

# CONFIDENCE IN NETWORK META-ANALYSIS



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**Institute of Social and Preventive Medicine**

**University of Bern**

**Switzerland**

**CINEMA**

**Confidence In Network Meta-Analysis**

The most critical question raised by patients and clinicians at the point of care is

“what is the drug of choice for the given condition?”

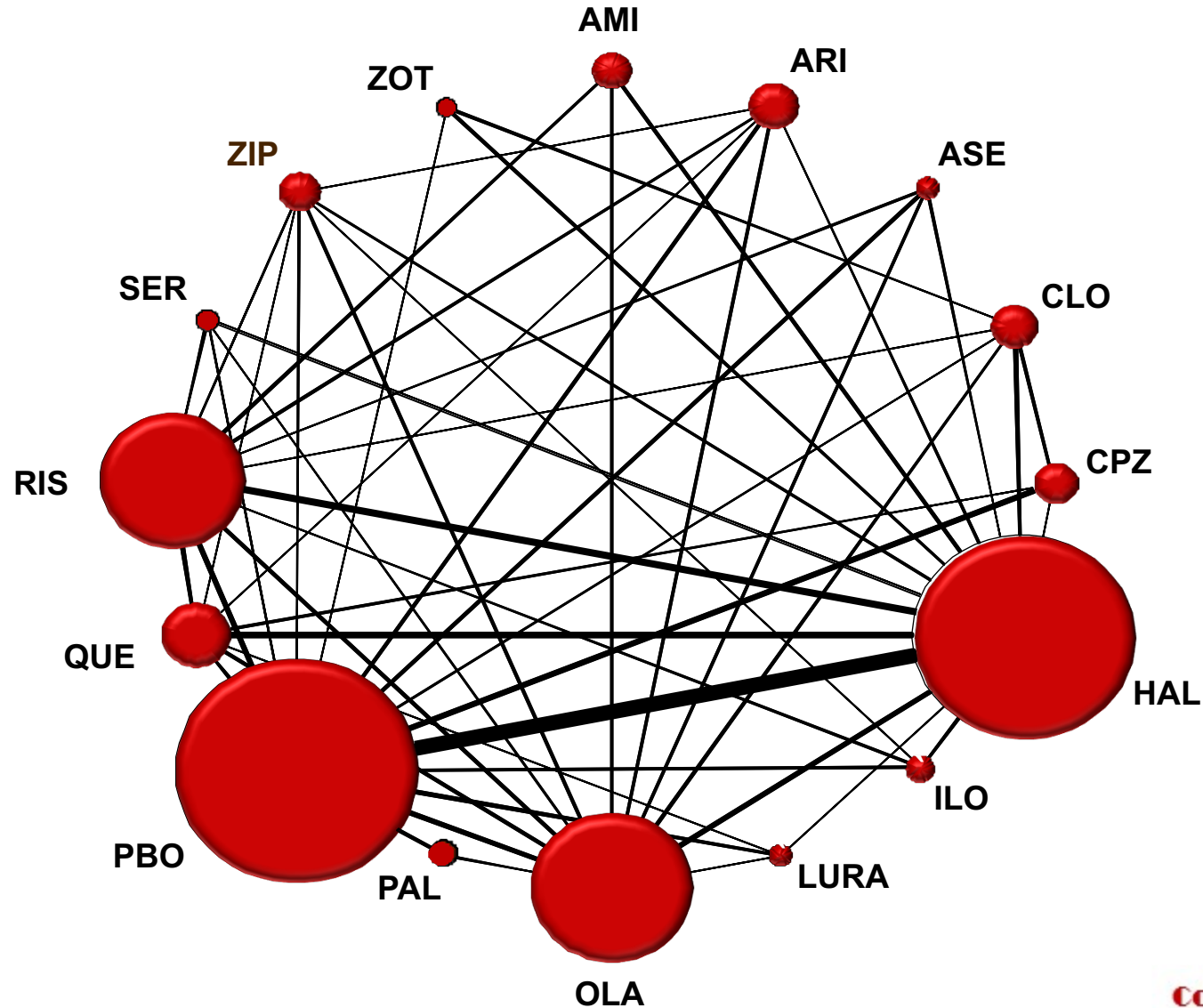
*Del Fiol G et al. Clinical questions raised by clinicians at the point of care: a systematic review. JAMA Intern Med. 2014*

**CINEMA**

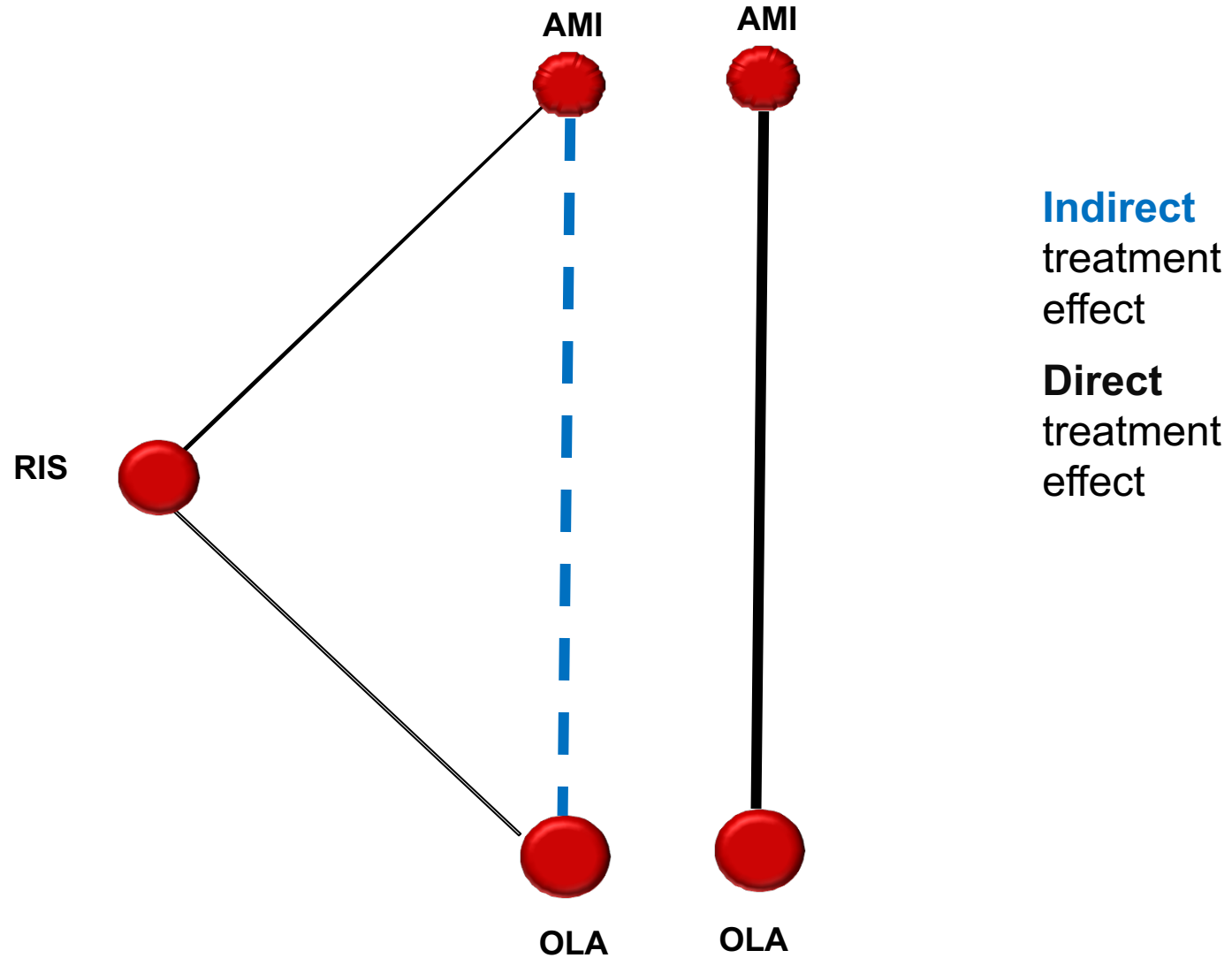
**Confidence In Network Meta-Analysis**

# NETWORK: INDIRECT, DIRECT AND MIXED EVIDENCE

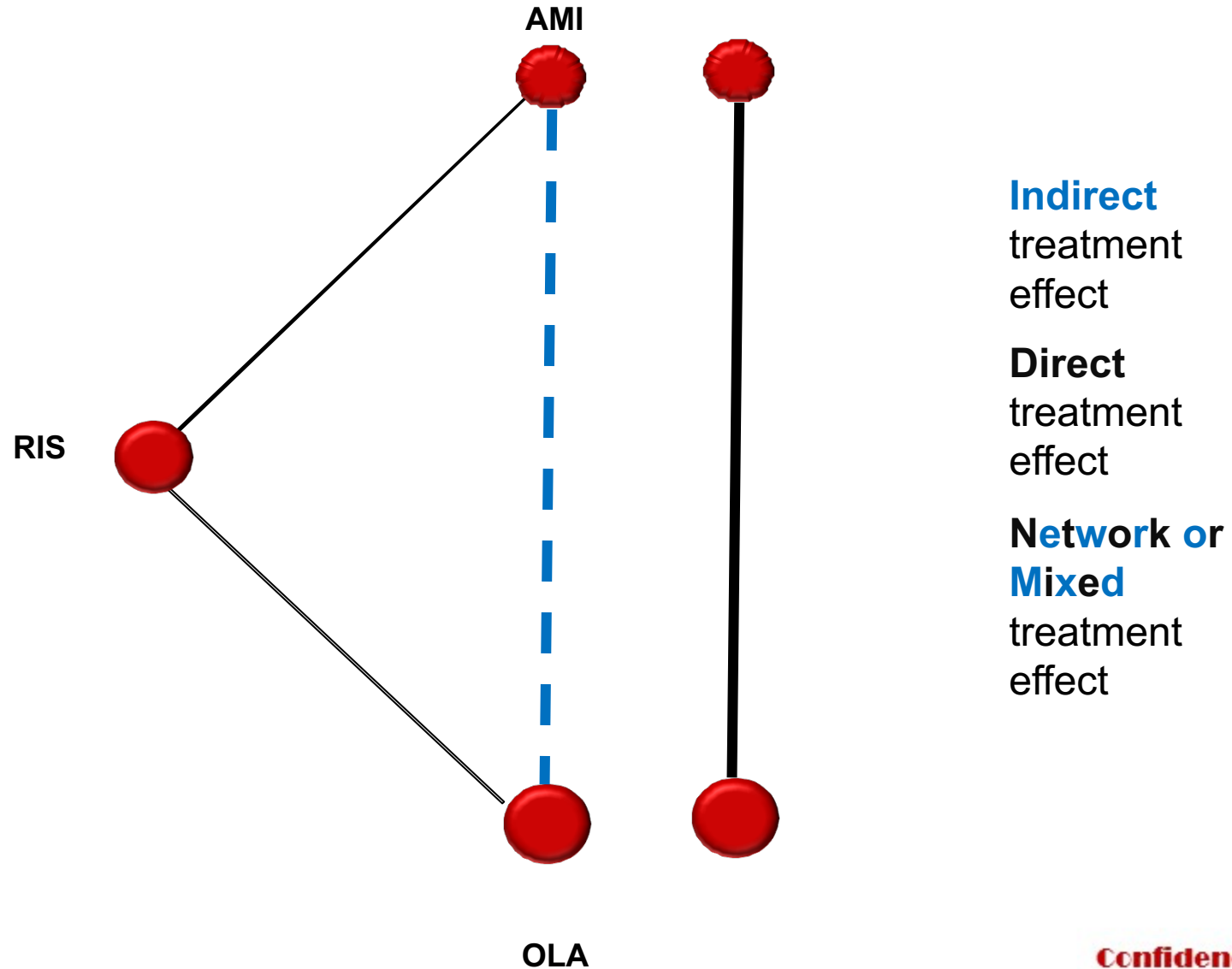
Leucht S et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia. Lancet 2013



# NETWORK: INDIRECT, DIRECT AND MIXED EVIDENCE

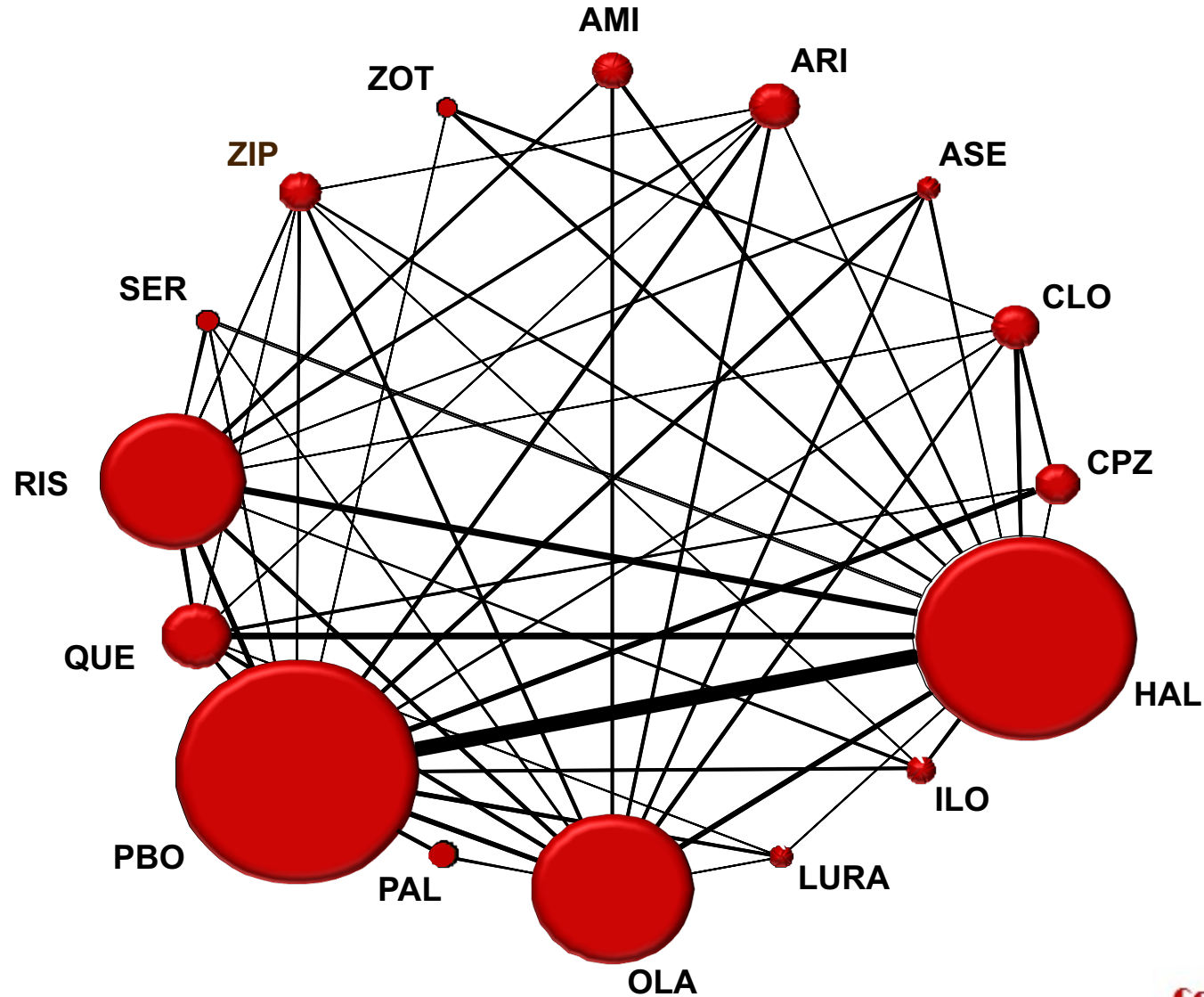


# NETWORK: INDIRECT, DIRECT AND MIXED EVIDENCE



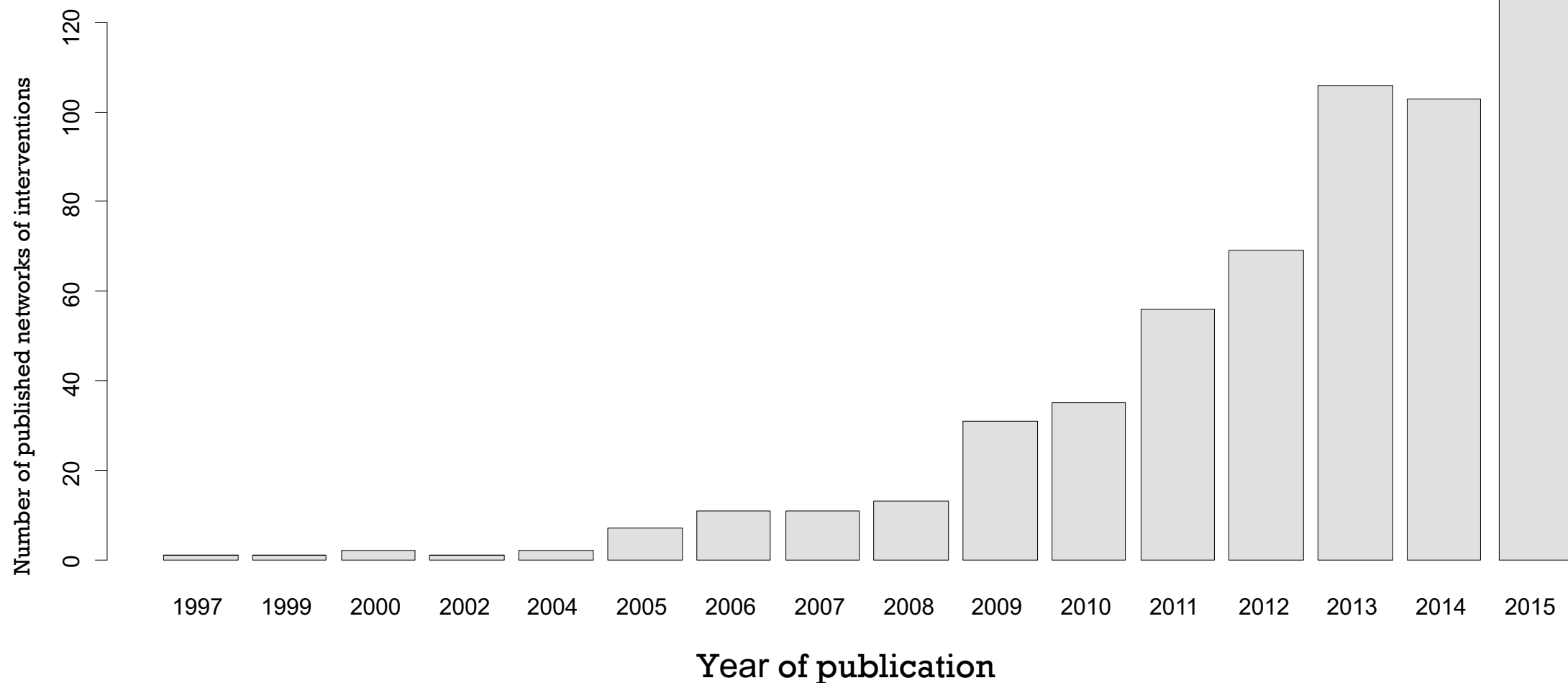
# NETWORK: INDIRECT, DIRECT AND MIXED EVIDENCE

Leucht S et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia. Lancet 2013



# 456 published networks in the medical literature comparing at least 4 medical interventions (March 2015)

*(Petropoulou et al. Journal of Clinical Epidemiology 2016, Zarin et al. BMC Medicine 2016)*



# None of the 456 NMAs published until 3/2015 attempted to evaluate the confidence in NMA results!

OPEN ACCESS Freely available online



## Evaluating the Quality of Evidence from a Network Meta-Analysis

Georgia Salanti<sup>1</sup>, Cinzia Del Giovane<sup>2</sup>, Anna Chaimani<sup>1</sup>, Deborah M. Caldwell<sup>3</sup>, Julian P. T. Higgins<sup>3,4\*</sup>

**1** Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece, **2** Statistics Unit, Department of Clinical and Diagnostic Medicine and Public Health, University of Modena and Reggio Emilia, Modena, Italy, **3** School of Social and Community Medicine, University of Bristol, Bristol, United Kingdom, **4** Centre for Reviews and Dissemination, University of York, York, United Kingdom

### Abstract

Systematic reviews that collate data about the relative effects of multiple interventions via network meta-analysis are highly informative for decision-making purposes. A network meta-analysis provides two types of findings for a specific outcome: the relative treatment effect for all pairwise comparisons, and a ranking of the treatments. It is important to consider the confidence with which these two types of results can enable clinicians, policy makers and patients to make informed decisions. We propose an approach to determining confidence in the output of a network meta-analysis. Our proposed approach is based on methodology developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group for pairwise meta-analyses. The suggested framework for evaluating a network meta-analysis acknowledges (i) the key role of indirect comparisons (ii) the contributions of each piece of direct evidence to the network meta-analysis estimates of effect size; (iii) the importance of the transitivity assumption to the validity of network meta-analysis; and (iv) the possibility of disagreement between direct evidence and indirect evidence. We apply our proposed strategy to a systematic review comparing topical antibiotics without steroids for chronically discharging ears with underlying eardrum perforations. The proposed framework can be used to determine confidence in the results from a

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Confidence in Network Meta-Analysis

BMJ 2014;349:g5

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Milo A Puha  
Brignardello  
Working Group



# CINEMA framework

Consider the **network estimates**

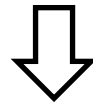
Study limitations  
 Indirectness  
 Inconsistency (heterogeneity, incoherence)  
 Imprecision  
 Publication bias

Rate each **network estimate**

No concerns

Some concerns

Major concerns



Network estimate	Study limitations	Indirectness	Inconsistency		Imprecision	Publication bias	Confidence
			Heterogeneity	Incoherence			
A vs B	Some concerns	Some concerns	Major concerns	Some concerns	Some concerns	undetected	Very low
A vs C	No concerns	No concerns	No concerns	Major concerns	No concerns	suspected	Low
....							

**Methods developed by:**  
Georgia Salanti  
Julian Higgins  
Adriani Nikolakopoulou

**Web developer:**  
Theodore  
Papakonstantinou

**Project supervision:**  
Matthias Egger

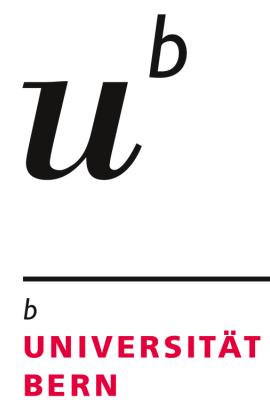
## Welcome to CINeMA!


*CINeMA (Confidence in Network Meta-Analysis) is a web application that simplifies the evaluation of confidence in the findings from network meta-analysis.*

It is based on a framework described in (1) which considers the five **GRADE** domains: **study limitations, indirectness, inconsistency, and publication bias**. The framework combines judgments about direct evidence with their statistical contribution to network meta-analysis, enabling evaluation of the credibility of **NMA** treatment effects.

*1. Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JPT. Evaluating the quality of evidence from a network meta-analysis. PLoS Med. 2014;9(7):e99682.*

To browse your projects or upload a new one go to [My Projects](#)



CINeMA is distributed, in the hope that it will be useful but without any warranty, under the  license

By using CINeMA you accept the following [DISCLAIMER](#)

# Incident diabetes in clinical trials of antihypertensive drugs: a network meta-analysis

William J Elliott, Peter M Meyer

## Summary

**Background** The effect of different classes of antihypertensive drugs on incident diabetes mellitus is controversial because traditional meta-analyses are hindered by heterogeneity across trials and the absence of trials comparing angiotensin-converting-enzyme (ACE) inhibitors with angiotensin-receptor blockers (ARB). We therefore undertook a network meta-analysis, which accounts for both direct and indirect comparisons to assess the effects of antihypertensive agents on incident diabetes.

*Lancet* 2007; 369: 201-07

Department of Preventive Medicine, Rush Medical College of Rush University at Rush University Medical Center, Chicago, IL 60612, USA

**Number of studies** 22

**Number of treatment nodes** 6

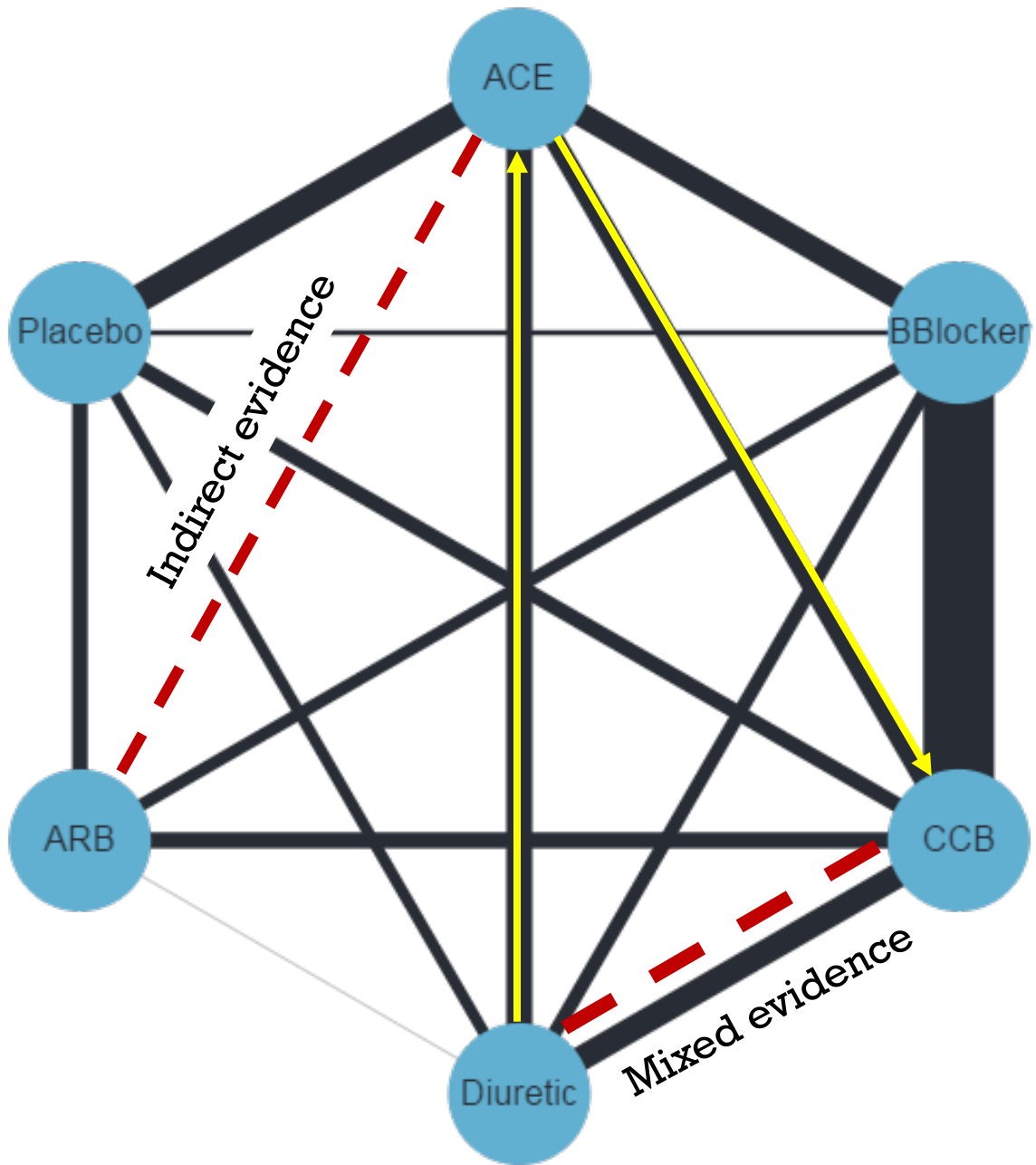
**Primary outcome** Effect of antihypertensives on incidence diabetes mellitus - proportion of patients who developed diabetes

**Measurement** Binary

**Intervention comparison type** pharmacological vs placebo

**CINEMA**

**Confidence In Network Meta-Analysis**



Comparison	Number of Studies	Study Limitations	Imprecision	Inconsistency			Publication bias	<u>CONFIDENCE</u>
				Heterogeneity	Incoherence	Indirectness		
Mixed evidence								
ACE vs BBLOCKER	3	No concerns	No concerns	Some concerns	Some concerns	No concerns	Undetected	MODERATE
ACE vs CCB	3	No concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	MODERATE
ACE vs Diuretic	2							MODERATE
ACE vs Placebo	3							LOW
ARB vs BBLOCKER	1							MODERATE
ARB vs CCB	1							LOW
ARB vs Diuretic	1							MODERATE
ARB vs Placebo	2							VERY LOW
BBLOCKER vs CCB	5							MODERATE
BBLOCKER vs Diuretic	2							MODERATE
BBLOCKER vs Placebo	1							VERY LOW
CCB vs Diuretic	2							MODERATE
CCB vs Placebo	1	No concerns	Some concerns	Some concerns	No concerns	No concerns	Suspected	LOW
Diuretic vs Placebo	3	No concerns	No concerns	Some concerns	No concerns	No concerns	Suspected	LOW
Indirect evidence								
ACE vs ARB	--	No concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	LOW

**Semi-automated process**

Explicit rules that classify each network meta-analysis effect for each domain to

**No concerns, Some concerns, Major concerns** as described in the documentation

**The rules can be overwritten!**



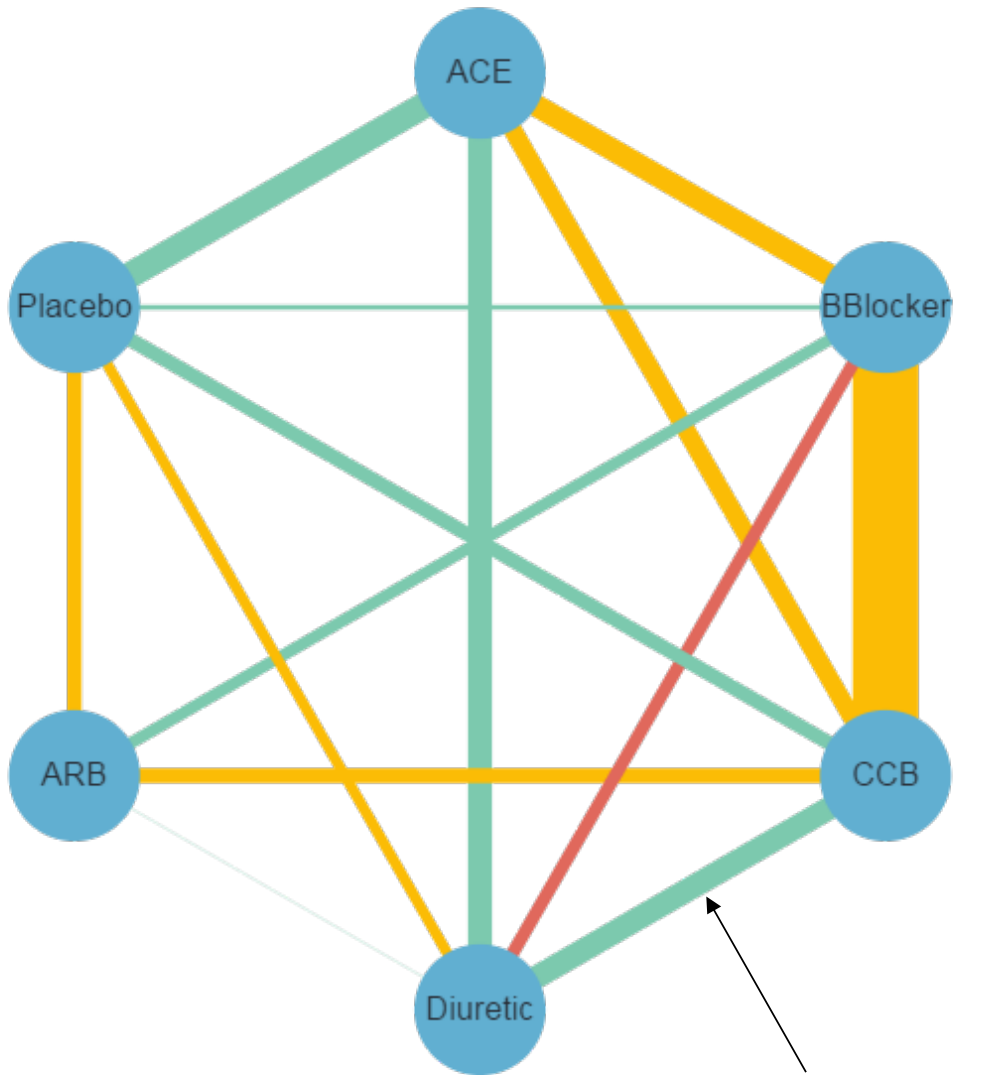
The aim of the webinar is to explain the methods used in CINeMA and present an alpha version of the web application

[pollev.com/gmhbe](https://pollev.com/gmhbe)

# STUDY LIMITATION

- Major concerns
- Some concerns
- No concerns

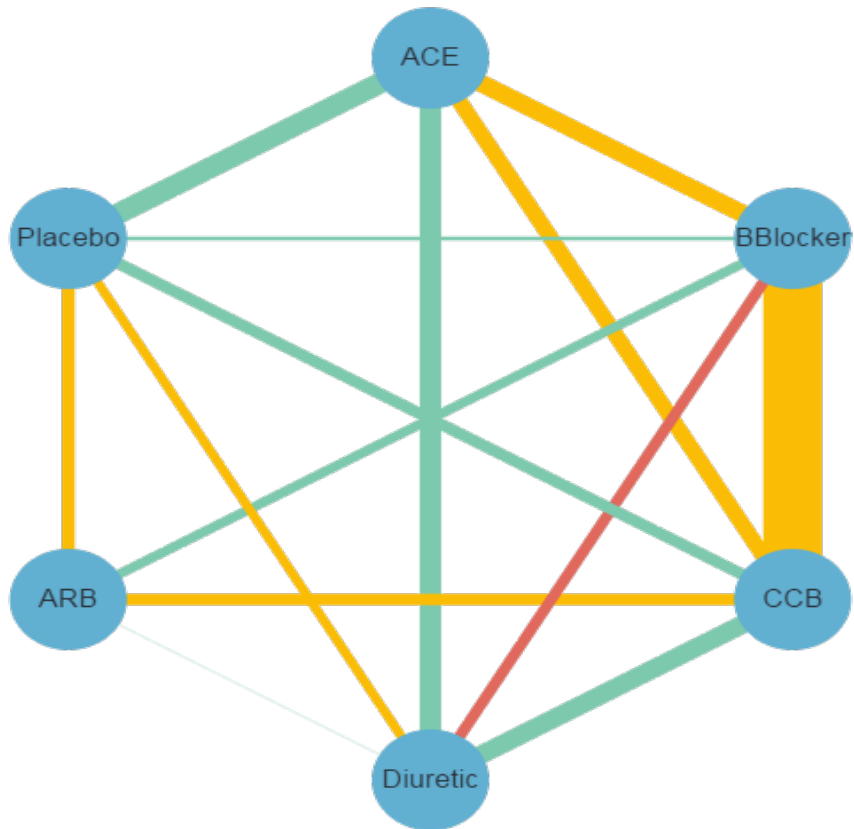
Form risk of bias judgements for each study.  
Consider selection, performance, attrition, detection and reporting bias



**CCB vs Diuretics:**  
overall low risk of bias

<u>Study name</u>	<u>Risk of Bias</u>
AASK	LOW
ALLHAT	LOW
ALPINE	LOW
ANBP-2	LOW
ASCOT	LOW
CAPPP	MODERATE
CHARM	LOW
DREAM	LOW
EWPHE	MODERATE
FEVER	LOW
HAPPHY	HIGH
HOPE	LOW
INSIGHT	LOW
INVEST	LOW
LIFE	LOW
MRC	LOW
NORDIL	LOW
PEACE	LOW
SCOPE	MODERATE
SHEP	LOW
STOP-2	MODERATE
VALUE	MODERATE





### Comparison

BB vs Placebo  
Diuretics  
CCB  
ACE  
ARB

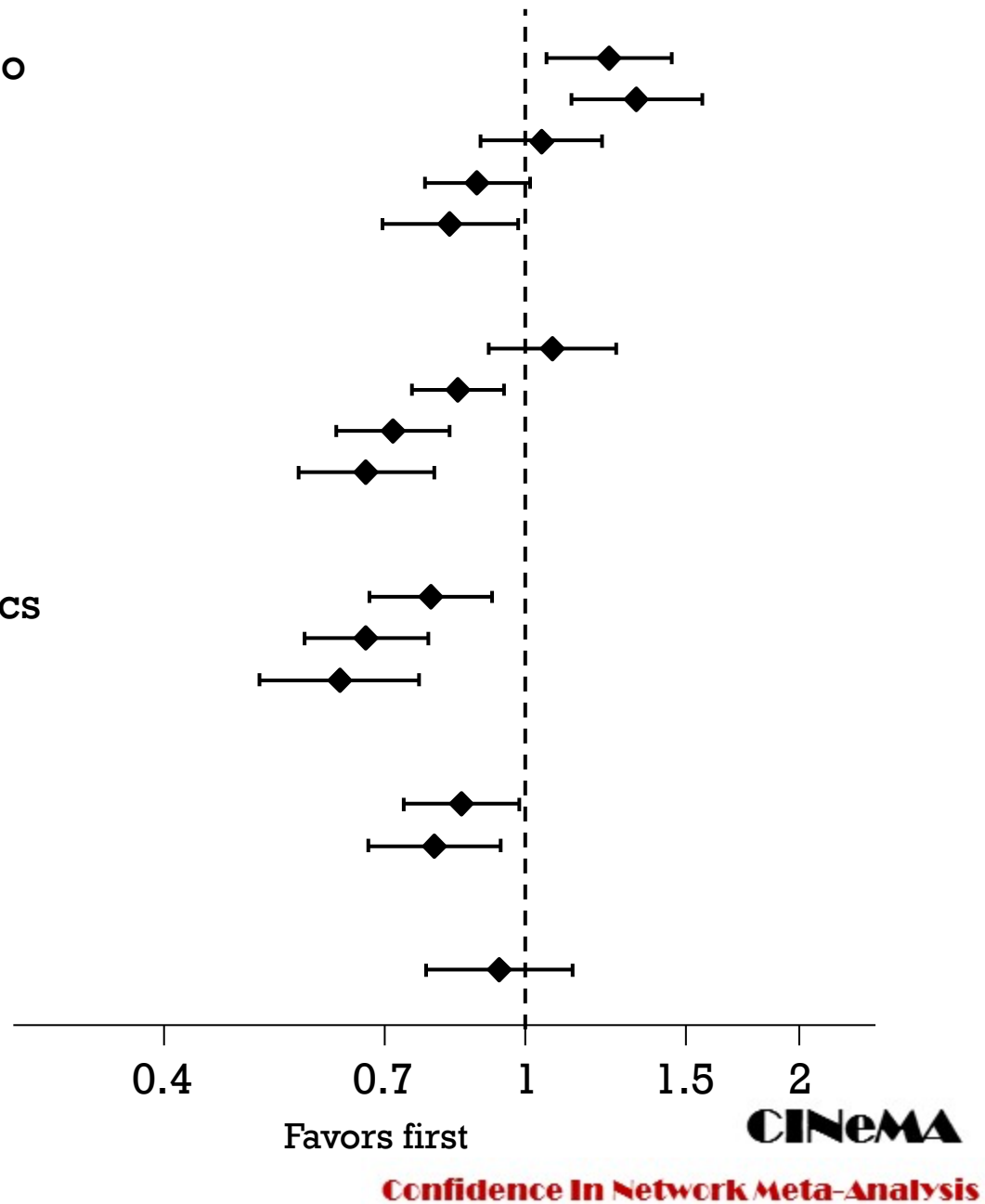
Diuretics vs BB  
CCB  
ACE  
ARB

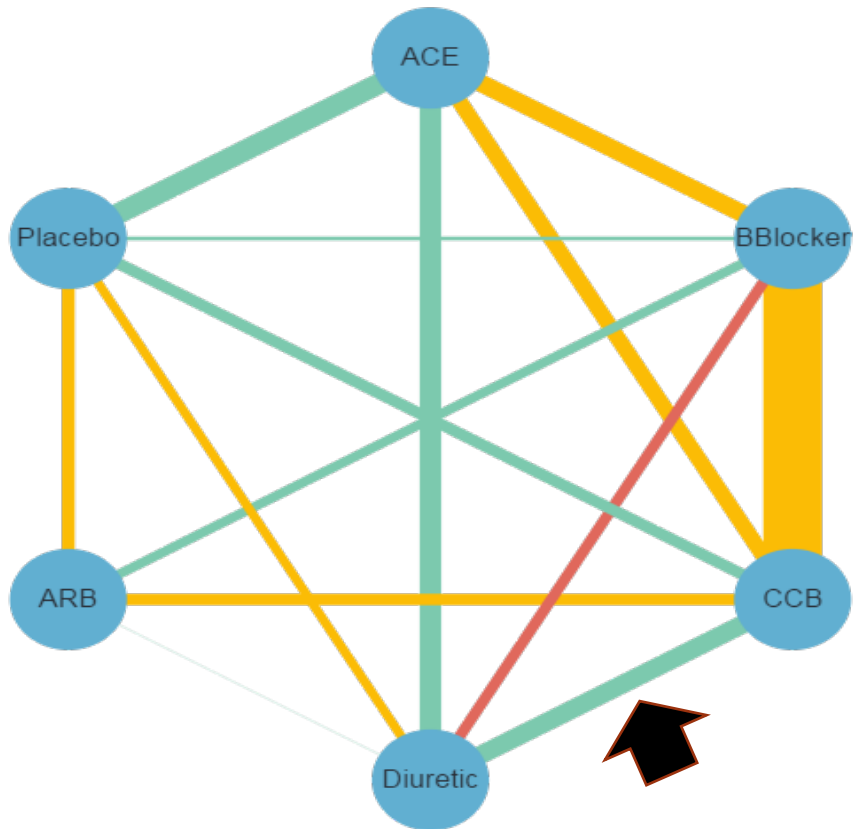
CCB vs Diuretics  
ACE  
ARB

ACE vs CCB  
ARB

ARB vs ACE

### OR from NMA





### Comparison

BB vs Placebo  
Diuretics  
CCB  
ACE  
ARB

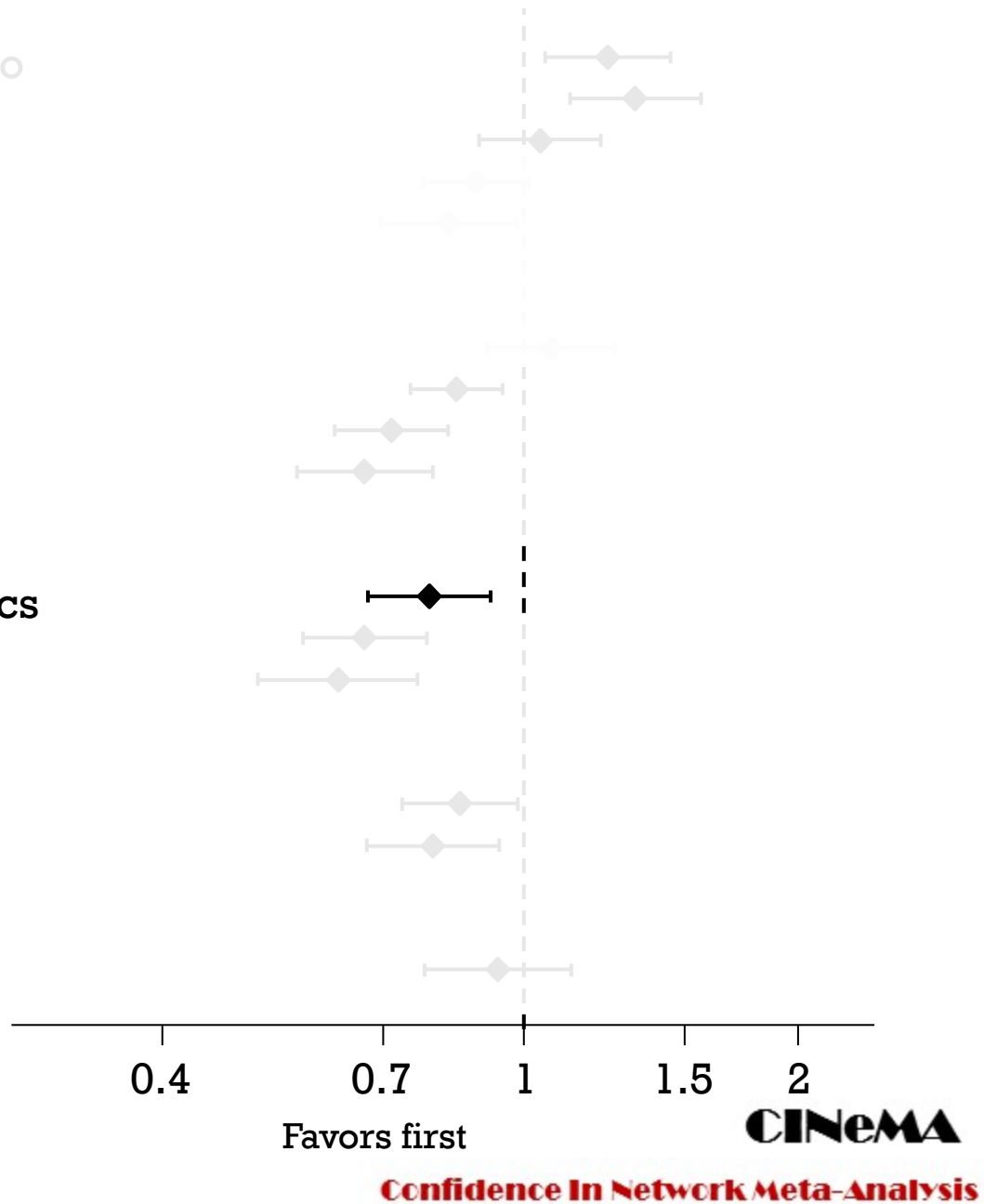
Diuretics vs BB  
CCB  
ACE  
ARB

**CCB vs Diuretics**  
ACE  
ARB

ACE vs CCB  
ARB

ARB vs ACE

### OR from NMA



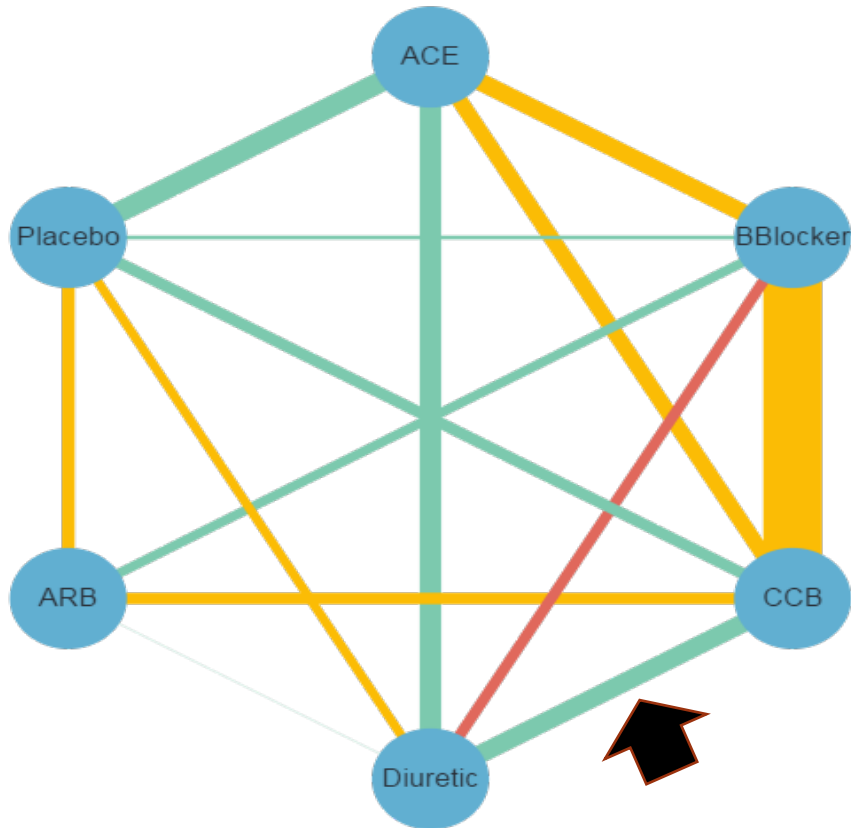
## Comparison

## OR from NMA

BB vs Placebo



*What is your judgement about study limitations for this (mixed) OR between CCB vs Diuretics estimated in network meta-analysis?*



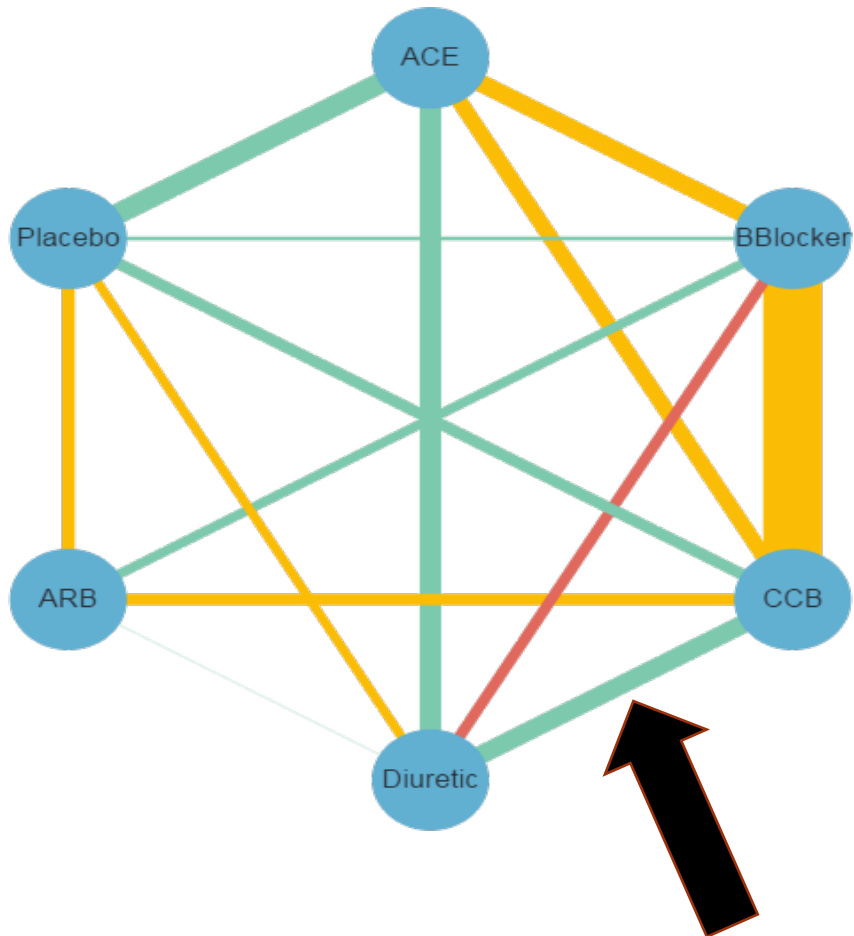
Major concerns

Some concerns

No concerns

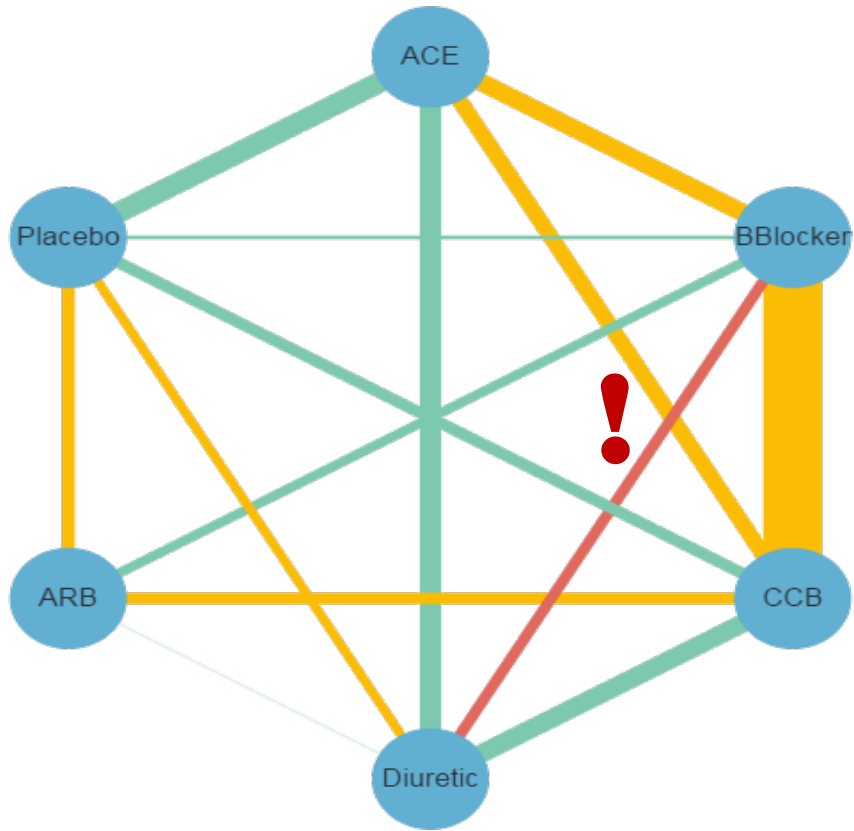
Go to:

[polllev.com/gmhbe](http://polllev.com/gmhbe)



your judgement about study limitations for the mixed OR between Diuretics estimated in network meta-analysis?



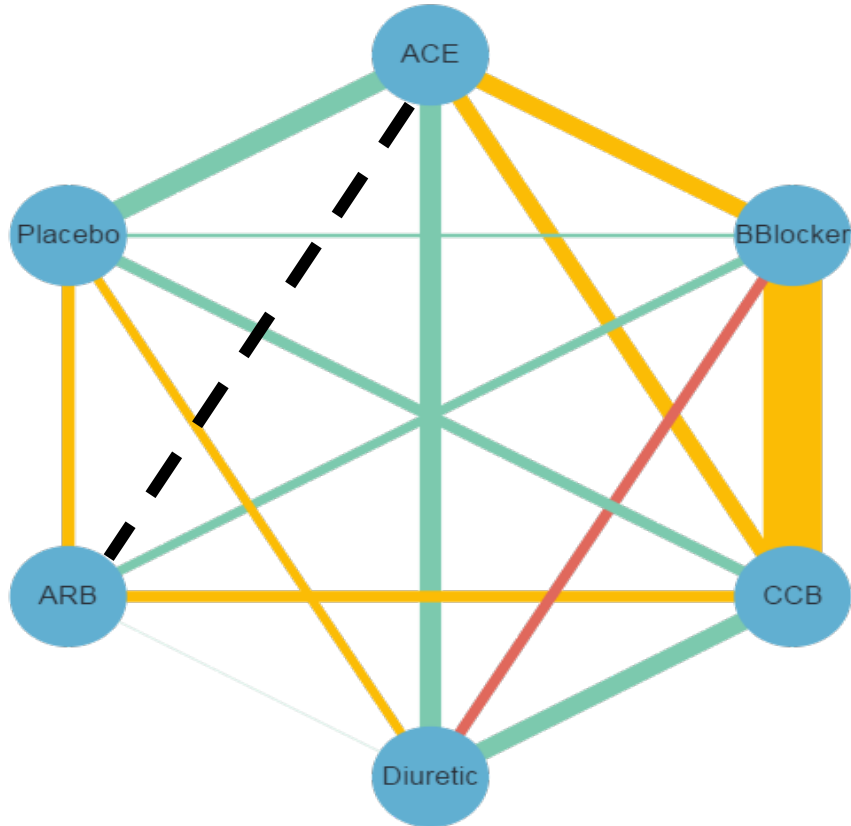


**Studies with high risk of bias contribute to the estimation of the OR CCB vs Diuretics!**

## Comparison

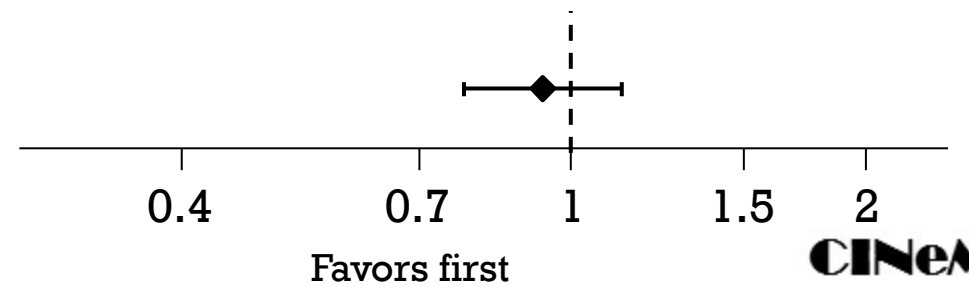
## OR from NMA

*What is your judgement about study limitations for this (indirect) OR for ACE vs ARB estimated in NMA?*

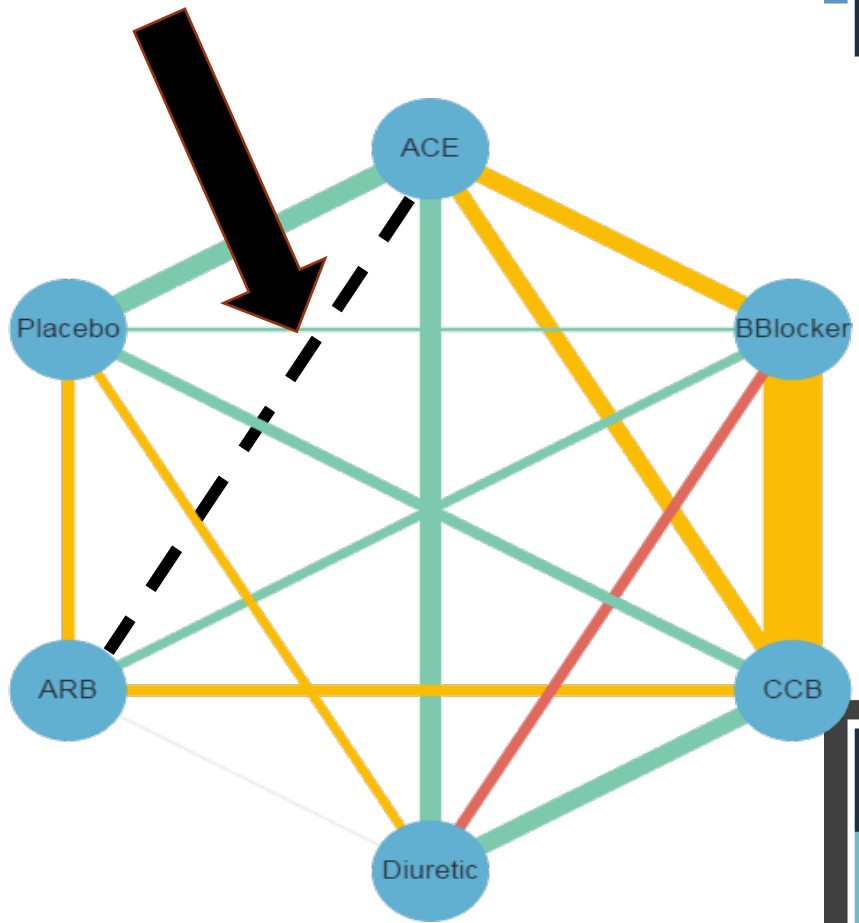


- Major concerns
- Some concerns
- No concerns

ARB vs ACE



our judgement about study limitations for the indirect OR between  
ARB estimated in network meta-analysis?



Major concerns

Some concerns

No concerns

**Start the presentation to activate live content**  
If you see this message in presentation mode, install the add-in or get help at [PollEv.com/app](https://PollEv.com/app)

An indirect or mixed treatment effect is a combination of the available direct treatment effects

## The contribution matrix

	ACE: BBlocker	ACE: CCB	ACE: Diuretic	ACE: Placebo	ARB: BBlocker	ARB: CCB	ARB: Diuretic	ARB: Placebo	BBlocker: CCB	BBlocker: Diuretic	BBlocker: Placebo	CCB: Diuretic	CCB: Placebo	Diuretic: Placebo
<b>Mixed estimates</b>														
ACE:BBlocker	32	10	10	8	6	1	0	4	15	6	2	5	2	0
ACE:CCB	10	26	13	11	1	6	0	4	9	1	0	13	6	0
ACE:Diuretic	6	7	57	5	0	2	0	2	1	5	0	12	2	2
ACE:Placebo	5	7	5	56	3	3	0	6	1	0	2	3	8	2
ARB:BBlocker	4	1	0	3	41	21	0	5	19	2	2	2	1	0
ARB:CCB	1	2	1	2	8	67	0	6	8	1	0	2	4	0
ARB:Diuretic	3	2	11	5	10	27	0	8	0	7	0	25	0	2
ARB:Placebo	3	3	2	7	6	15	0	49	0	1	2	2	10	1
BBlocker:CCB	6	4	1	1	11	12	0	0	53	4	2	5	2	0
BBlocker:Diuretic	10	1	13	2	5	3	0	2	19	20	2	21	0	2
BBlocker:Placebo	10	2	2	14	13	3	0	16	16	4	8	1	11	2
CCB:Diuretic	2	6	11	3	1	3	0	2	7	6	0	56	3	2
CCB:Placebo	2	6	4	12	1	15	0	16	6	0	2	5	28	2
Diuretic:Placebo	0	0	20	20	2	7	0	9	0	5	2	17	11	7
<b>Indirect estimates</b>														
ACE:ARB	10	11	8	16	11	20	0	14	1	1	0	7	2	0

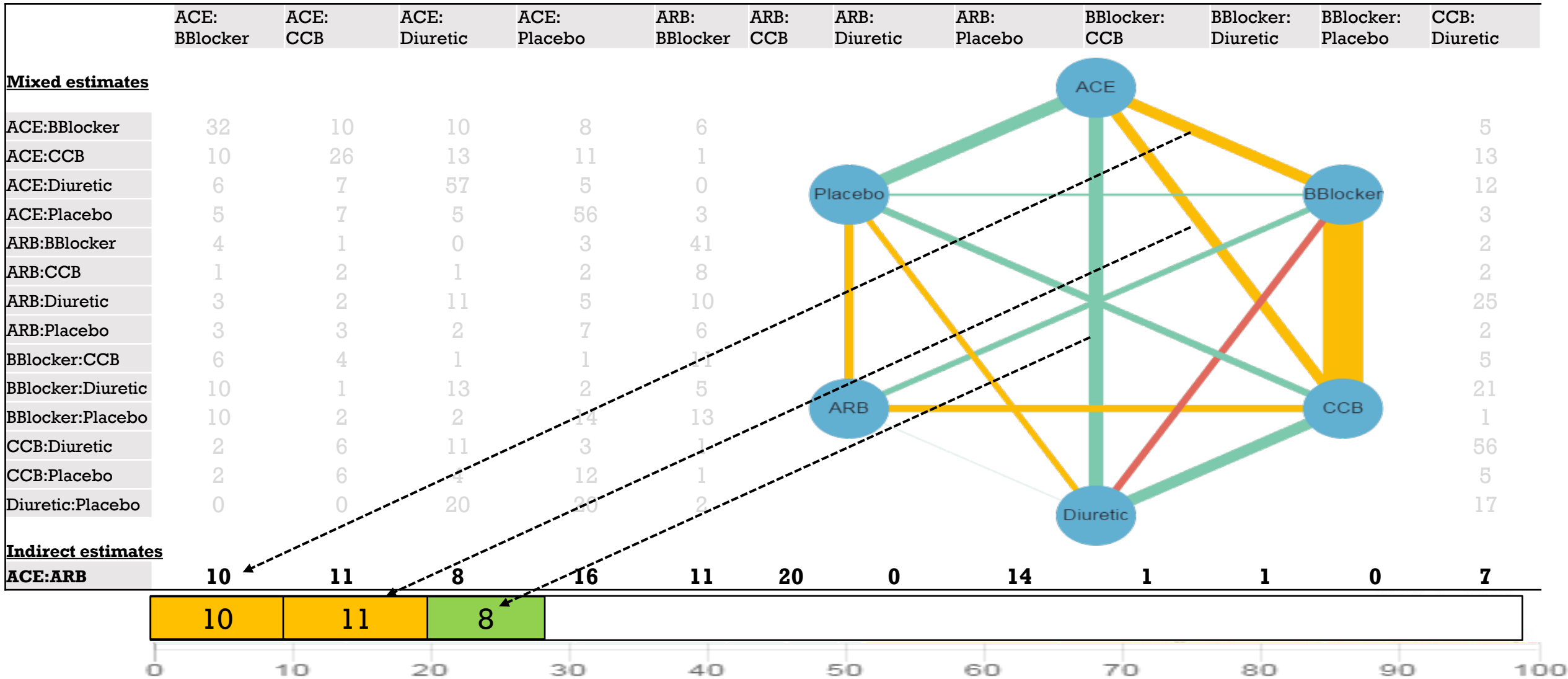


An indirect or mixed treatment effect is a combination of the available direct treatment effects

## The contribution matrix

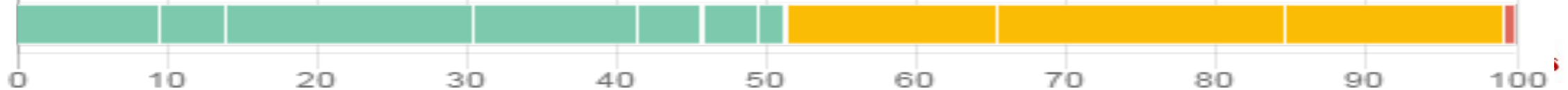
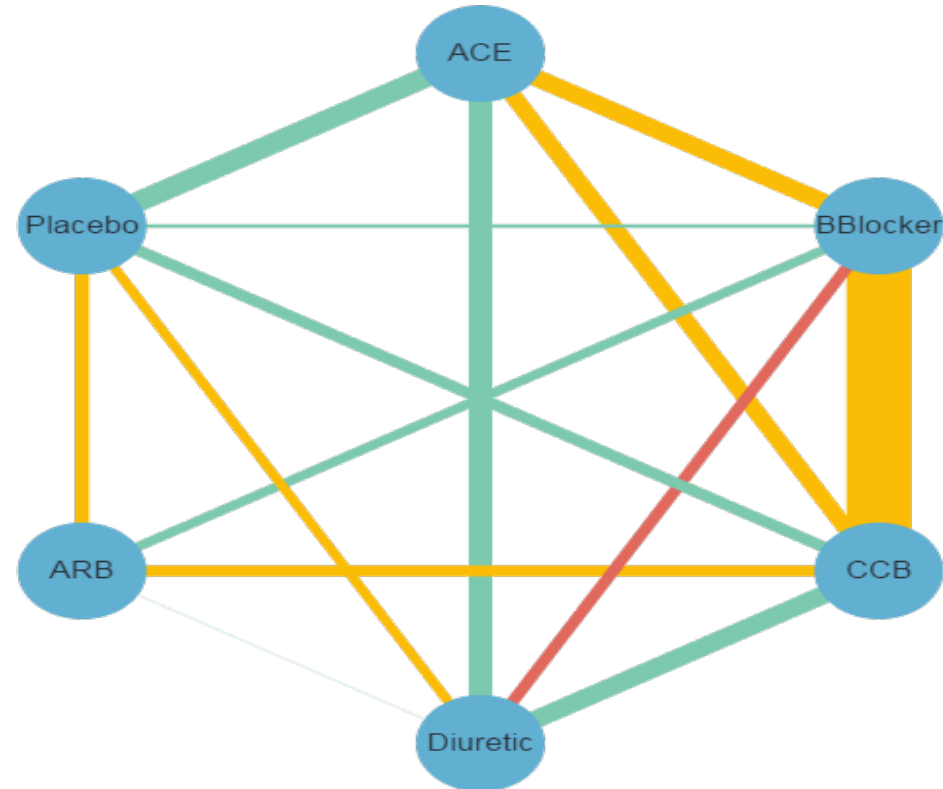
	ACE: BBlocker	ACE: CCB	ACE: Diuretic	ACE: Placebo	ARB: BBlocker	ARB: CCB	ARB: Diuretic	ARB: Placebo	BBlocker: CCB	BBlocker: Diuretic	BBlocker: Placebo	CCB: Diuretic	CCB: Placebo	Diuretic: Placebo
<b>Mixed estimates</b>														
ACE:BBlocker	32	10	10	8	6	1	0	4	15	6	2	5	2	0
ACE:CCB	10	26	13	11	1	6	0	4	9	1	0	13	6	0
ACE:Diuretic	6	7	57	5	0	2	0	2	1	5	0	12	2	2
ACE:Placebo	5	7	5	56	3	3	0	6	1	0	2	3	8	2
ARB:BBlocker	4	1	0	3	41	21	0	5	19	2	2	2	1	0
ARB:CCB	1	2	1	2	8	67	0	6	8	1	0	2	4	0
ARB:Diuretic	3	2	11	5	10	27	0	8	0	7	0	25	0	2
ARB:Placebo	3	3	2	7	6	15	0	49	0	1	2	2	10	1
BBlocker:CCB	6	4	1	1	11	12	0	0	53	4	2	5	2	0
BBlocker:Diuretic	10	1	13	2	5	3	0	2	19	20	2	21	0	2
BBlocker:Placebo	10	2	2	14	13	3	0	16	16	4	8	1	11	2
CCB:Diuretic	2	6	11	3	1	3	0	2	7	6	0	56	3	2
CCB:Placebo	2	6	4	12	1	15	0	16	6	0	2	5	28	2
Diuretic:Placebo	0	0	20	20	2	7	0	9	0	5	2	17	11	7
<b>Indirect estimates</b>														
ACE:ARB	10	11	8	16	11	20	0	14	1	1	0	7	2	0

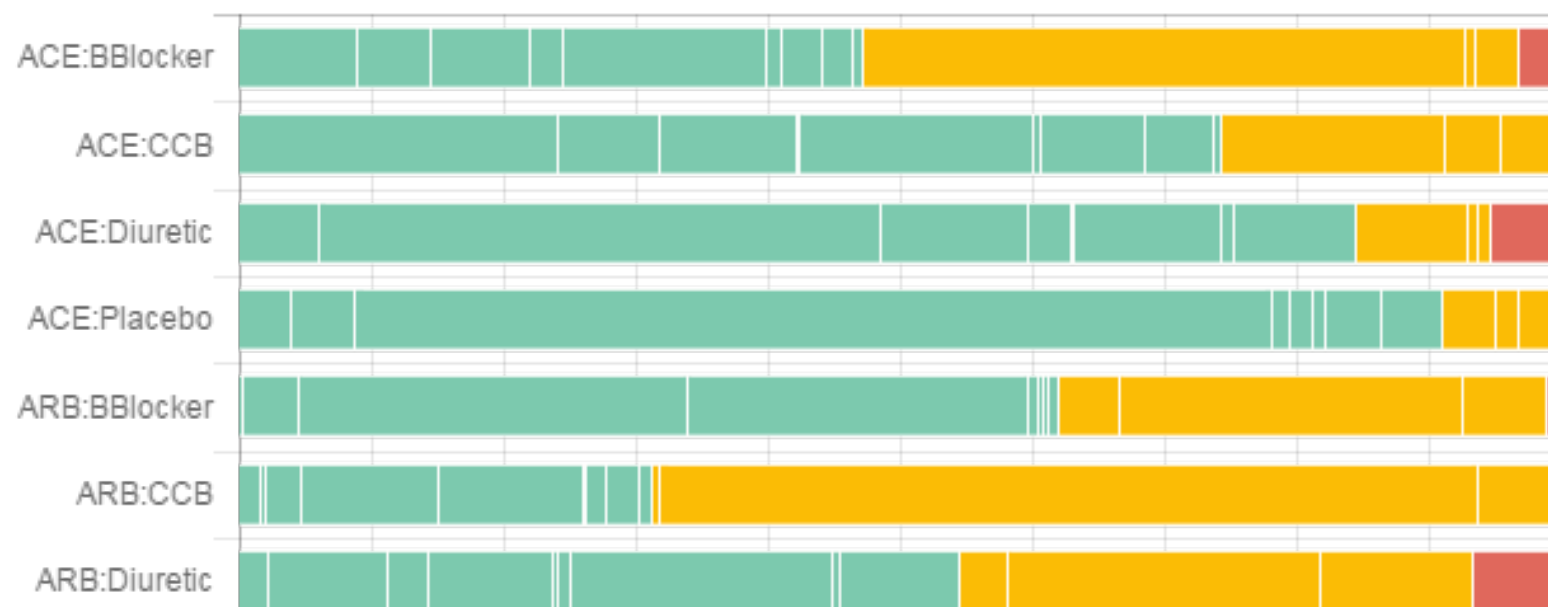
# The contribution matrix



# The contribution matrix

	ACE: BBlocker	ACE: CCB	ACE: Diuretic	ACE: Placebo	ARB: BBlocker	ARB: CCB	ARB: Diuretic	ARB: Placebo	BBlocker: CCB	BBlocker: Diuretic	BBlocker: Placebo	CCB: Diuretic
<b>Mixed estimates</b>												
ACE:BBlocker	32	10	10	8	6							5
ACE:CCB	10	26	13	11	1							13
ACE:Diuretic	6	7	57	5	0							12
ACE:Placebo	5	7	5	56	3							3
ARB:BBlocker	4	1	0	3	41							2
ARB:CCB	1	2	1	2	8							2
ARB:Diuretic	3	2	11	5	10							25
ARB:Placebo	3	3	2	7	6							2
BBlocker:CCB	6	4	1	1	11							5
BBlocker:Diuretic	10	1	13	2	5							21
BBlocker:Placebo	10	2	2	14	13							1
CCB:Diuretic	2	6	11	3	1							56
CCB:Placebo	2	6	4	12	1							5
Diuretic:Placebo	0	0	20	20	2							17
<b>Indirect estimates</b>												
<b>ACE:ARB</b>	<b>10</b>	<b>11</b>	<b>8</b>	<b>16</b>	<b>11</b>	<b>20</b>	<b>0</b>	<b>14</b>	<b>1</b>	<b>1</b>	<b>0</b>	<b>7</b>



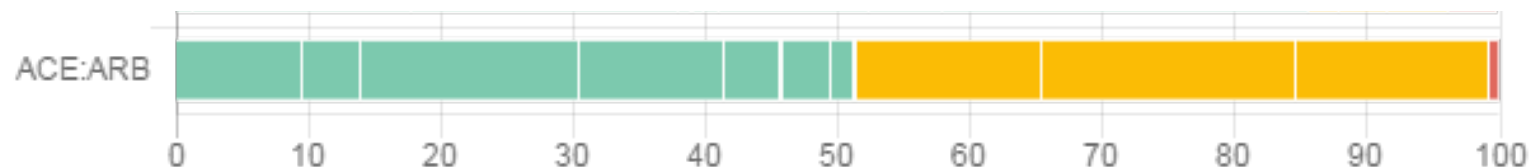


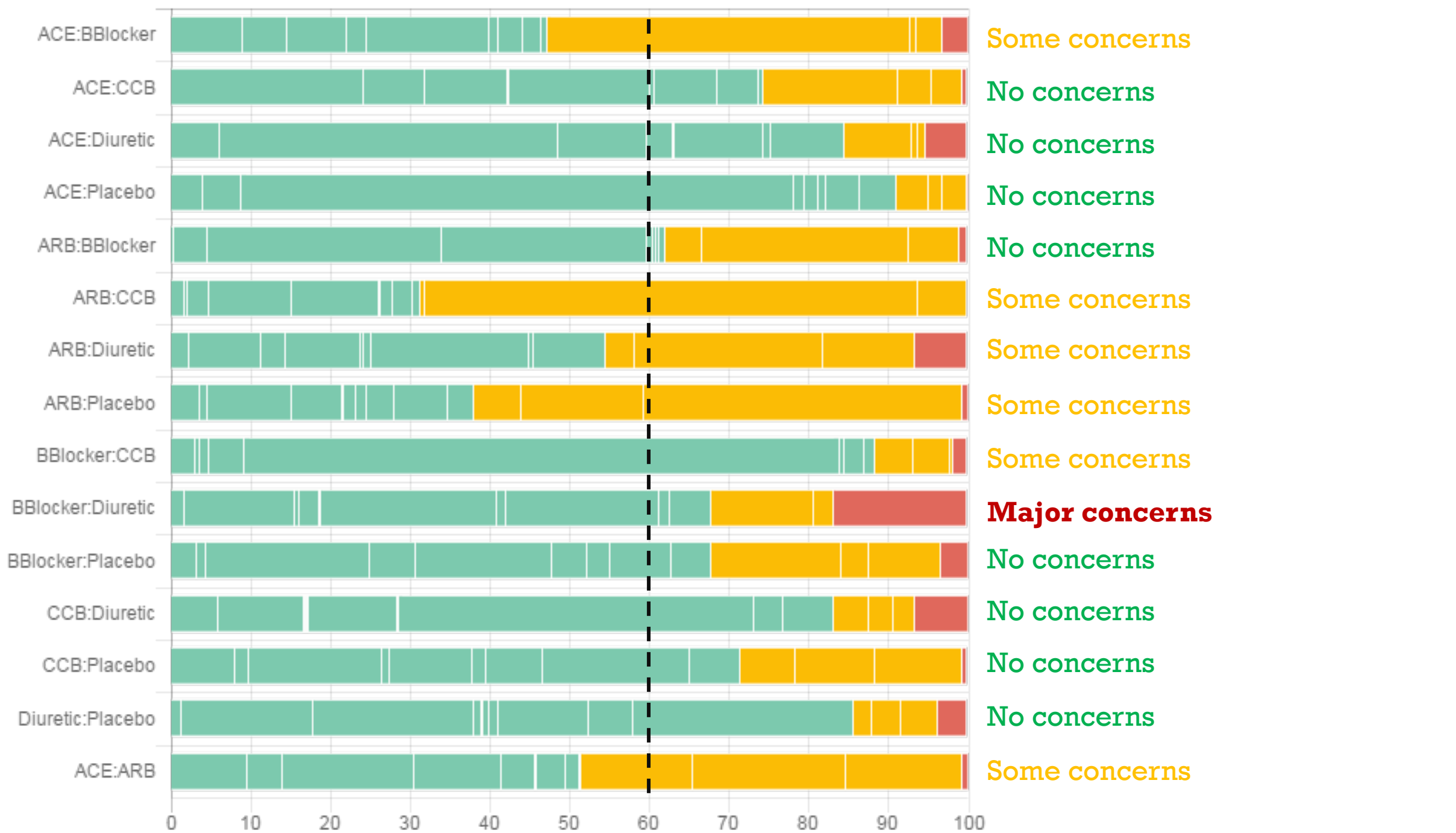
*What is your judgement about study limitation for this (indirect) OR for ACE vs ARB estimated in NMA?*

Major concerns

Some concerns

No concerns





# INDIRECTNESS

- Major concerns
- Some concerns
- No concerns

# INDIRECTNESS

- Considerations similar to those in a pairwise meta-analysis
- **How relevant is the study PICO and setting to the research question?**
- **Score each study at 3 levels**
  - **Low indirectness** to the research question
  - **Moderate indirectness** to the research question
  - **High indirectness** to the research question
- Then study-level judgements are summarized within pairwise comparisons and across the network using the contribution matrix exactly as with the Risk of Bias.
- This also addresses the condition of transitivity!
  - If the studies across comparisons have differences in important characteristics (e.g. effect modifiers) compared to the target population, then the transitivity assumption is challenged

Now it is time for....

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**Confidence In Network Meta-Analysis**



# IMPRECISION

- Major concerns
- Some concerns
- No concerns

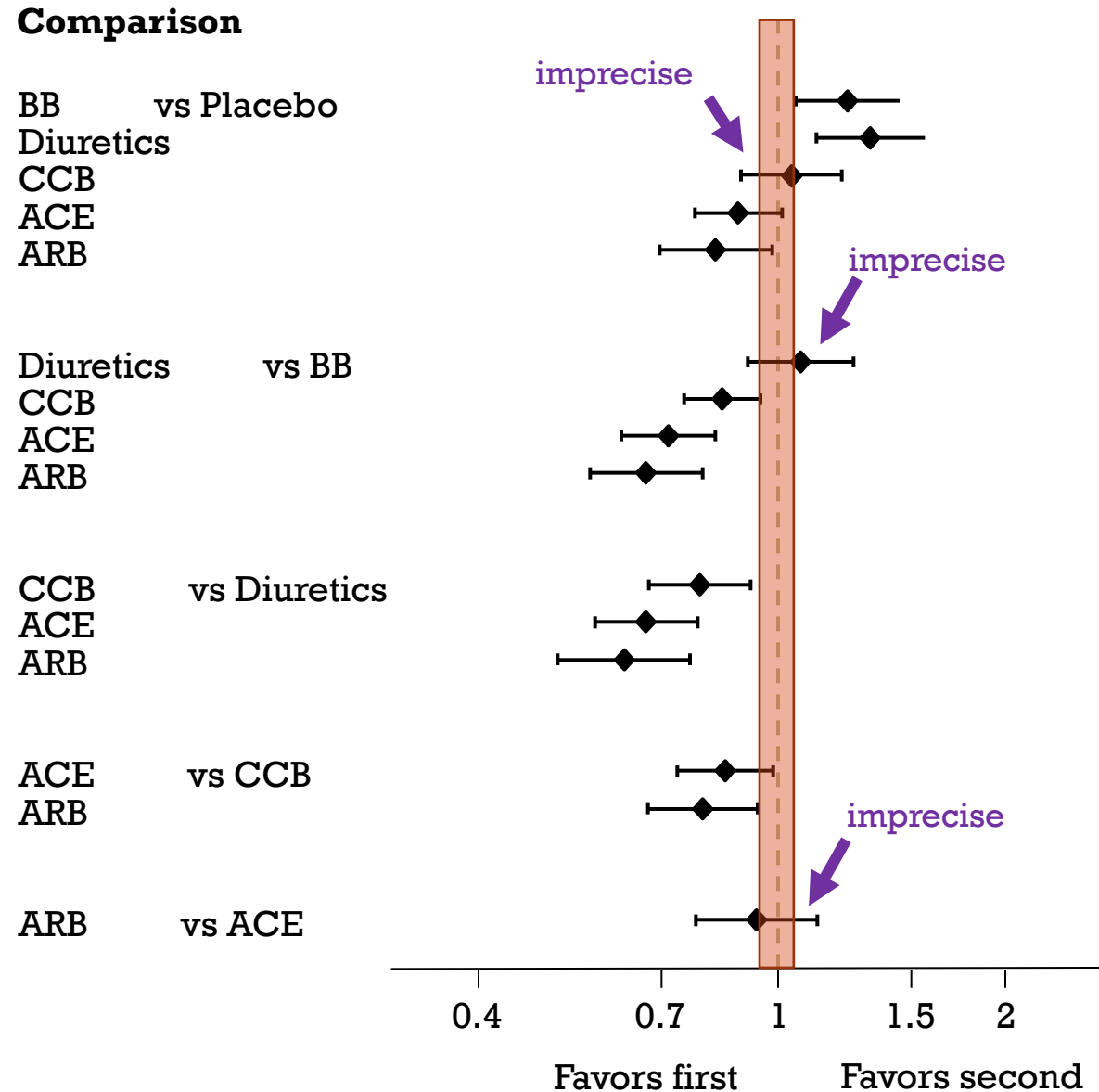
# IMPRECISION

- Traditional GRADE considers, among others, the total sample size available and compares it with the Optimal Information Size
- The sample size in a NMA relative effect makes little sense (as studies in the network contribute direct and indirect information!)
- Imprecision relates to the width of the 95% confidence interval:

**Does the 95% CI include values that lead to different clinical decisions?**

- Set a "[margin of equivalence](#)"
  - the range of relative treatment effect around the no-effect line that do not signify important differences between the interventions
  - Could be set using the Minimum Clinically Important Difference

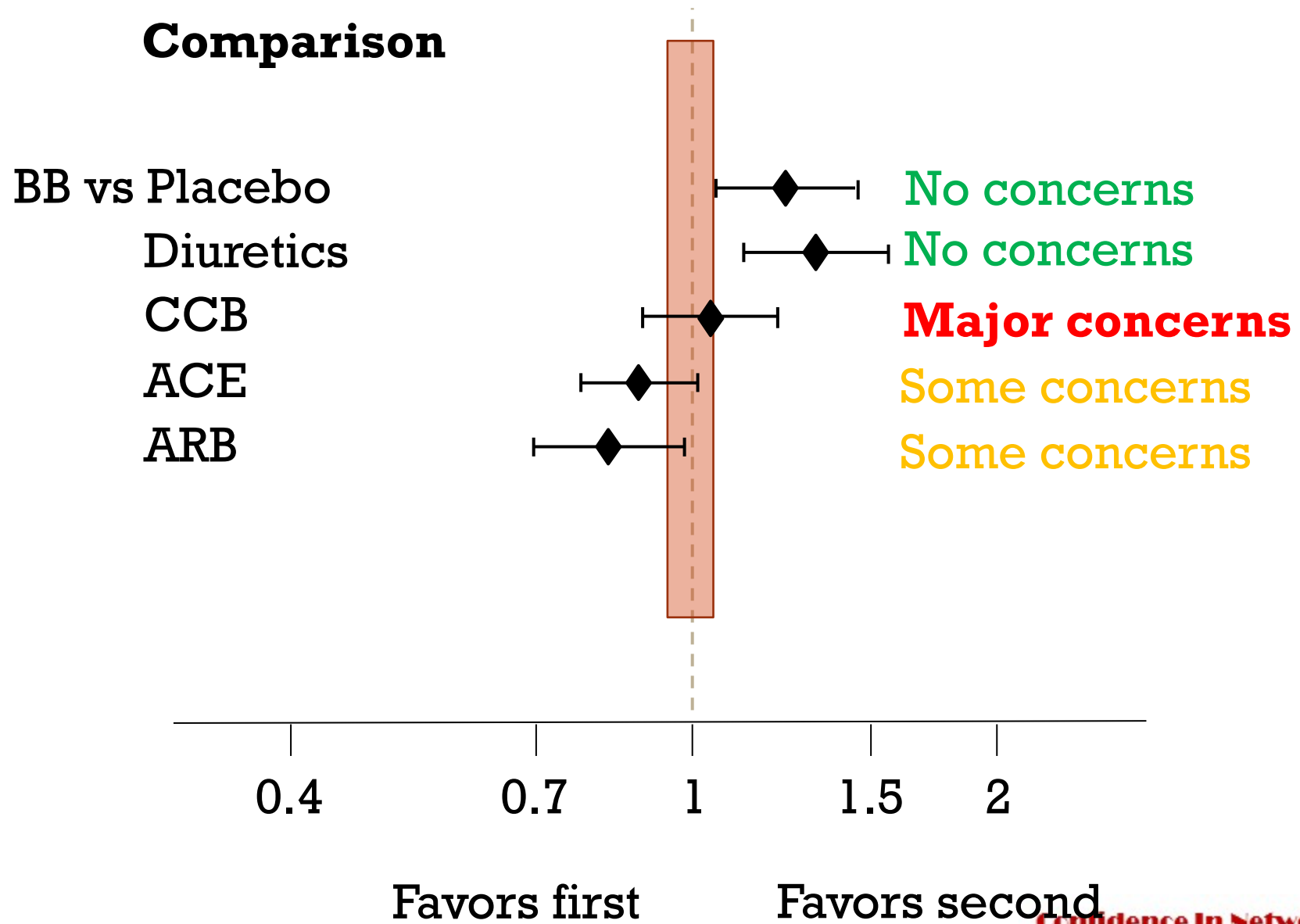
# NMA estimated odds ratios for diabetes



**Imprecision:** Confidence intervals include values that lead into different clinical decisions

Margin of equivalence:  
OR=1.05 in either direction  
Imprecision when the confidence interval **crosses both 0.95 and 1.05**

# NMA estimated odds ratios for diabetes



Now it is time for....

**CINEMA**

**CINEMA**

**Confidence In Network Meta-Analysis**

# INCONSISTENCY

## HETEROGENEITY

- Major concerns
- Some concerns
- No concerns

## INCOHERENCE

- Major concerns
- Some concerns
- No concerns

# INCONSISTENCY

## **Heterogeneity**

disagreement between  
variance within a  
comparison

# INCONSISTENCY HETEROGENEITY

- The major driver in judging heterogeneity is whether it impacts on clinical decisions
- Heterogeneity is represented by the **predictive intervals**: the intervals within which we expect to find the true effect size of a new study
- They are extensions of the confidence intervals



# INCONSISTENCY HETEROGENEITY

## Treatment Effect

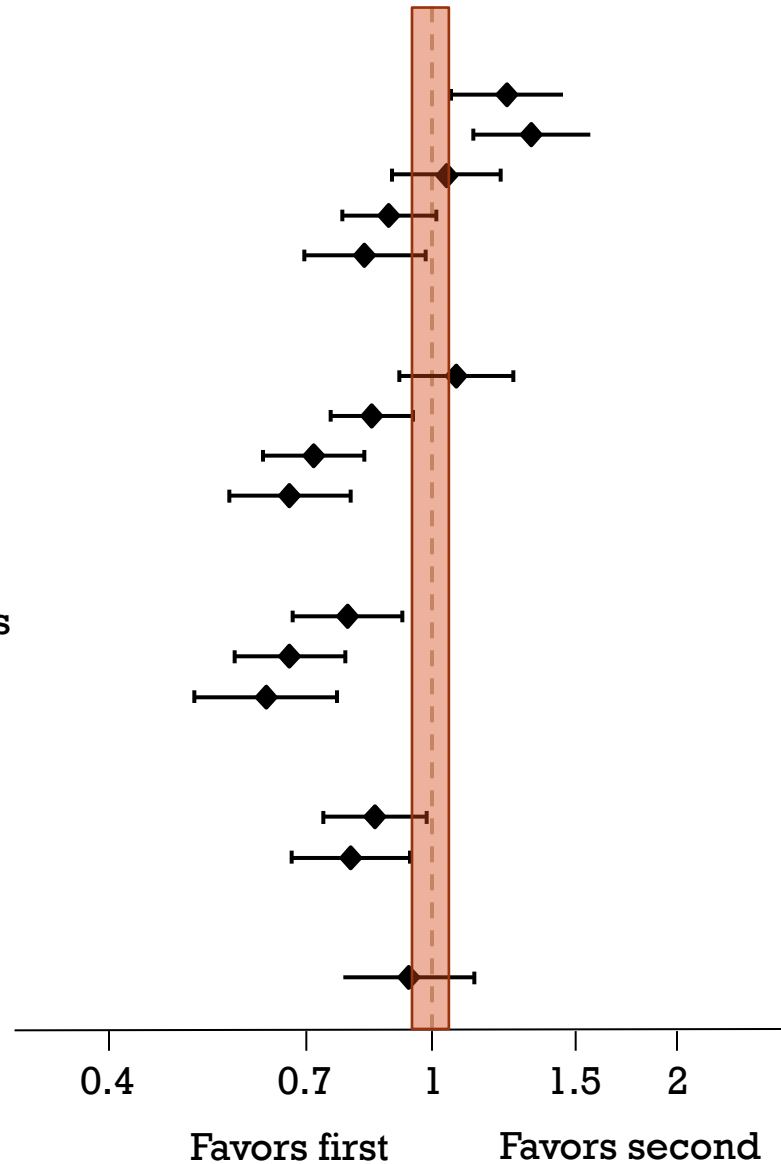
BB vs Placebo  
Diuretics  
CCB  
ACE  
ARB

Diuretics vs BB  
CCB  
ACE  
ARB

CCB vs Diuretics  
ACE  
ARB

ACE vs CCB  
ARB

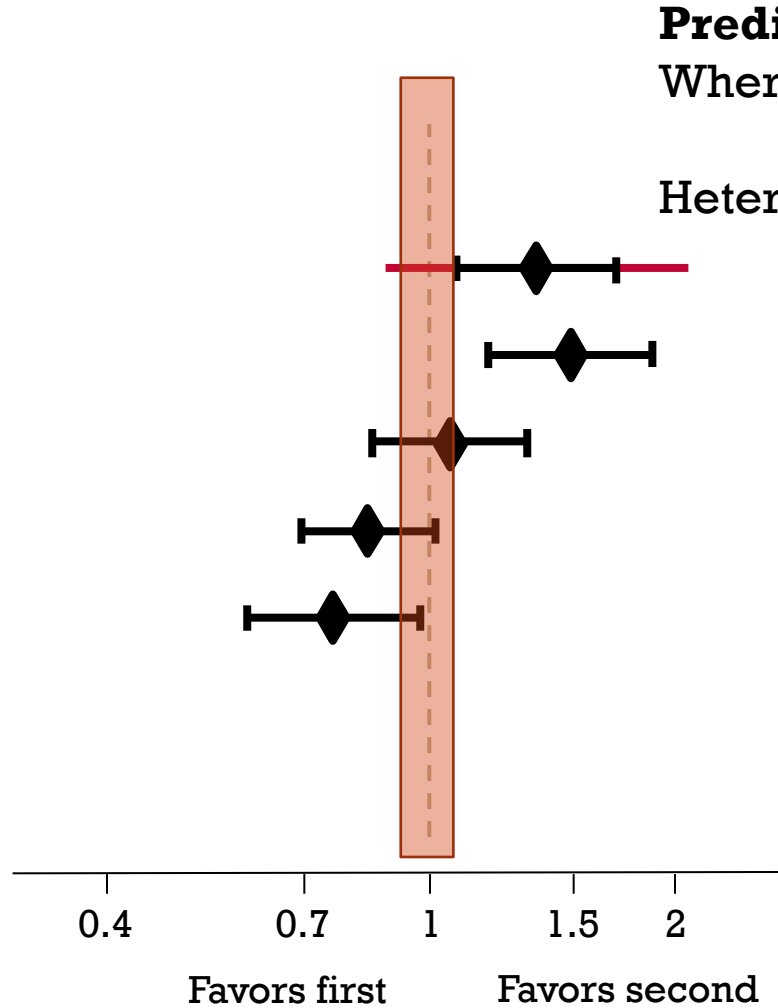
ARB vs ACE



# INCONSISTENCY HETEROGENEITY

**Treatment Effect**

BB vs Placebo  
Diuretics  
CCB  
ACE  
ARB



**Prediction interval:**

Where is the true effect in a new study?

Heterogeneity changes conclusions!

# INCONSISTENCY HETEROGENEITY

## Treatment Effect

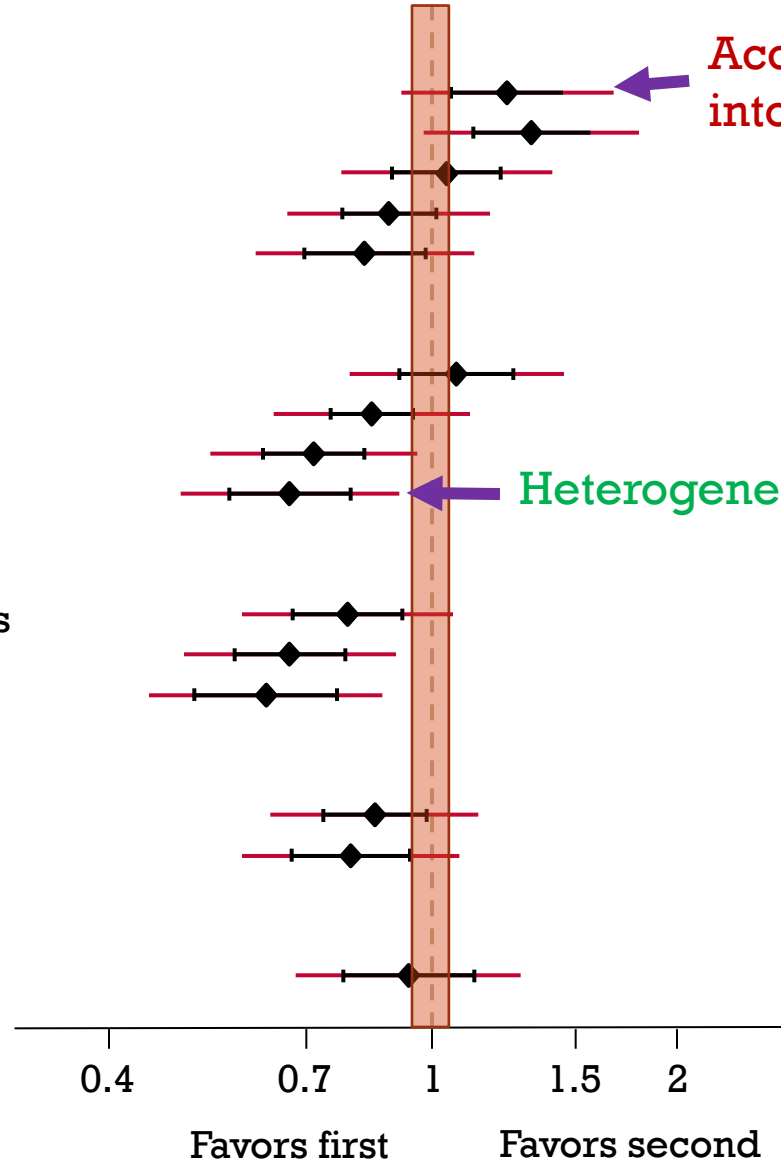
BB vs Placebo  
Diuretics  
CCB  
ACE  
ARB

Diuretics vs BB  
CCB  
ACE  
ARB

CCB vs Diuretics  
ACE  
ARB

ACE vs CCB  
ARB

ARB vs ACE

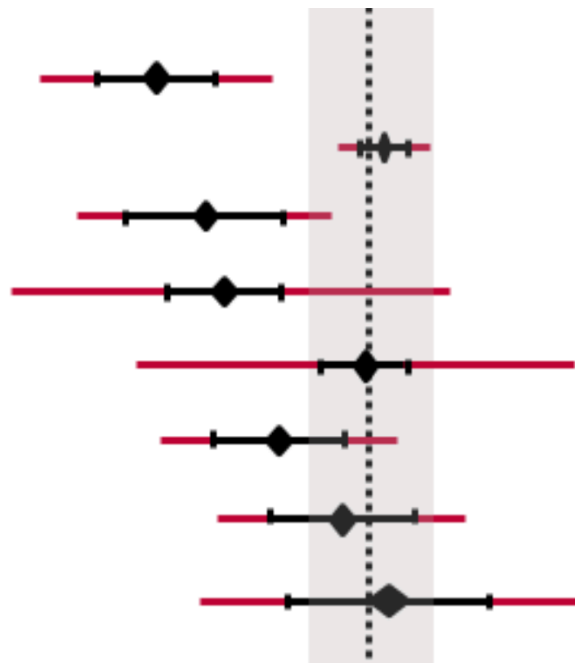


Accounting for heterogeneity leads into different clinical decisions!

Heterogeneity does not changes conclusions!

# INCONSISTENCY HETEROGENEITY

## Rules implemented in the software



↑  
Margin of  
equivalence

No concerns: Confidence and prediction intervals agree in relation to clinically important effect

No concerns: Confidence and prediction intervals agree in relation to clinically important effect

Some concerns: Prediction interval extends into clinically important or unimportant effects

Major concerns: Prediction interval extends into clinically important effects in both directions

Major concerns: Prediction interval extends into clinically important effects in both directions

No concerns: Confidence and prediction intervals agree in relation to clinically important effect

Some concerns: Prediction interval extends into clinically important or unimportant effects

No concerns: Confidence and prediction intervals agree in relation to clinically important effect

**Prediction interval** ———  
**Confidence interval** ———

# INCONSISTENCY HETEROGENEITY

- The major driver of our decisions is whether the heterogeneity impacts on clinical decisions
- Heterogeneity is represented by the **predictive intervals**: the intervals within which we expect to find the true effect size of a new study
- They are extensions of the confidence intervals
- **Pairwise meta-analysis heterogeneity variances  $\tau^2$  can be estimated**
  - But their estimation makes sense when you have enough studies
  - The observed values of  $\tau^2$  can be compared with the expected values from empirical evidence (*Turner et al Int J Epidemiol. 2012, Rhodes et al. J Clin Epidemiol. 2015*)
  - The expected values depend on the nature of the outcome and the treatments being compared

# INCONSISTENCY HETEROGENEITY

Comparison	ACE:BBlocker
Evidence: mixed	
Between-study heterogeneity for each direct comparison	
$I^2$ :	49.8%
Estimated $\tau^2$ :	0.019
Reference Values for $\tau^2$	
first quantile:	0.003
median:	0.014
third quantile:	0.061
95% intervals for NMA estimate	
Confidence interval:	(1.245,1.498)
Prediction interval:	(0.992,1.879)
<i>Prediction interval extends into clinically important or unimportant effects</i>	
Heterogeneity judgement	Serious

Comparison	ARB:BBlocker
Evidence: mixed	
Between-study heterogeneity for each direct comparison	
$I^2$ :	NA
Estimated $\tau^2$ :	NA
Reference Values for $\tau^2$	
first quantile:	0.003
median:	0.014
third quantile:	0.061
95% intervals for NMA estimate	
Confidence interval:	(1.372,1.657)
Prediction interval:	(1.094,2.077)
<i>Confidence and prediction intervals agree in relation to clinically important effect</i>	
Heterogeneity judgement	No serious

Comparison	BBlocker:CCB
Evidence: mixed	
Between-study heterogeneity for each direct comparison	
$I^2$ :	62.5%
Estimated $\tau^2$ :	0.013
Reference Values for $\tau^2$	
first quantile:	0.003
median:	0.014
third quantile:	0.061
95% intervals for NMA estimate	
Confidence interval:	(0.768,0.871)
Prediction interval:	(0.600,1.115)
<i>Prediction interval extends into clinically important effects in both directions</i>	
Heterogeneity judgement	Very Serious

# INCONSISTENCY

**Heterogeneity**  
between-study  
variance within a  
comparison

**Incoherence**  
disagreement between  
different sources of  
evidence

We consider prediction intervals for the **impact of heterogeneity** in clinical decision making

# INCONSISTENCY

**Heterogeneity**  
between-study  
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We consider prediction intervals for the **impact of heterogeneity** in clinical decision making

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disagreement between  
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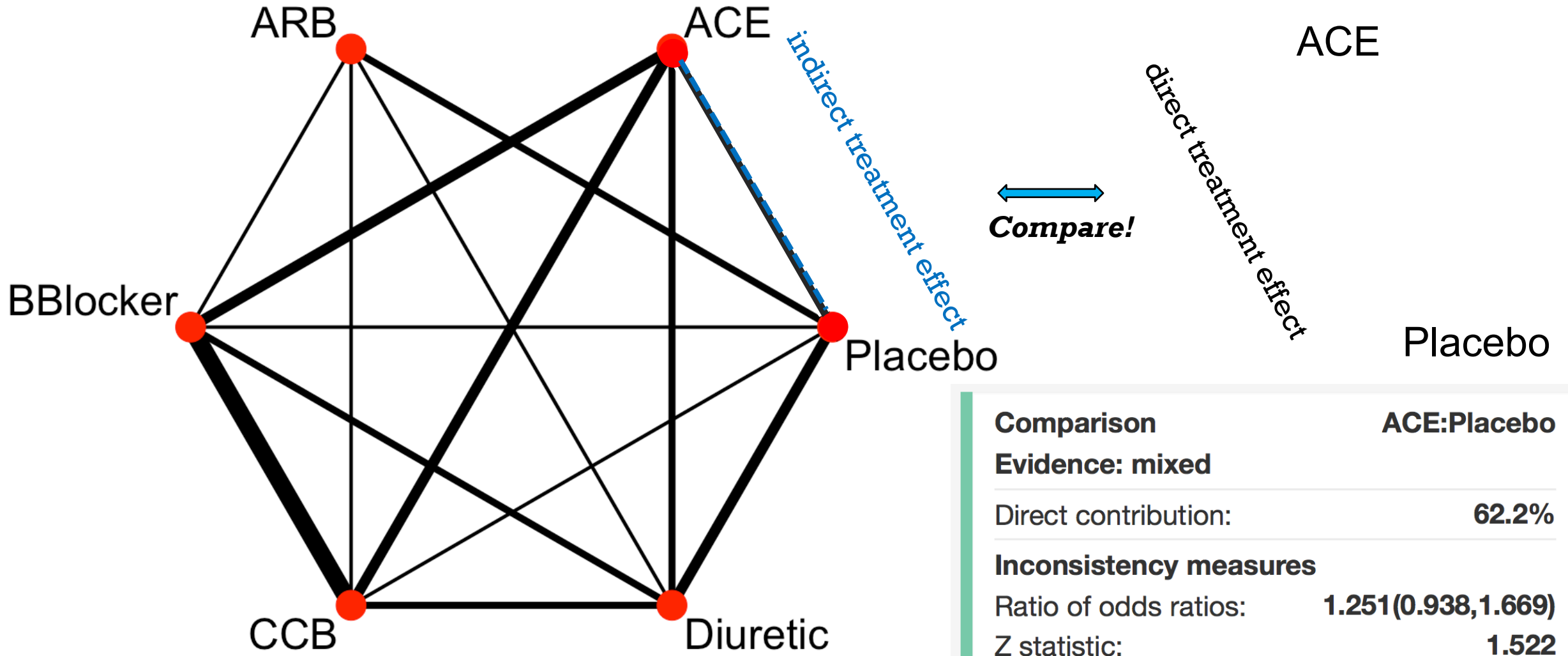
**Separate Direct from Indirect Evidence test** (node-splitting)  
: Compare direct and indirect relative treatment effects using a Z-test  
: one test for each treatment comparisons

**Design-by-treatment test  $X^2$**   
: one test for the network



# INCONSISTENCY INCOHERENCE

Separate Direct from Indirect Evidence test



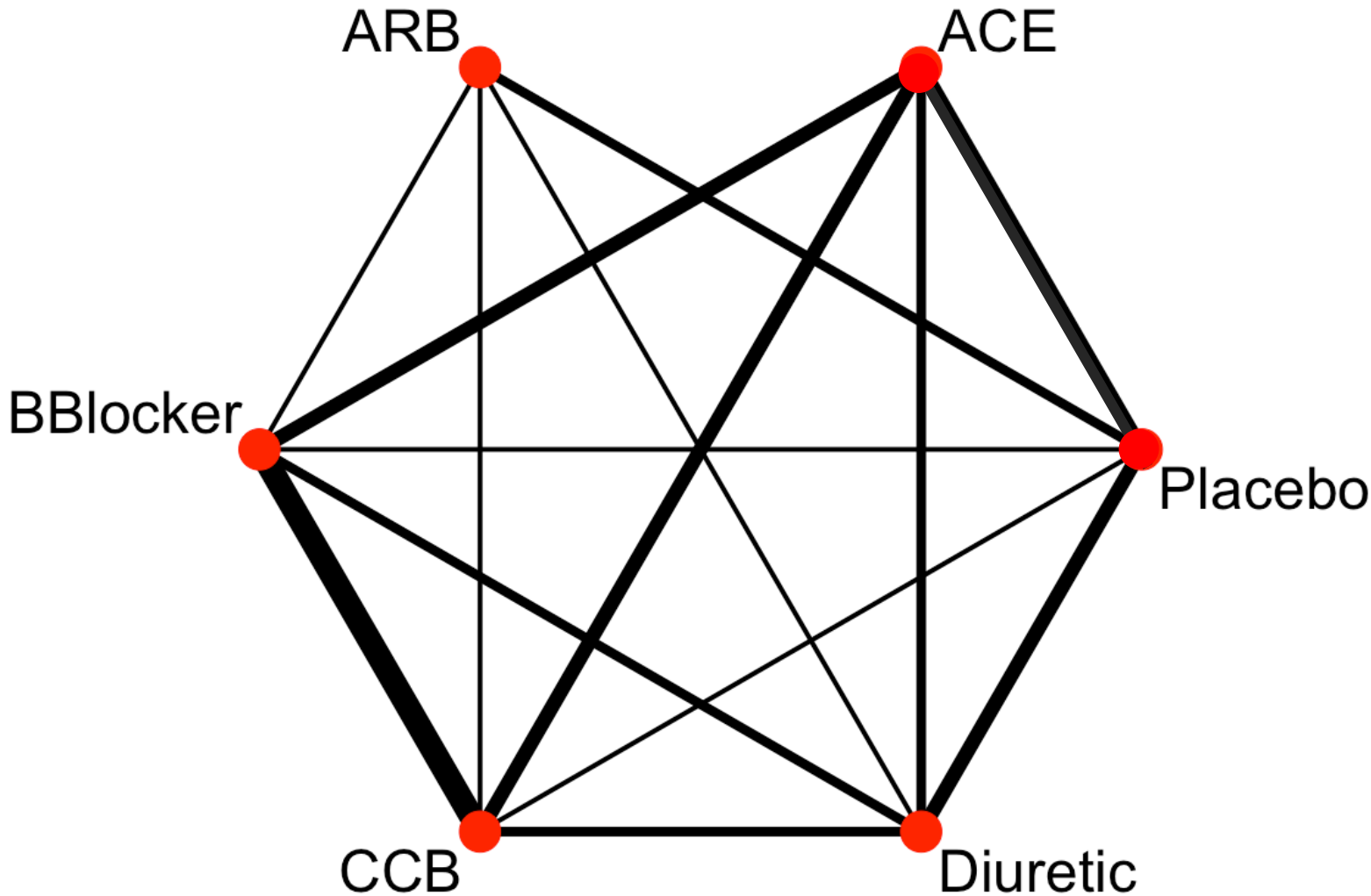
Comparison	ACE:Placebo
Evidence: mixed	
Direct contribution:	62.2%
<b>Inconsistency measures</b>	
Ratio of odds ratios:	1.251 (0.938, 1.669)
Z statistic:	1.522
P value:	0.128

# INCONSISTENCY INCOHERENCE

Design-by-treatment  $\chi^2$  test

Does the assumption of coherence hold for the entire network?

$\chi^2 = 19.325$  (13 df)  
P-value=0.113



CINEMA

Confidence In Network Meta-Analysis

# INCONSISTENCY INCOHERENCE

Treatment comparisons that take at least 90% of the information from direct evidence have no concerns for incoherence

For comparisons with at least 10% of information derived from indirect evidence we use the following rules

## Design-by-treatment interaction model

		$p\text{-value} > 0.1$	$0.01 < p\text{-value} < 0.1$	$p\text{-value} < 0.01$
<b>SIDE</b>	$p\text{-value} > 0.1$	No concerns	No concerns	Some concerns
	$0.01 < p\text{-value} < 0.1$	Some concerns	Some concerns	Major concerns
	$p\text{-value} < 0.01$	Some concerns	Major concerns	Major concerns

# INCONSISTENCY INCOHERENCE

**Comparison** ACE:BBlocker

**Evidence: mixed**

Direct contribution: 51.4%

**Inconsistency measures**

Ratio of odds ratios: 0.719(0.533,0.969)

Z statistic: -2.165

P value: 0.030

Incoherence judgement

Some concerns

**Comparison** ACE:CCB

**Evidence: mixed**

Direct contribution: 41.5%

**Inconsistency measures**

Ratio of odds ratios: 1.099(0.810,1.490)

Z statistic: 0.605

P value: 0.545

Incoherence judgement

No concerns

**Comparison** ARB:CCB

**Evidence: mixed**

Direct contribution: 41.7%

**Inconsistency measures**

Ratio of odds ratios: 1.012(0.709,1.444)

Z statistic: 0.066

P value: 0.948

Incoherence judgement

No concerns

**Comparison** ARB:Diuretic

**Evidence: mixed**

Direct contribution: 1.0%

**Inconsistency measures**

Ratio of odds ratios: 5.247(0.634,43.445)

Z statistic: 1.537

P value: 0.124

Incoherence judgement

No concerns

**Comparison** BBlocker:Placebo

**Evidence: mixed**

Direct contribution: 9.5%

**Inconsistency measures**

Ratio of odds ratios: 0.524(0.299,0.918)

**Comparison** CCB:Diuretic

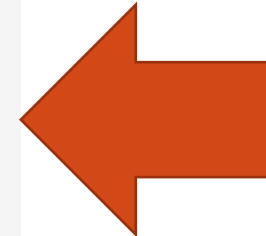
**Evidence: mixed**

Direct contribution: 48.0%

**Inconsistency measures**

Ratio of odds ratios: 0.932(0.676,1.286)

Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis. Res Synth Meth 2012



# PUBLICATION BIAS

- Suspected
- Undetected

<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>ACE:BBlocker</b> <input checked="" type="checkbox"/> Undetected <input type="checkbox"/> Suspected	<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>ACE:CCB</b> <input type="checkbox"/> Undetected
<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>ACE:Placebo</b> <input type="checkbox"/> Undetected	<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>ARB:BBlocker</b> <input type="checkbox"/> Undetected
<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>ARB:Diuretic</b> <input type="checkbox"/> Undetected	<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>ARB:Placebo</b> <input type="checkbox"/> Undetected
<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>BBlocker:Diuretic</b> <input type="checkbox"/> Undetected	<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>BBlocker:Placebo</b> <input type="checkbox"/> Undetected
<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>CCB:Placebo</b> <input type="checkbox"/> Undetected	<b>Comparison</b> <b>Evidence: mixed</b> Publication bias judgement	<b>Diuretic:Placebo</b> <input type="checkbox"/> Undetected

Now it is time for....

**CINEMA**

**CINEMA**

**Confidence In Network Meta-Analysis**

# DISCLAIMER

You are welcome to use CINeMA with the understanding that it is still under development

- We will improve the data input module
- We will fix some known bugs in the calculations
- For some calculations CINeMA the `netmeta` package in R, so updates/debugging in `netmeta` affect CINeMA too
- Please notify us for any problems you come across [cinema.ispm@gmail.com](mailto:cinema.ispm@gmail.com)
- If you use it in a publication you can cite

**CINeMA: Confidence in Network Meta-Analysis [Software].  
University of Bern 2017. Available from [cinema.ispm.ch](http://cinema.ispm.ch)**

**CINeMA**

**Confidence In Network Meta-Analysis**