATMENTS

rankings in network meta-analysis

Anna Chaimani

University of Ioannina School of Medicine

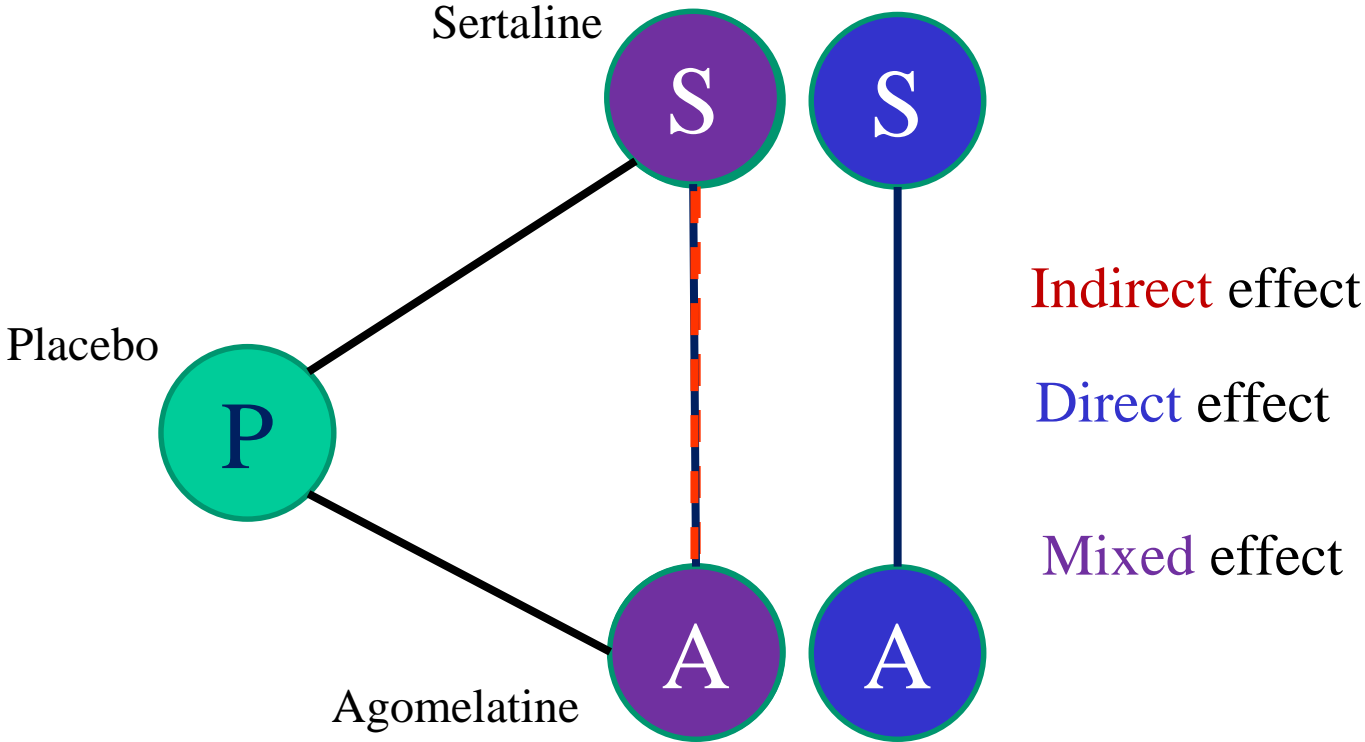
Greece



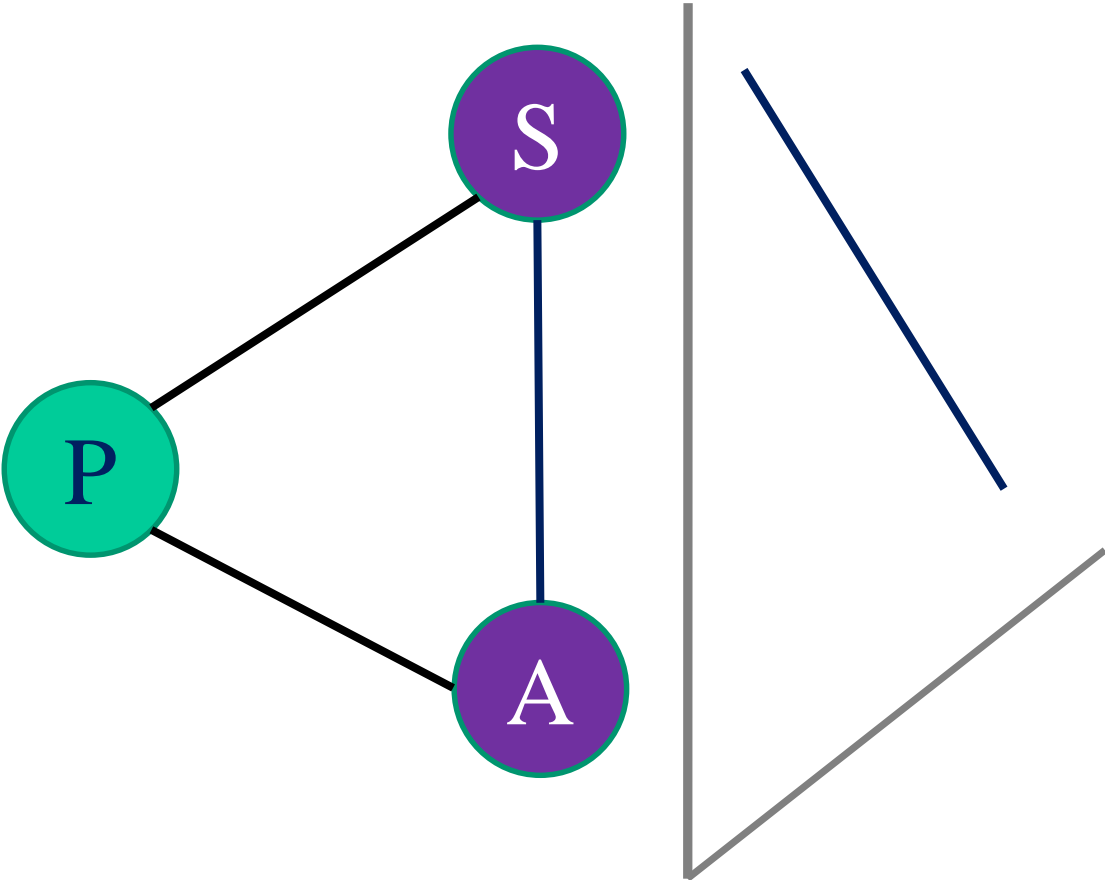
*Johns Hopkins Bloomberg School of Public Health
Baltimore, 16 August 2016*

The idea of network meta-analysis

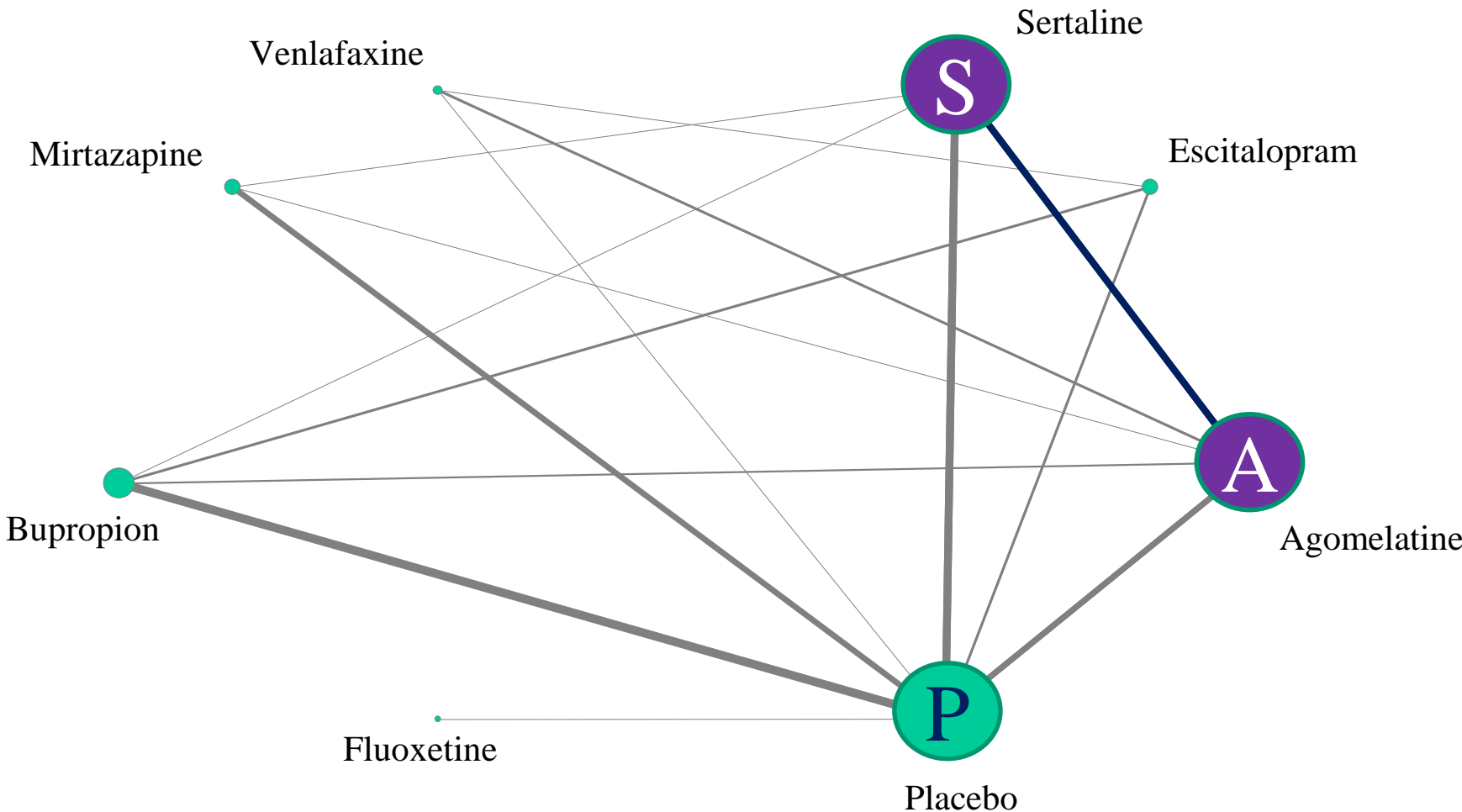
TREATMENTS FOR DEPRESSION



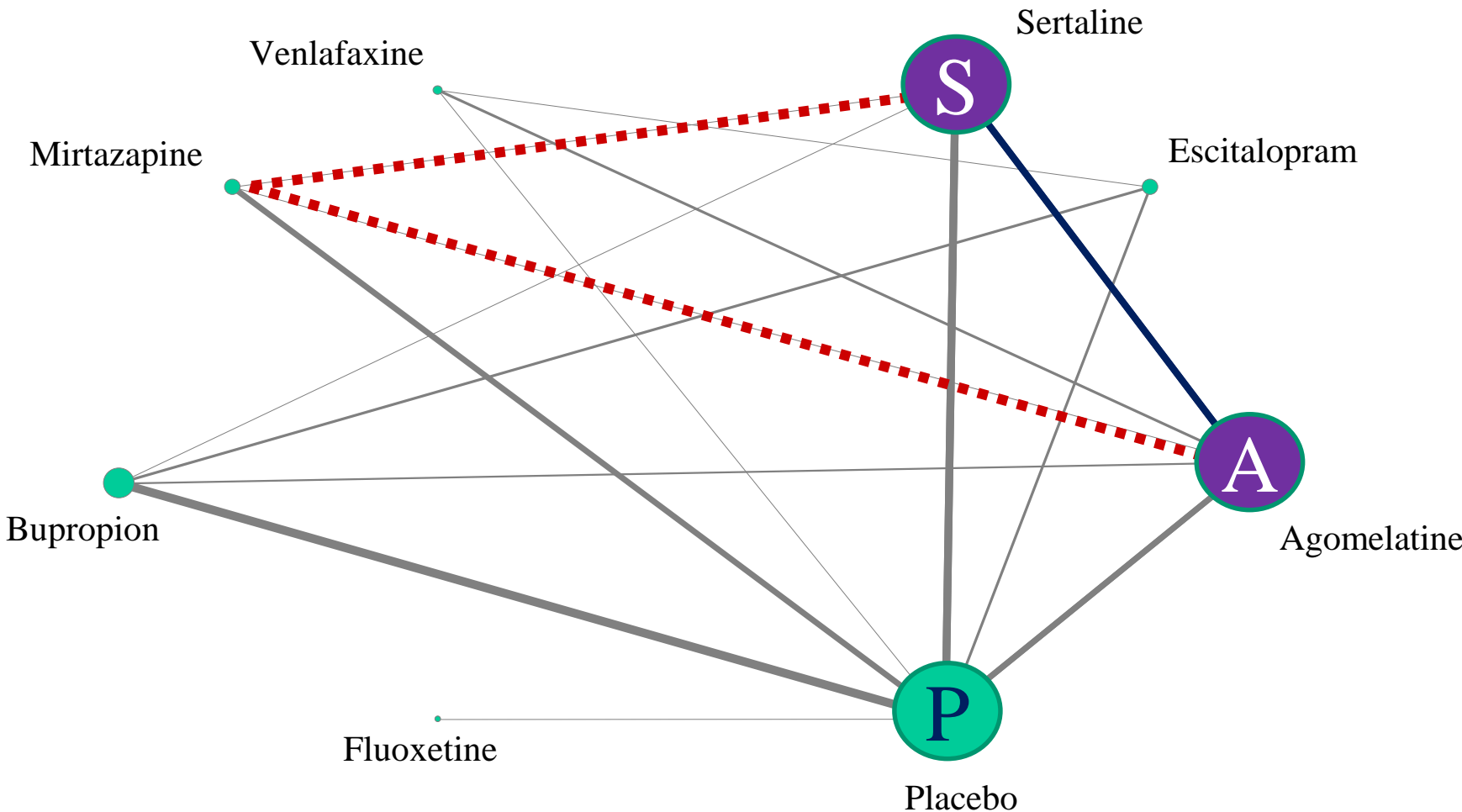
TREATMENTS FOR DEPRESSION



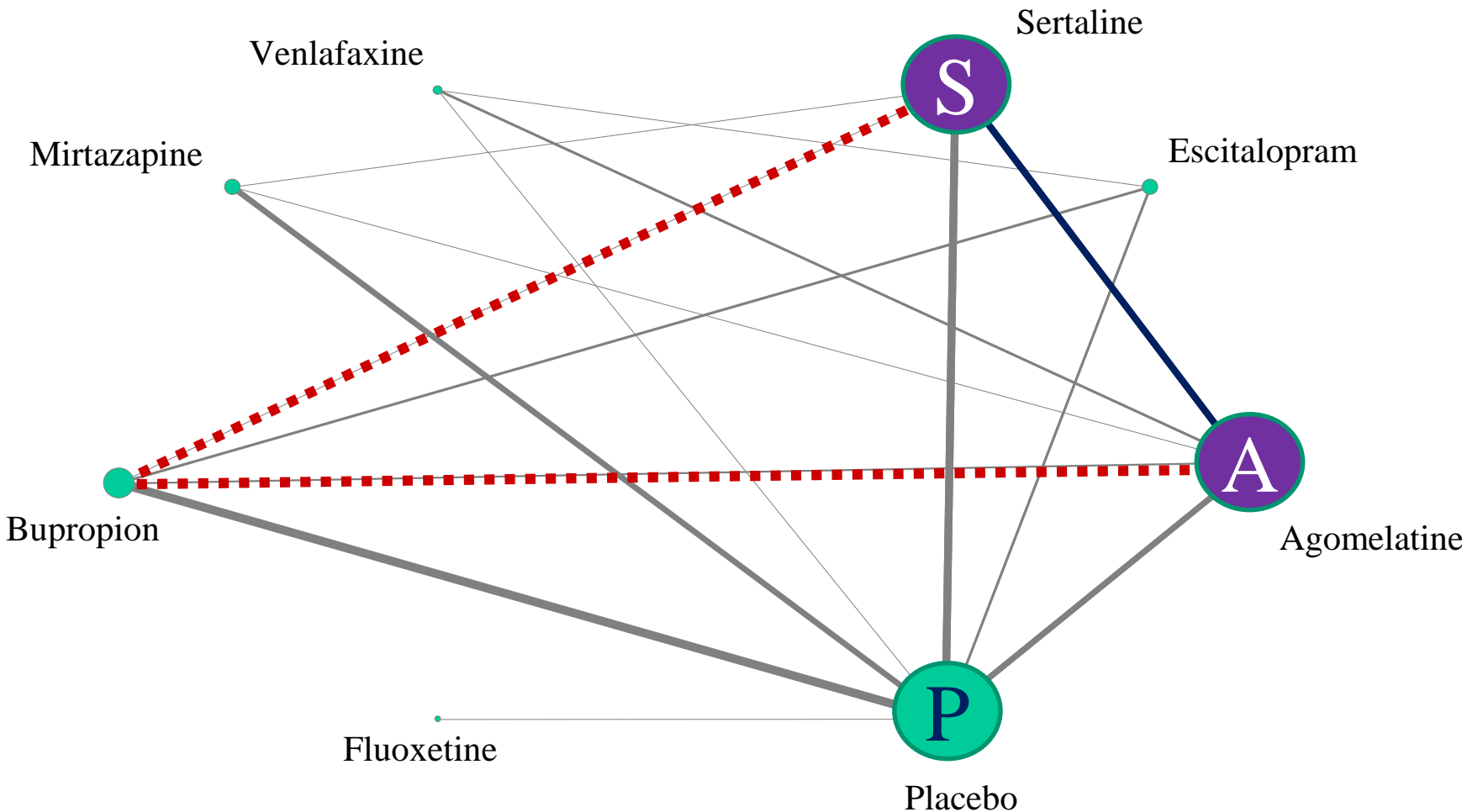
TREATMENTS FOR DEPRESSION



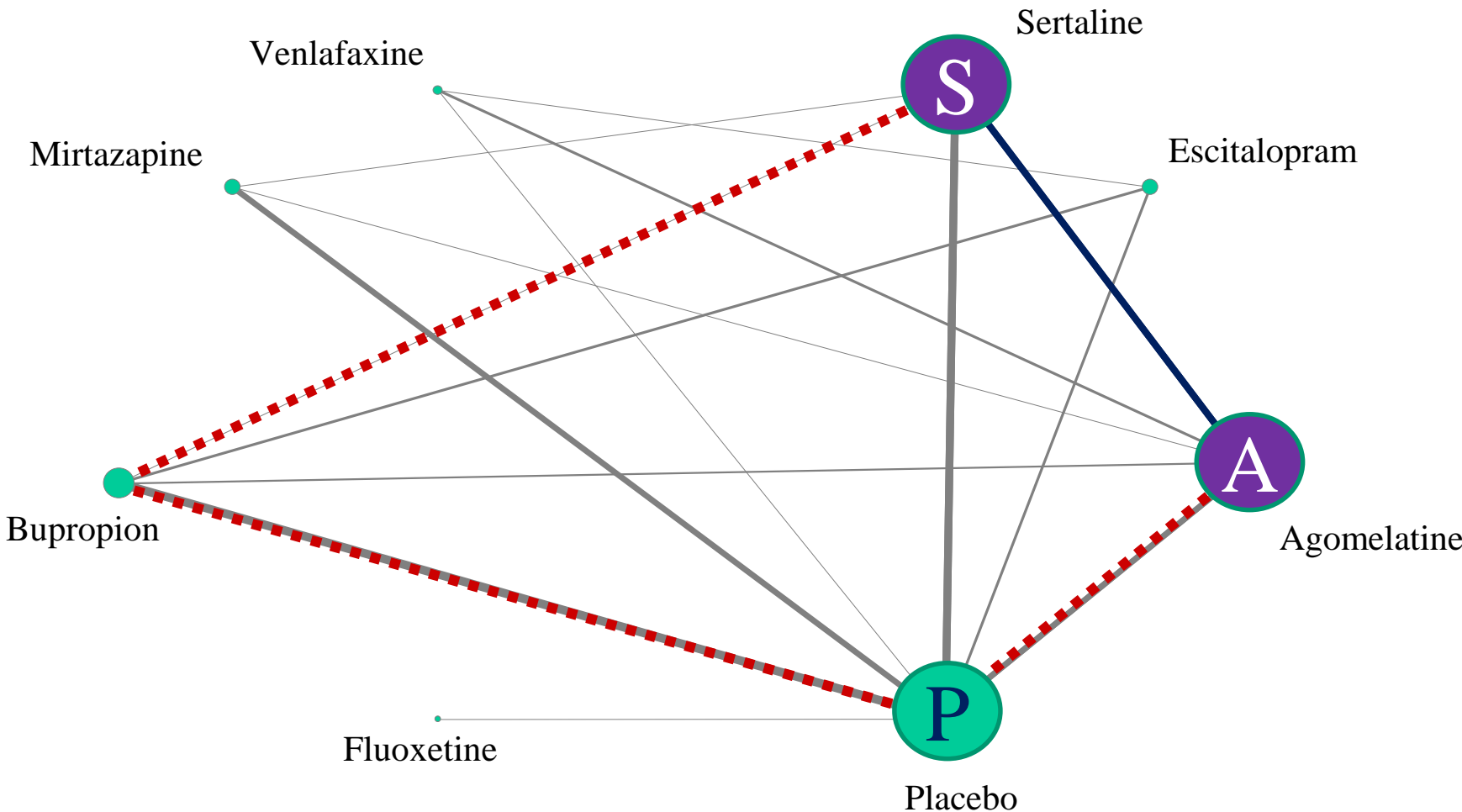
TREATMENTS FOR DEPRESSION



TREATMENTS FOR DEPRESSION



TREATMENTS FOR DEPRESSION



NETWORK RESULTS

escitalopram is more effective than agomelatine

venlafaxine is more effective than sertraline

bupropion is more acceptable than agomelatine

all drugs are more effective than placebo

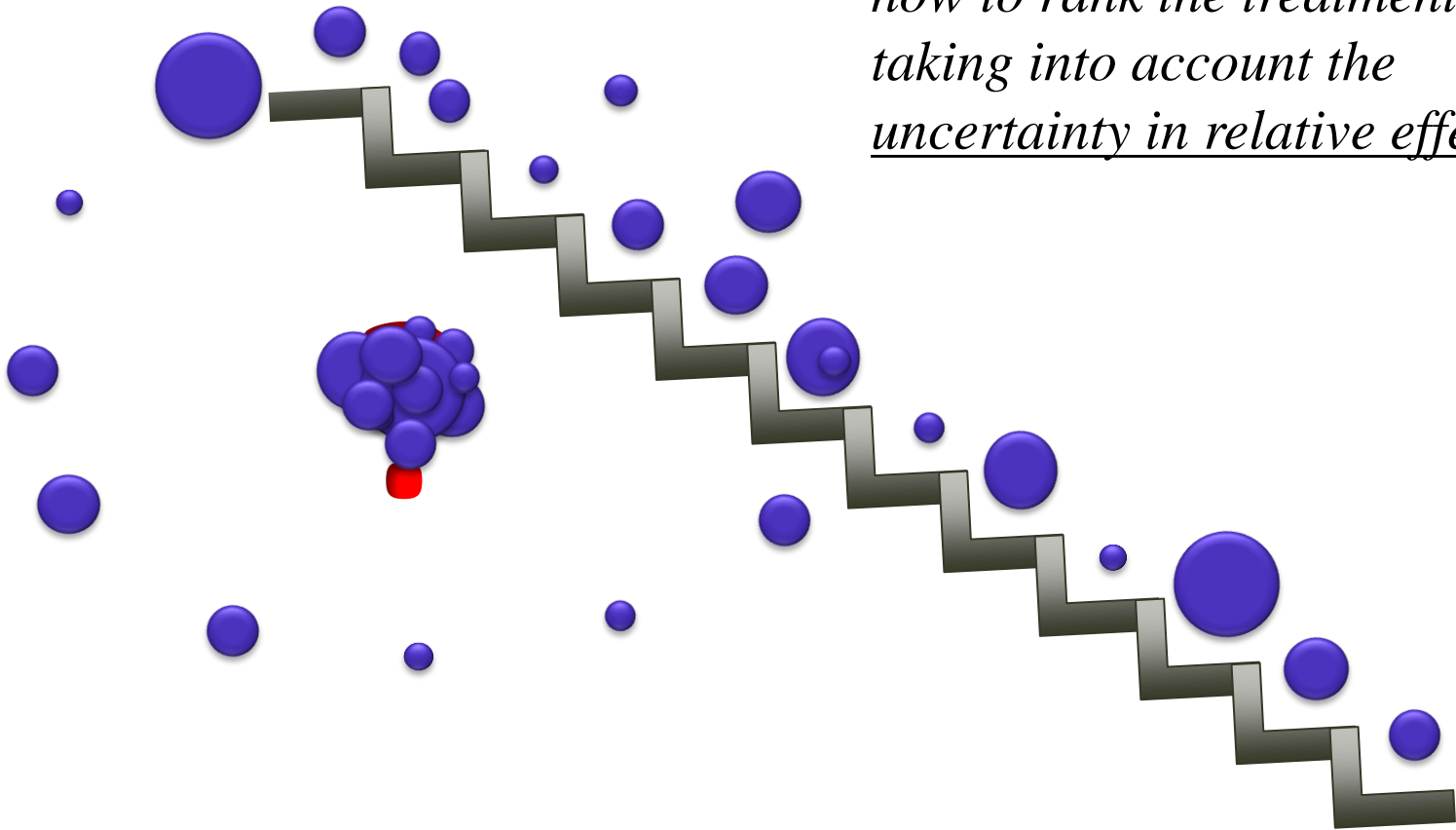
Effectiveness

Acceptability

ESC	1.40 (0.93,2.11)	1.11 (0.75,1.66)	1.16 (0.63,2.14)	0.85 (0.62,1.15)
-0.06 (-0.22,0.11)	MIRT	0.80 (0.51,1.25)	0.83 (0.44,1.57)	0.61 (0.44,0.83)
-0.12 (-0.28,0.02)	-0.07 (-0.22,0.08)	VEN	<u>0.54</u> (0.37,0.79)	0.88 (0.44,1.44)
<u>-0.19</u> (-0.36,-0.01)	-0.13 (-0.30,0.04)	?	0.06 (-0.12,0.10)	AGO
<u>-0.19</u> (-0.37,-0.01)	-0.13 (-0.31,0.04)	-0.07 (-0.24,0.11)	-0.01 (-0.18,0.17)	BUP
<u>-0.19</u> (-0.36,-0.02)	-0.13 (-0.31,0.05)	<u>-0.11</u> (-0.23,-0.06)	-0.01 (-0.18,0.17)	0.00 (-0.19,0.20)
<u>-0.20</u> (-0.36,-0.01)	-0.14 (-0.42,0.12)	-0.08 (-0.34,0.18)	-0.02 (-0.28,0.24)	-0.01 (-0.29,0.26)
<u>-0.56</u> (-0.69,-0.43)	<u>-0.50</u> (-0.63,-0.38)	<u>-0.43</u> (-0.54,-0.32)	<u>-0.37</u> (-0.63,-0.11)	<u>-0.37</u> (-0.51,-0.23)
				<u>-0.37</u> (-0.51,-0.23)
				SERT
				0.73 (0.42,1.28)
				FLUO
				<u>-0.36</u> (-0.60,-0.11)
				PBO

NETWORK RESULTS

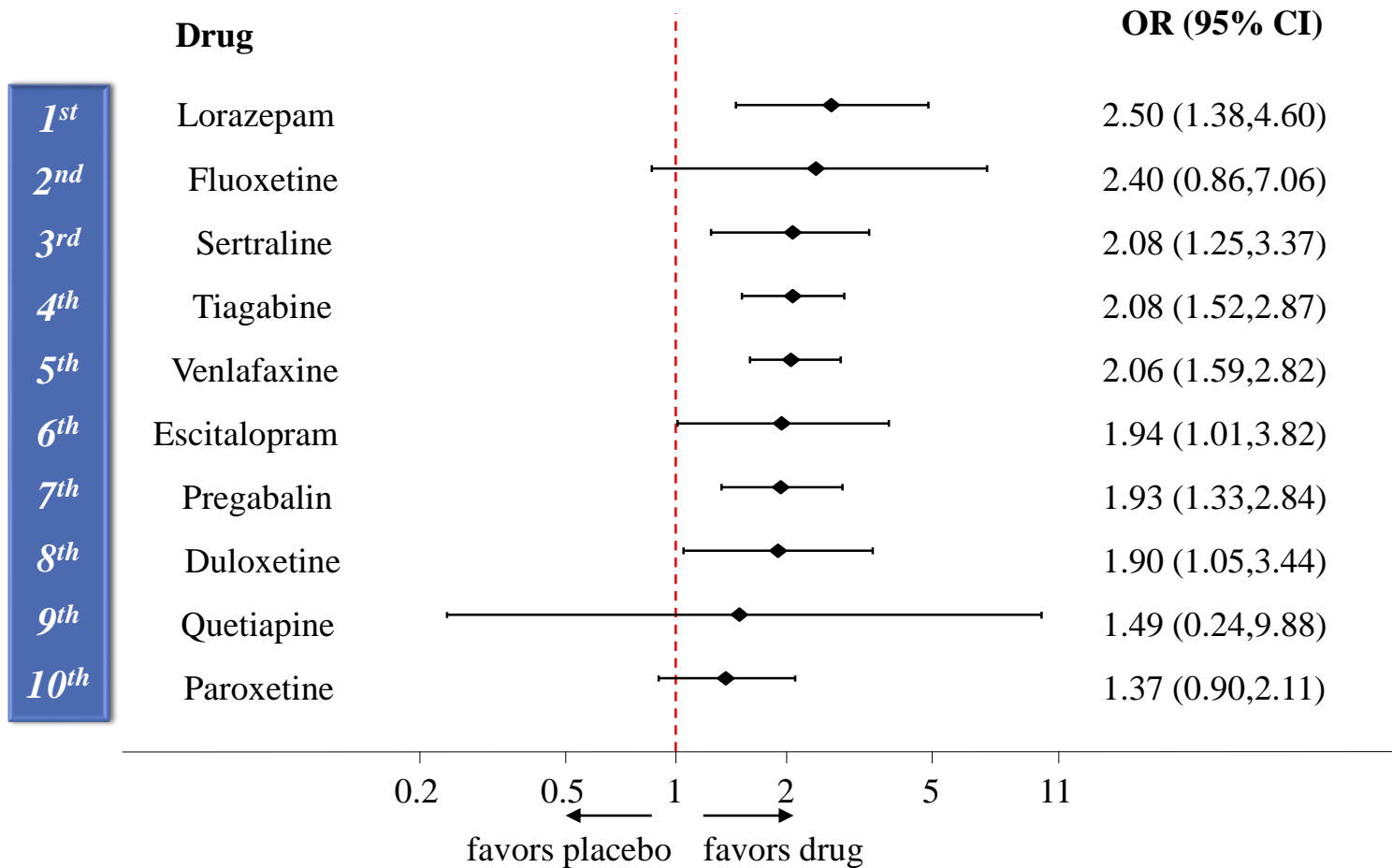
*how to rank the treatments
taking into account the
uncertainty in relative effects*



Ranking in network meta-analysis

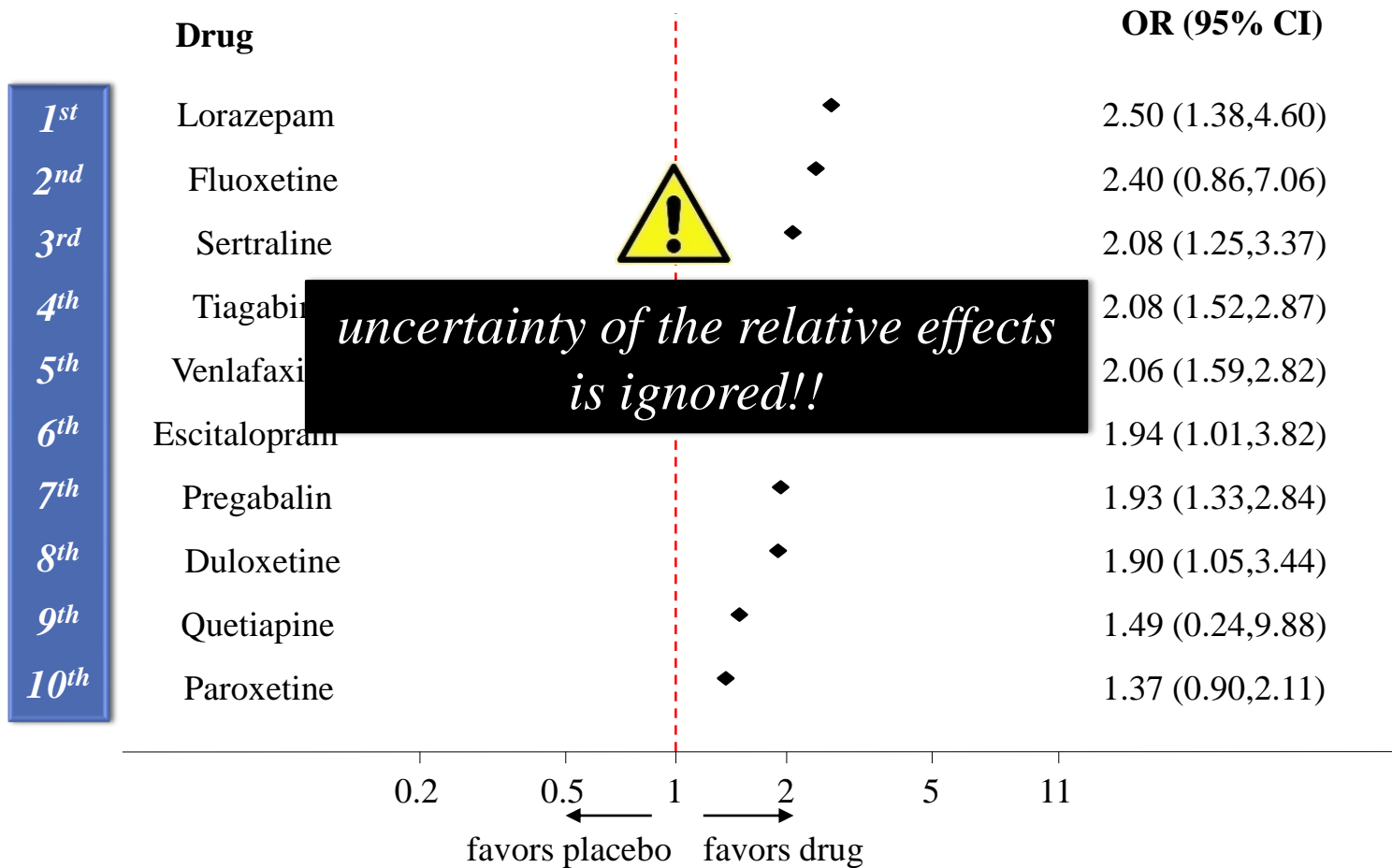
RANKING BASED ON RELATIVE EFFECTS

treatments for anxiety disorder



RANKING BASED ON RELATIVE EFFECTS

treatments for anxiety disorder



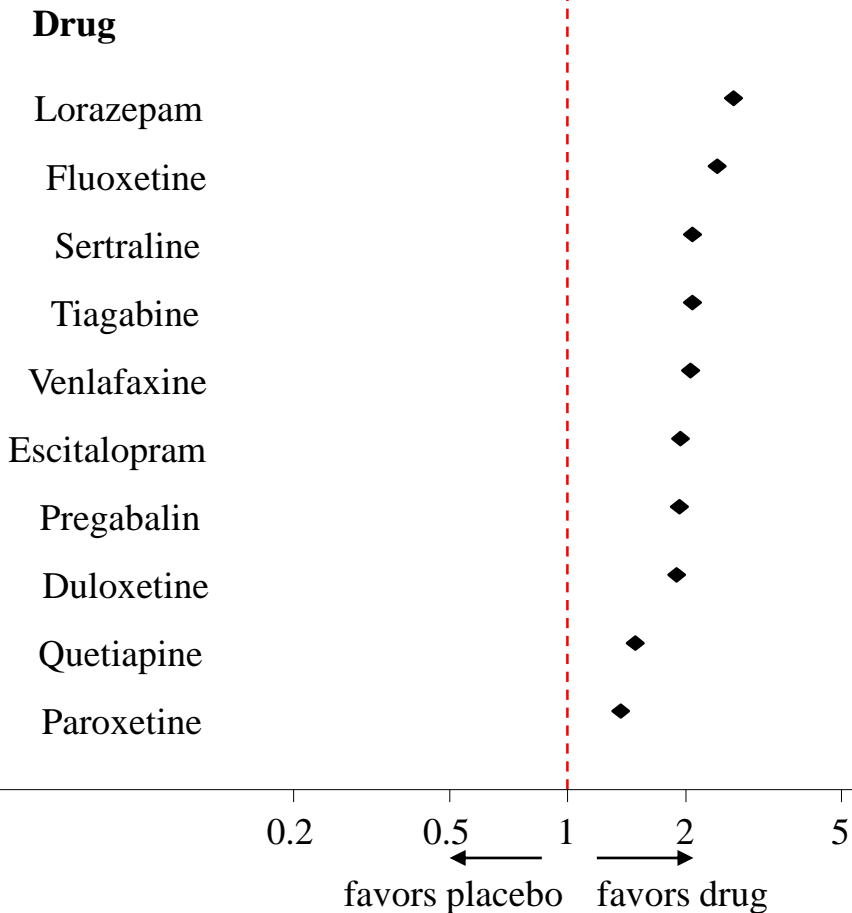
RANKING PROBABILITIES

- ranking probability \rightarrow the probability for a treatment of being at a particular rank
- estimation of such probabilities is straightforward within a Bayesian framework
 - *in each MCMC cycle rank the treatments*
 - *run 100 000 cycles*
 - *$(\#J=1)/100\,000$ is the probability that J is the best treatment*
- we can do the same in frequentist framework using a re-sampling method (e.g. bootstrap)

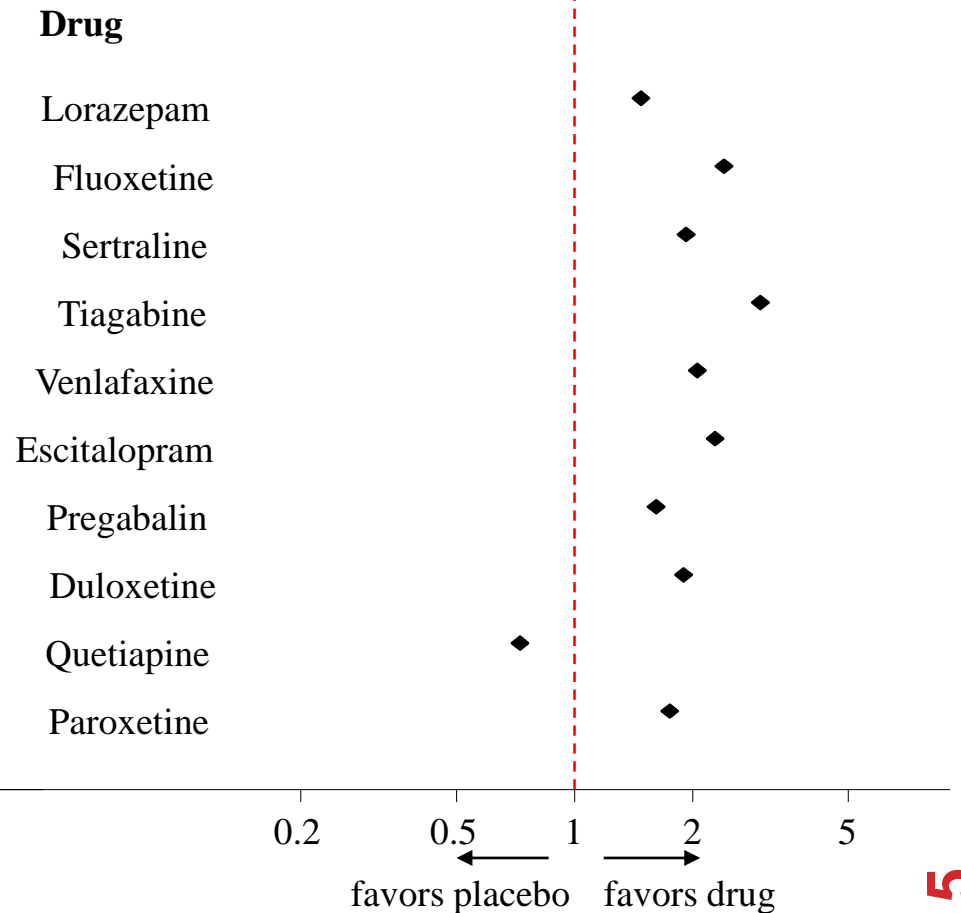
RANKING PROBABILITIES

treatments for anxiety disorder

1st cycle

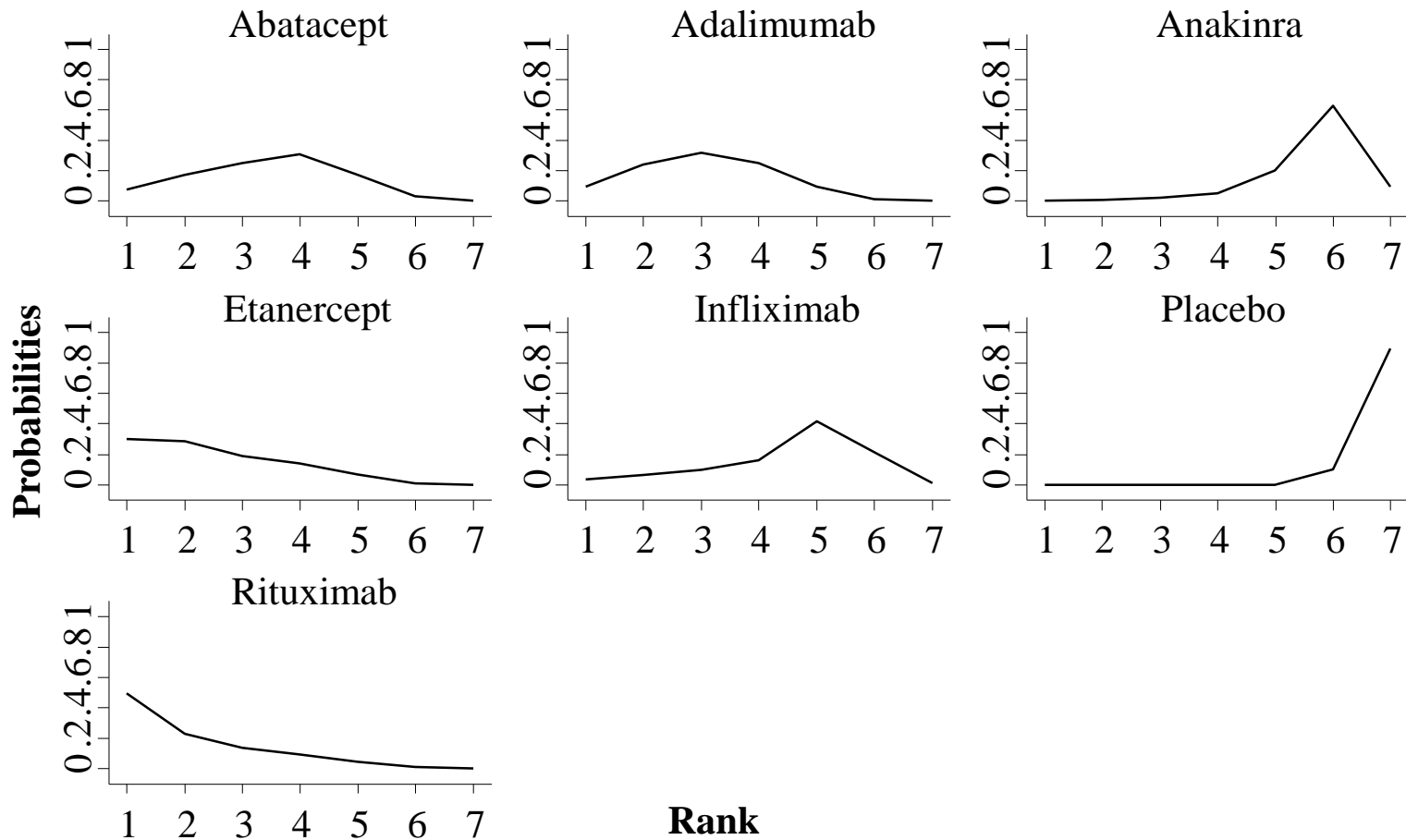


2nd cycle



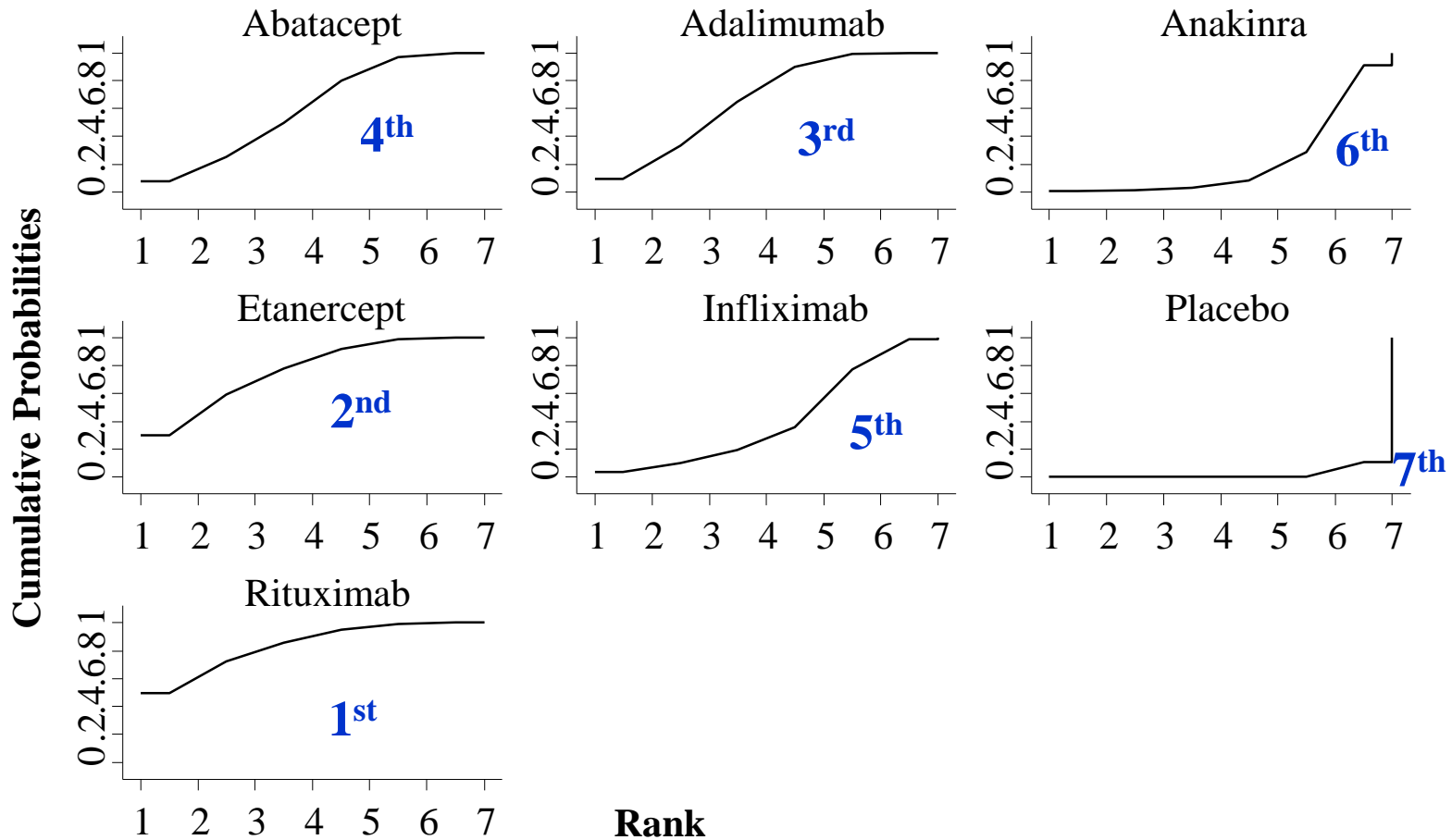
DISTRIBUTION OF RANKING PROBABILITIES

treatments for rheumatoid arthritis



CUMULATIVE RANKING PROBABILITIES

treatments for rheumatoid arthritis



MEASURES FOR RELATIVE RANKING

Use cumulative probabilities for each treatment to be among the n -best options

$$SUCRA_j = \frac{\sum_{l=1}^{T-1} \text{cum}_j^l}{T-1}$$

Treatment j
Ranks l

Total number of treatments T

$SUCRA_j$ = The percentage of the effectiveness/safety of a treatment that would be ranked first without any uncertainty

MEASURES FOR RELATIVE RANKING

Use the weighted average of all possible ranks with weights the ranking probabilities for each treatment

Total number of treatments T

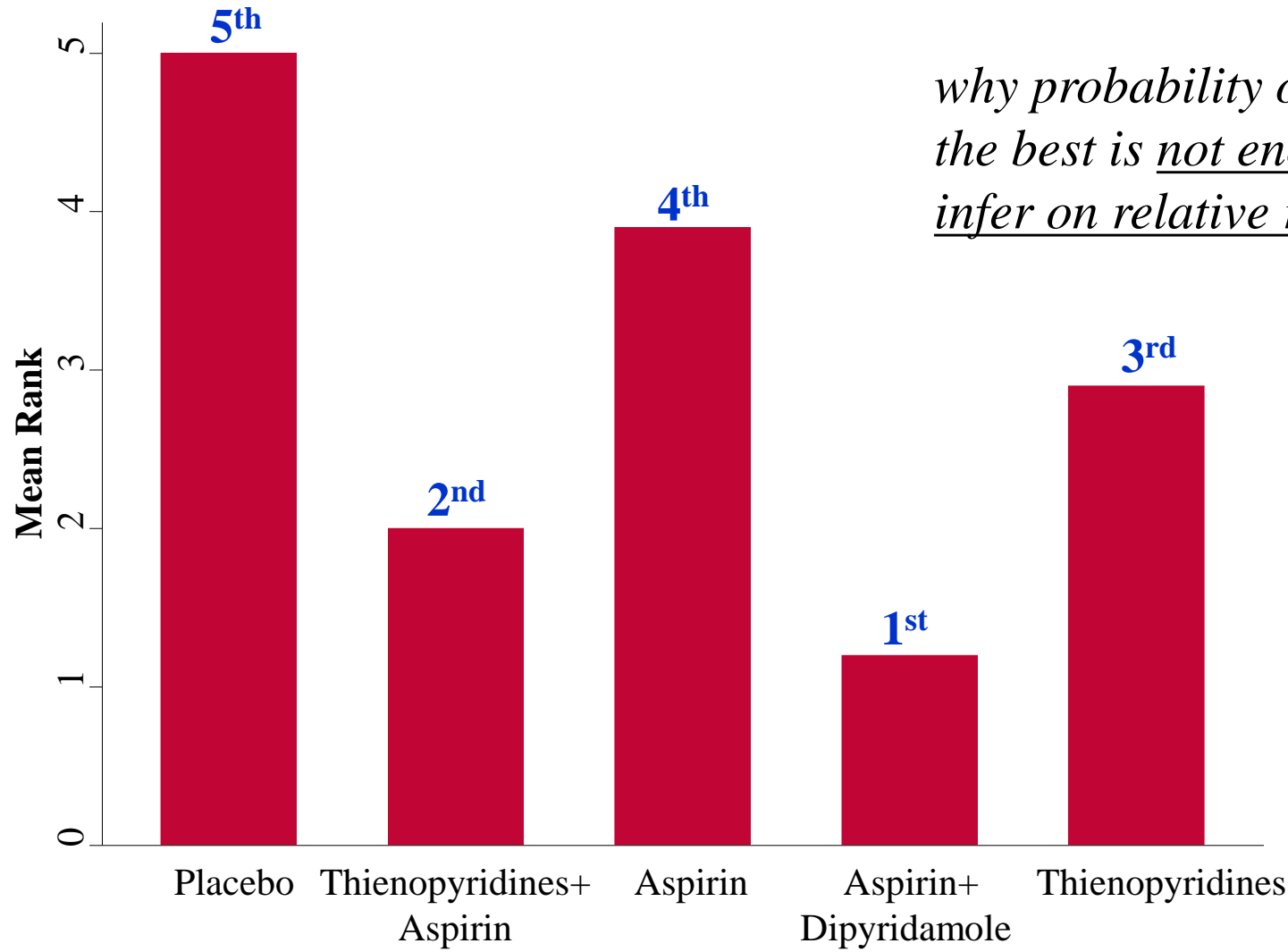
Treatment j
Ranks l

$$\text{Mean rank}_j = \frac{1}{T} \sum_{l=1}^T (p_{j,l} \cdot l)$$

Smaller mean rank values correspond to more effective/safer treatments

MEASURES FOR RELATIVE RANKING

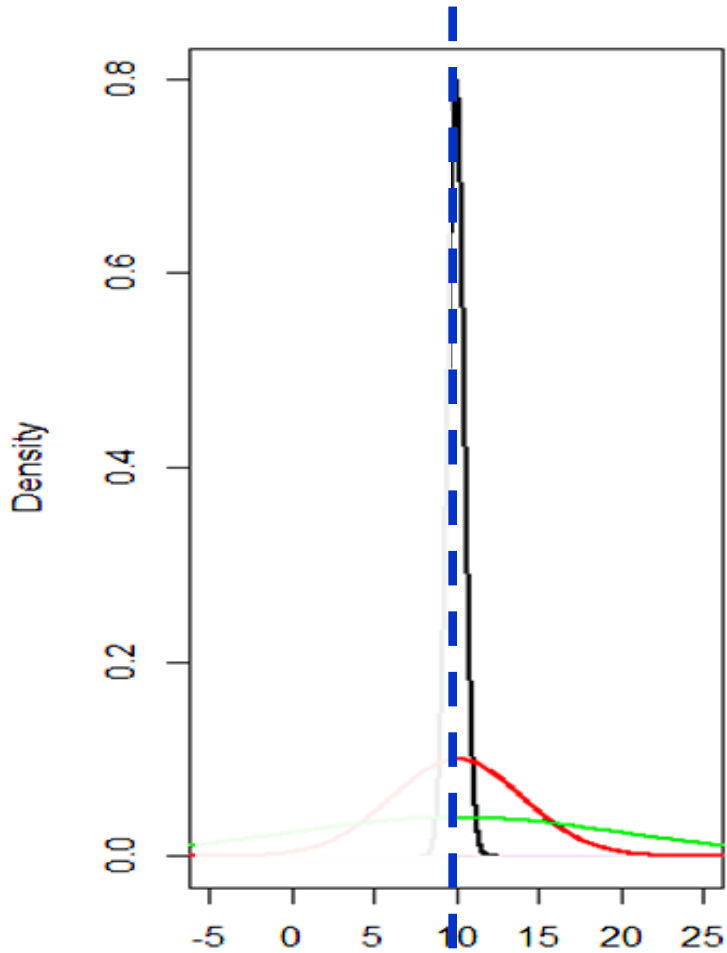
treatments for serious vascular events



why probability of being the best is not enough to infer on relative ranking

Uncertainty in relative ranking

HYPOTHETICAL EXAMPLE (1)



treatment outcomes

treatment x: mean=10, variance=4

treatment y: mean=10, variance=5

treatment z: mean=10, variance=10

	x	y	z
<i>P (best)</i>	25%	31%	44%
<i>P (sec)</i>	50%	38%	12%
<i>P (third)</i>	25%	31%	44%
<i>Mean ranks</i>	2	2	2
<i>SUCRAs</i>	50%	50%	50%

Conclusion:
treatment z is the most effective

Conclusion:
treatments x, y, z are equally effective

HYPOTHETICAL EXAMPLE (2)

A
B
C
D

	<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>	<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>
<i>Best</i>	28	24	24	24	97	1	1	1
<i>Second</i>	24	28	24	24	1	97	1	1
<i>Third</i>	24	24	28	24	1	1	97	1
<i>Last</i>	24	24	24	28	1	1	1	97

**Network ranking with
high imprecision**

**Network ranking with
high precision**

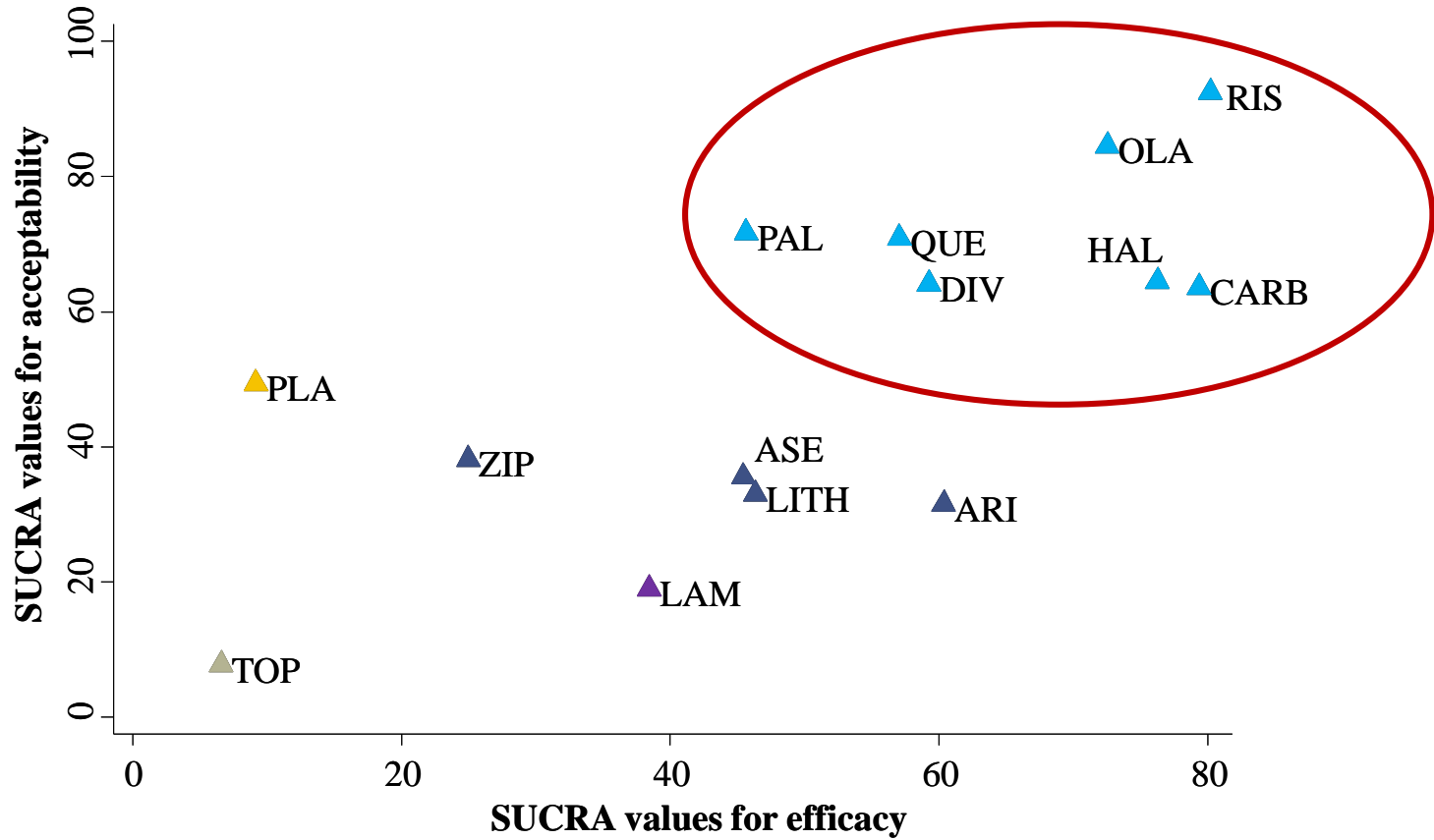
Relative ranking for different outcomes

TREATMENTS FOR SCHIZOPHRENIA

- the same intervention often does not perform equally well for different outcomes

	Efficacy		Acceptability			Efficacy		Acceptability	
ARI	60.2	5	32.4	12	OLA	72.4	4	85.5	2
ASE	45.3	11	36.4	10	PAL	45.5	10	72.6	4
CARB	79.2	2	64.5	7	PLA	9.00	14	50.3	8
DIV	59.1	7	65.0	14	QUE	56.9	8	71.8	5
HAL	76.1	3	65.4	6	RIS	80.4	1	93.4	1
LAM	38.3	12	19.9	13	TOP	6.40	6	8.60	3
LITH	46.2	9	33.9	11	ZIP	24.8	13	39.1	9

TREATMENTS FOR SCHIZOPHRENIA



IN SUMMARY

- relative ranking should be based on measures that account for the uncertainty of the relative effects
- inference on the relative ranking should take into consideration the uncertainty of the relative ranking
- relative ranking and relative effects should be interpreted jointly and always in light of several factors and outcomes



Thank You!