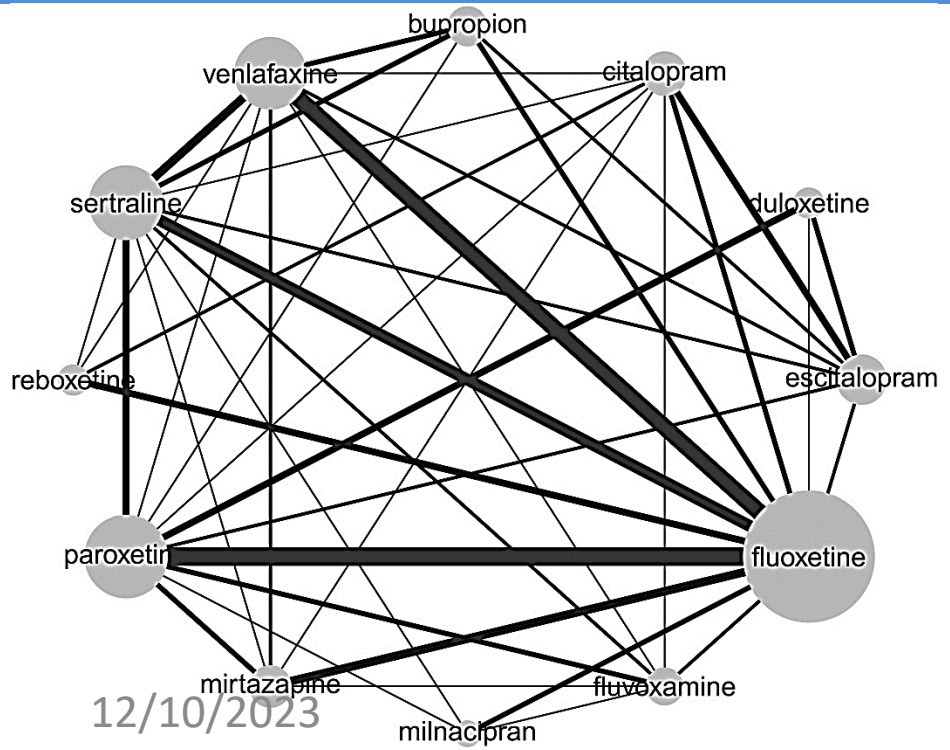
متاآنالیز شبکه ای : درک مفاهیم و کاربرد عملی



دکتر محمد حیدری

استادیار اپیدمیولوژی

گروه اپیدمیولوژی و آمار زیستی ، دانشکده پزشکی

دانشگاه علوم پزشکی ارومیه

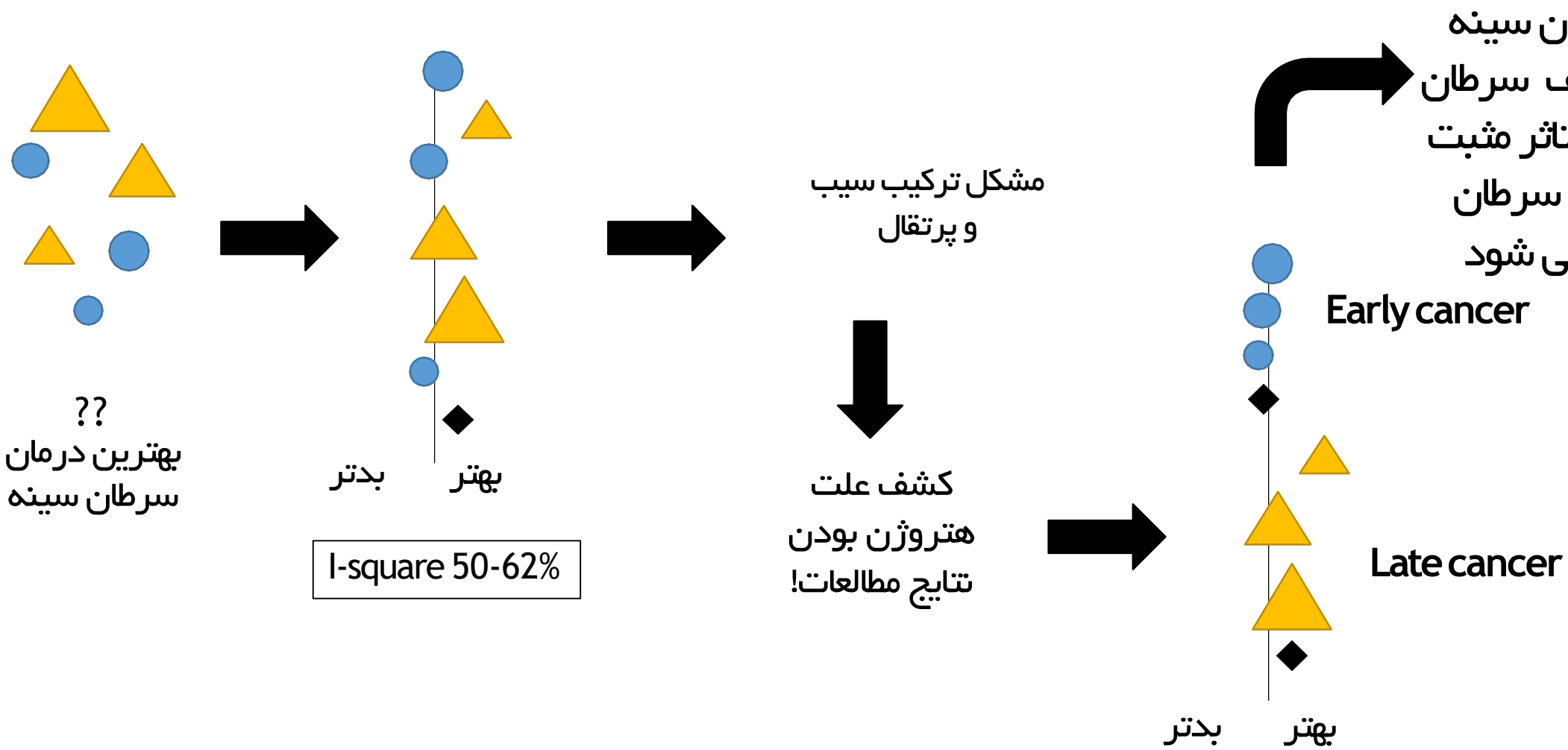
۱۹ آذر ۱۴۰۲

ایمیل : heidari.m@umsu.ac.ir

مشکل بزرگ پزشکی مدرن :

- وجود دریایی از داده ها و مقالات
- تفسیر نتایج متناقض

قصه متاآنالیز:



مزایای متاآنالیز:

- فهم اینکه تاثیر درمان های مختلف در شرایط متفاوت چگونه است
- یافتن اینکه چه وقت درمان نتیجه منفی دارد
- ترکیب حجم عظیمی از اطلاعات بصورت چیزی قابل استفاده
- شناخت کیفیت مطالعات مختلف
- بسیار مورد علاقه سیاستگذاران سلامت
- ارجاع خوردن بالا و بسیار تاثیرگذار

David M. Eddy:آغاز متاآنالیز شبکه ای

THE CONFIDENCE PROFILE METHOD: A BAYESIAN METHOD FOR ASSESSING HEALTH TECHNOLOGIES

DAVID M. EDDY

Duke University, Durham, North Carolina

(Received November 1986; revisions received September 1987, February 1988; accepted April 1988)

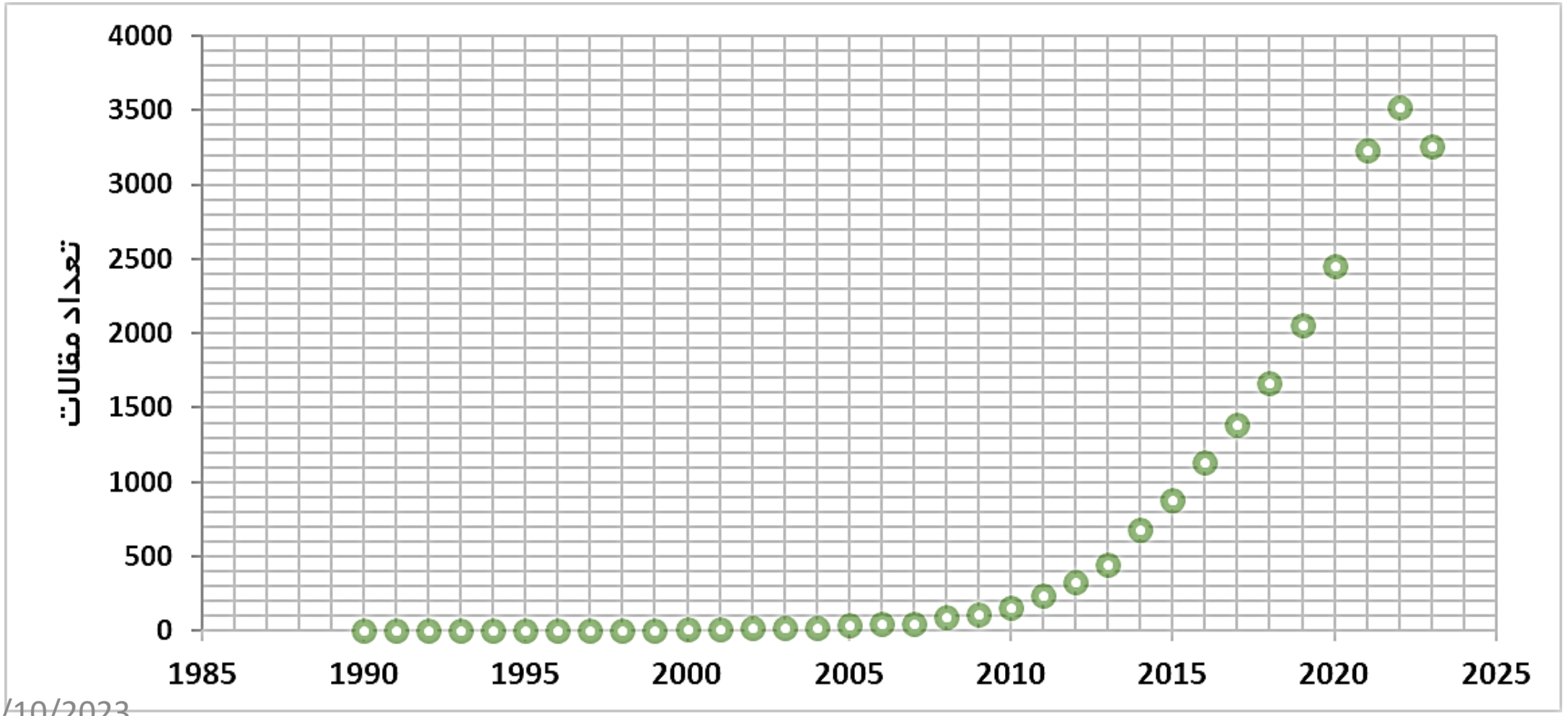
The Confidence Profile Method is a Bayesian method for adjusting and combining pieces of evidence to estimate parameters, such as the effect of health technologies on health outcomes. The information in each piece of evidence is captured in a likelihood function that gives the likelihood of the observed results of the evidence as a function of possible values of the parameter. A posterior distribution is calculated from Bayes formula as the product of the likelihood function and a prior distribution. Multiple pieces of evidence are incorporated by successive applications of Bayes' formula. Pieces of evidence are adjusted for biases to internal or external validity by modeling the biases and deriving "adjusted" likelihood functions that incorporate the models. Likelihood functions have been derived for one-, two- and multi-arm prospective studies; 2×2, $2 \times n$ and matched case-control studies, and cross-sectional studies. Biases that can be incorporated in likelihood functions include crossover in controlled trials, error in measurement outcomes, patient selection biases, differences in technologies, and differences in length of follow-up. Effect measures include differences of rates, ratios of rates, and odds ratios. The elements of the method are illustrated with an analysis of the effect of a thrombolytic agent on the difference in probability of 1-year survival after a heart attack.

The first step in the assessment of a health technology is to evaluate the existing evidence to estimate how the technology affects the magnitude or probability of important health outcomes—its bene-

tive, which leaves it vulnerable to oversimplification, errors in reasoning, wishful thinking, and self-interest.

This paper introduces a Bayesian method for syn-

تعداد مقالات نمایه شده در PUBMED با موضوع متاآنالیز شبکه ای



نام های دیگر متاآنالیز شبکه ای: Network Meta Analysis

- Multiple treatments meta-analysis
- Mixed treatment comparisons

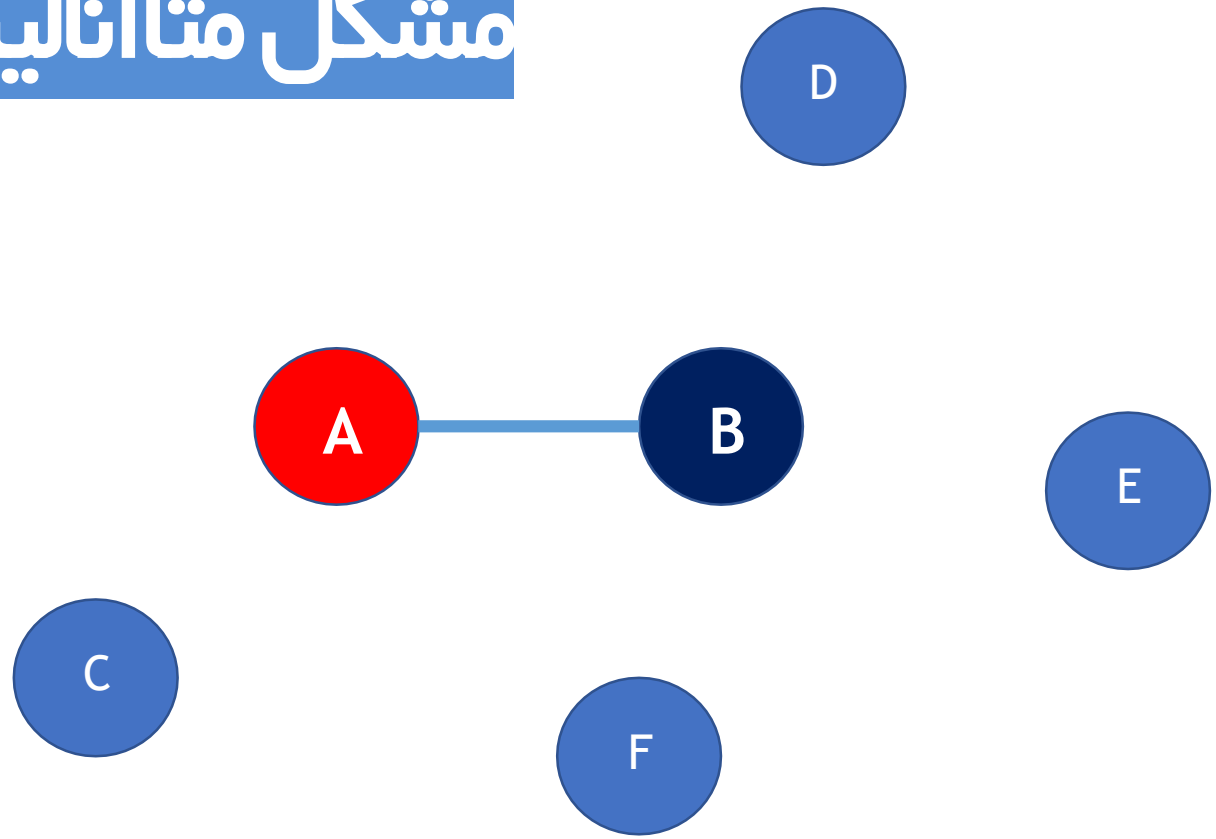
فهم منطق متاآنالیز شبکه ای

- اثر غیر مستقیم : Indirect Effect
- اثر ترکیبی : Mixed Effect

متاآنالیز دو به دو - pairwise

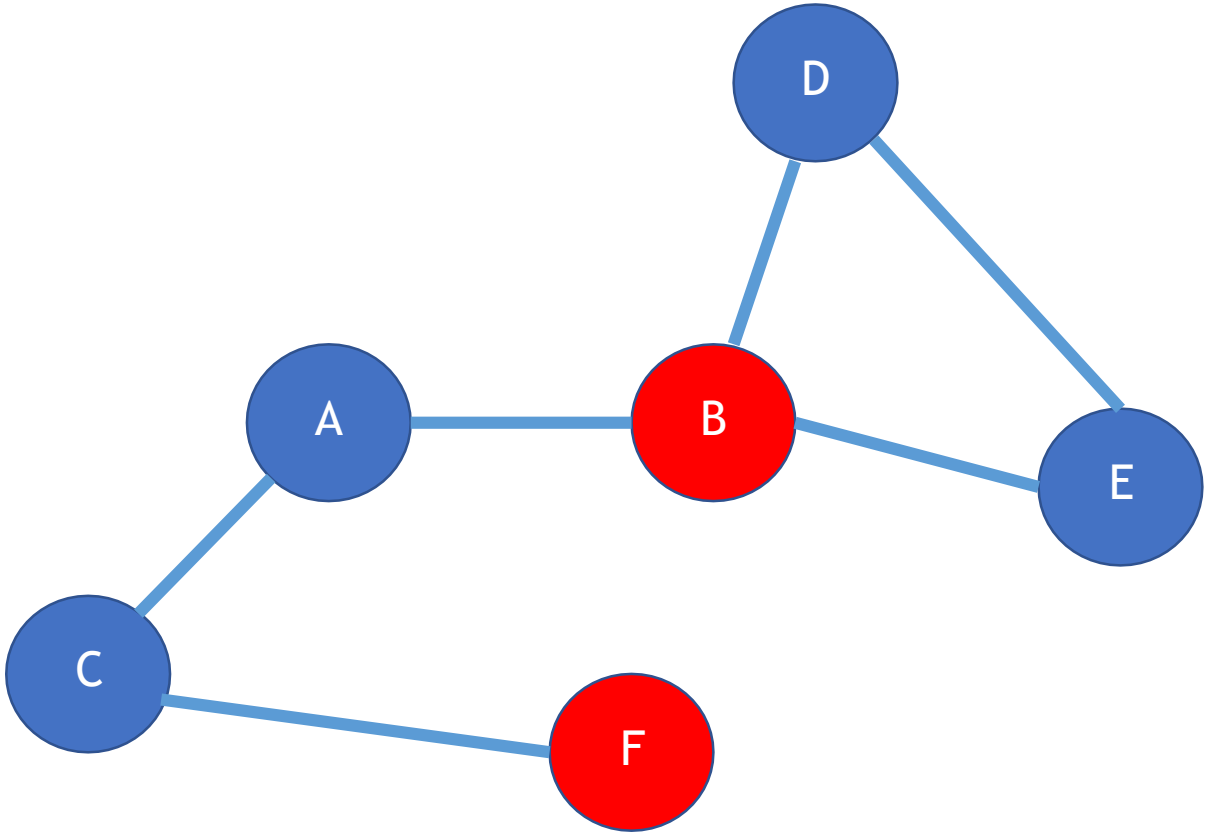
سوال پژوهش: آیا درمان A از درمان B بهتر است؟

مشکل متاآنالیز دو به دو



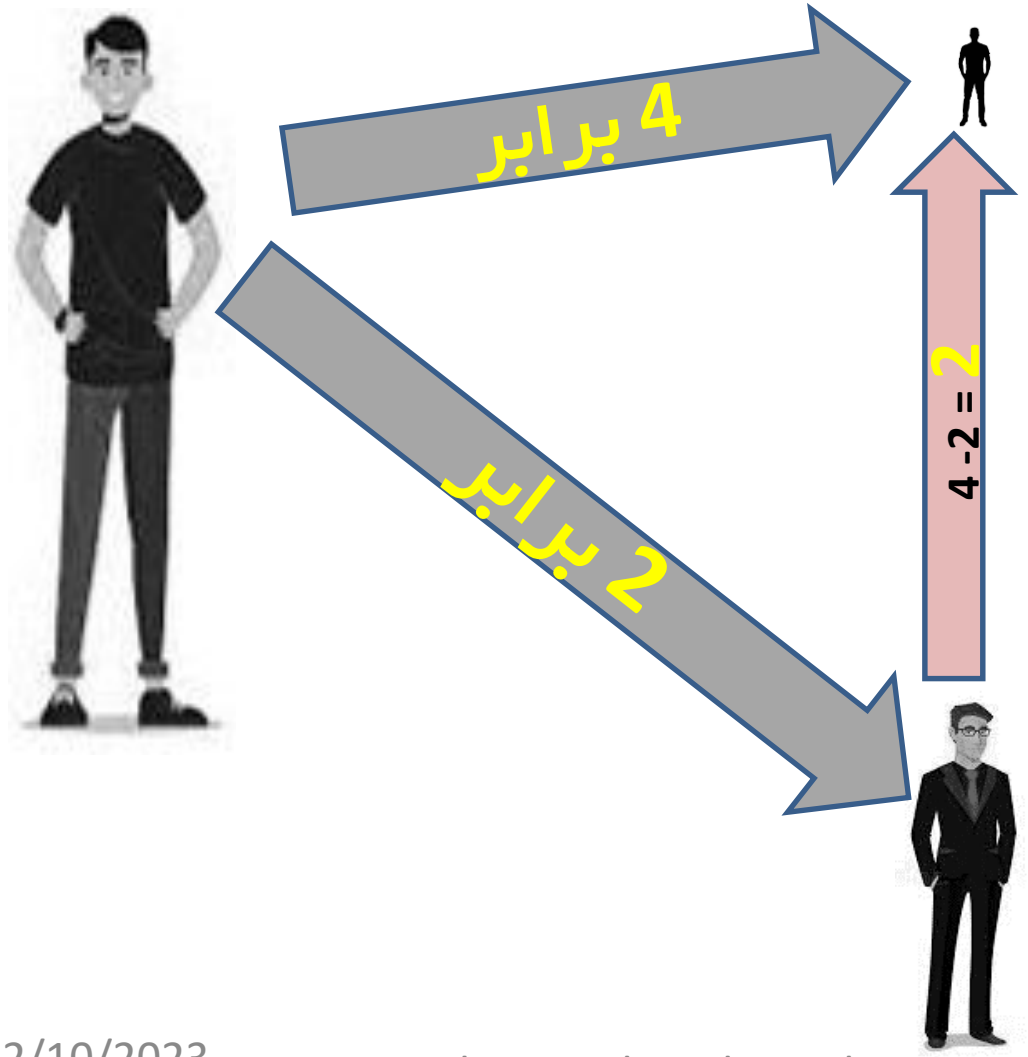
آیا درمان A از درمان B بهتر است؟

اما سوال واقعی چیست؟



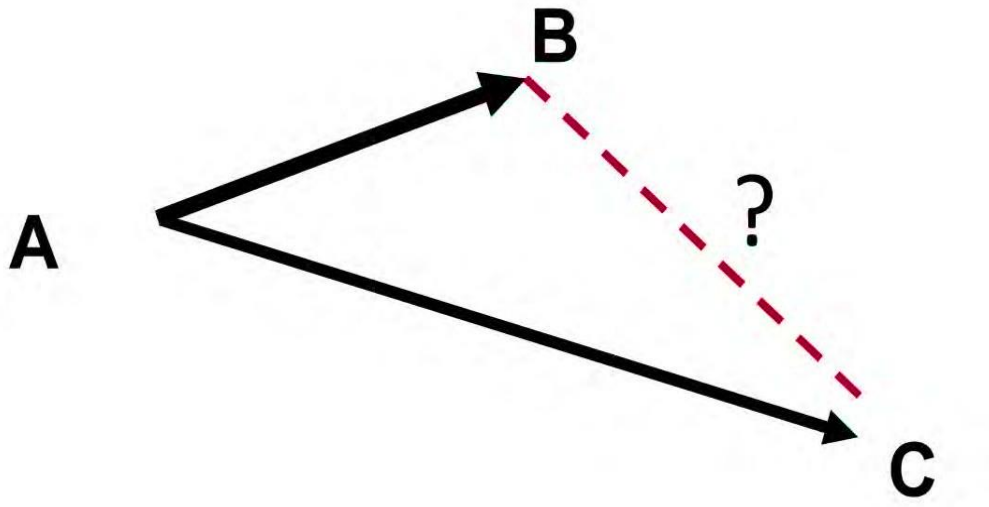
- کدامیک از **۶ درمان** موجود بیش از بقیه موثر است؟
- آیا درمان F از درمان B بهتر است؟

منطق محاسبه مقایسه غیر مستقیم:



مقایسه غیر مستقیم چیست؟

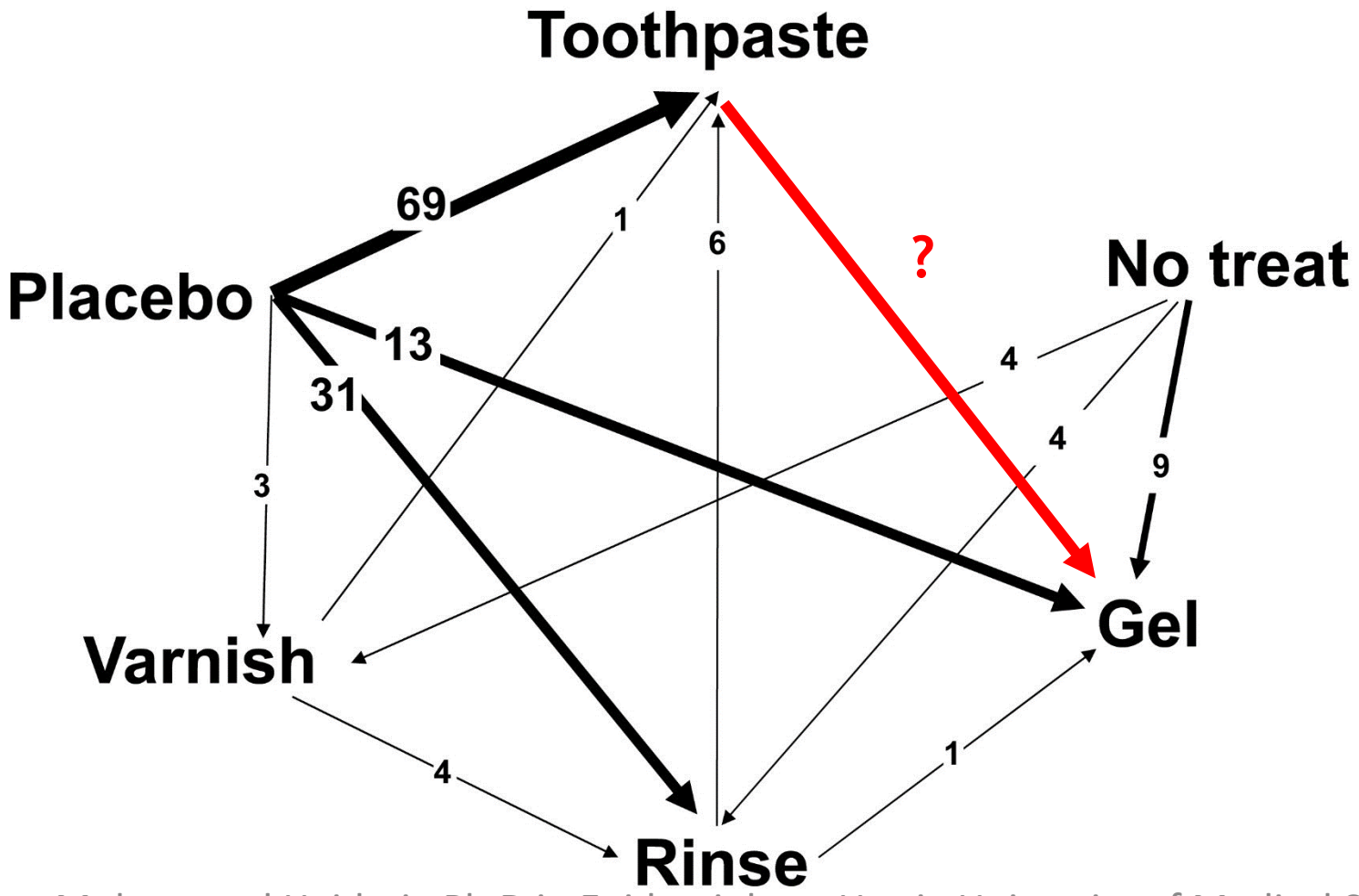
تخمین غیرمستقیم اثر درمان B در مقابل C از کارآزمایی‌هایی که A v B و A v C را مقایسه می‌کنند.



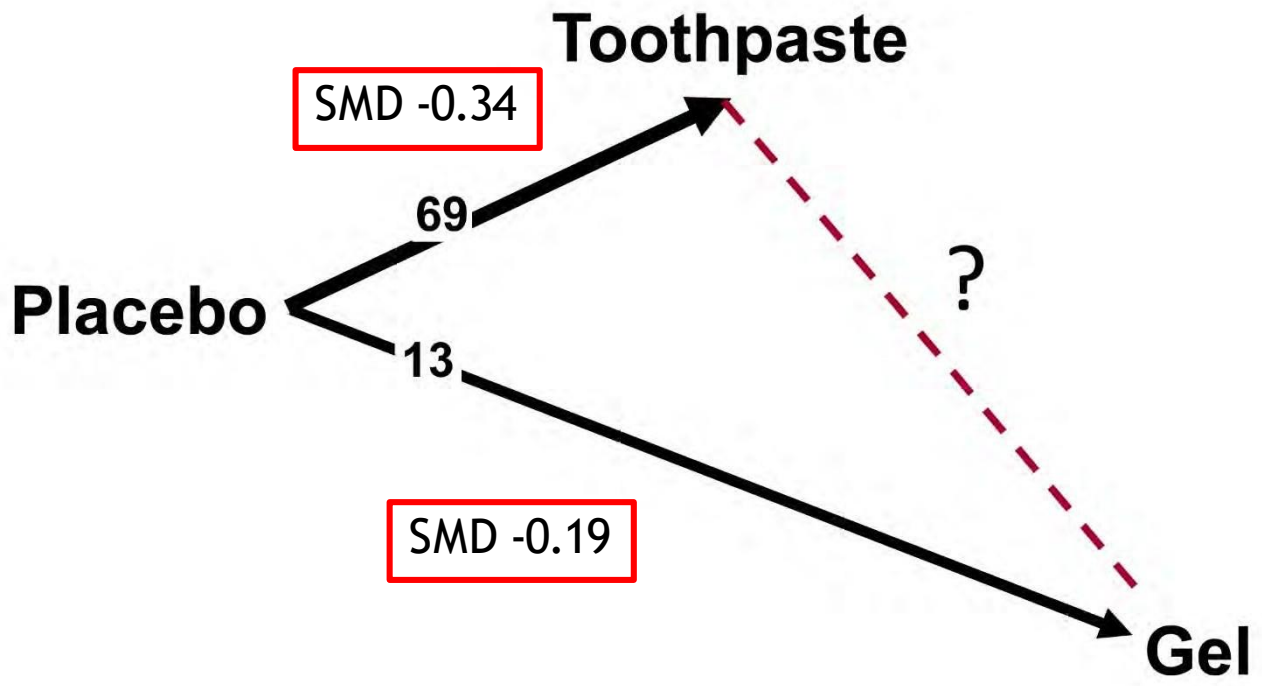
Treatment effect BC = Treatment effect AC **-** Treatment effect AB

Variance BC = variance AC **+** variance AB

مثال : مقایسه اثر مداخلات مختلف در پوسیدگی دندان

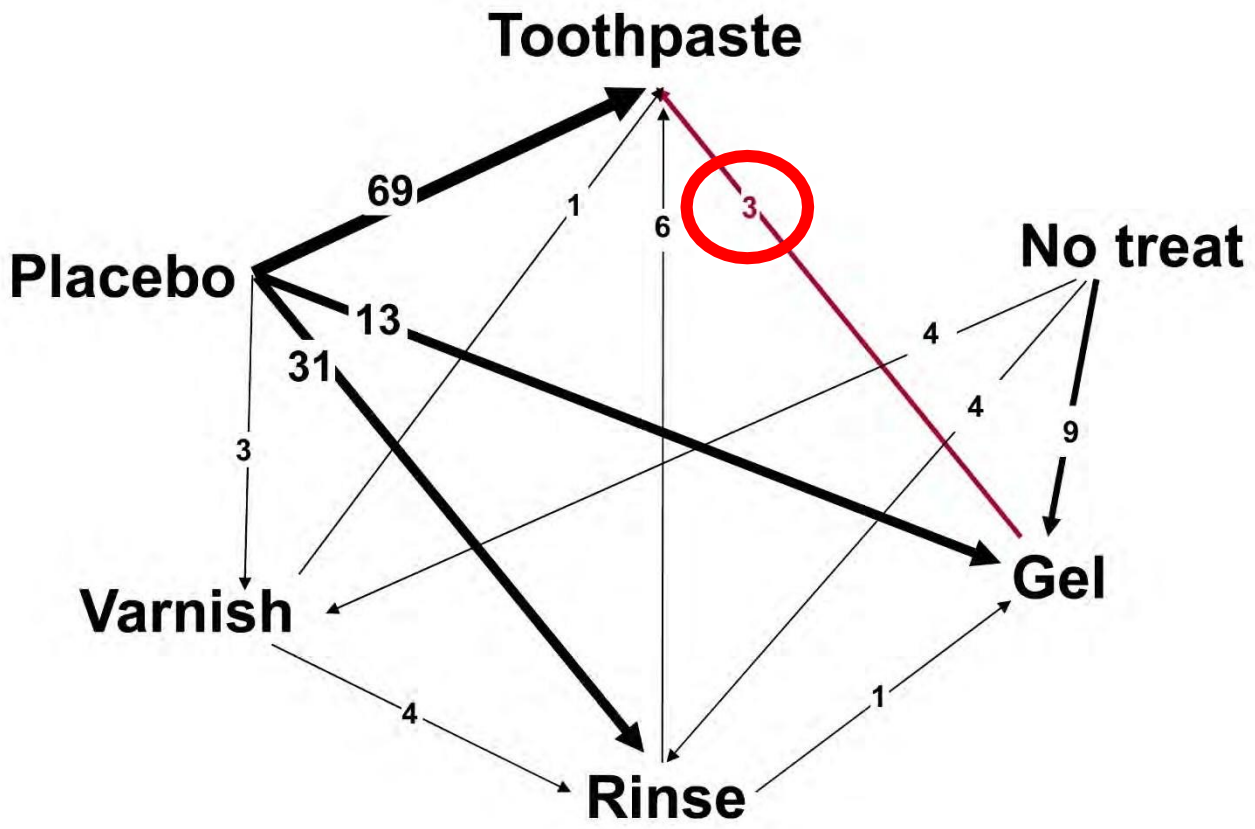


مثال : مقایسه اثر خمیردندان و ژل

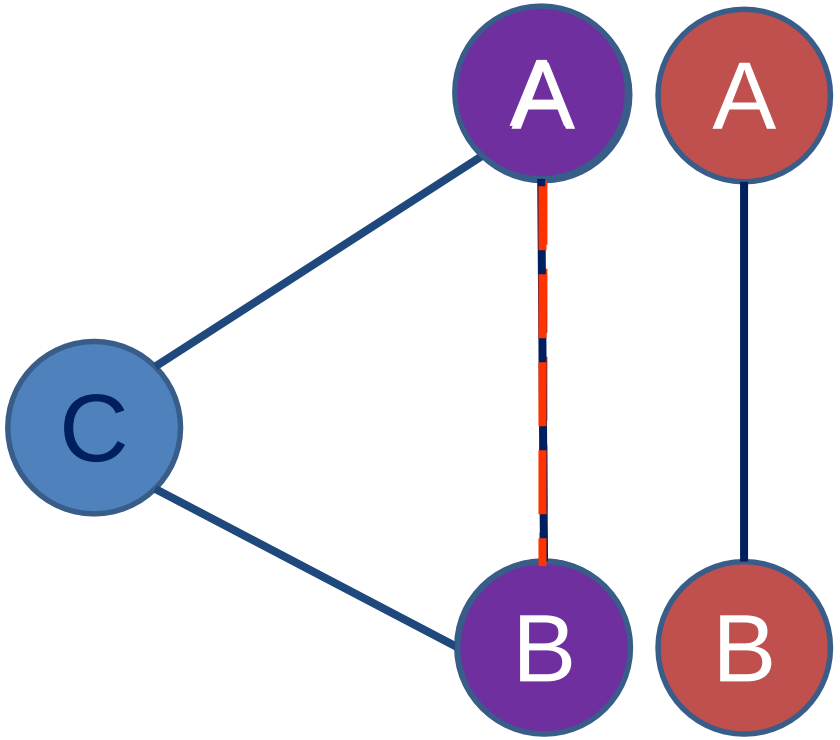


SMD = -0.34 - (-0.19) = -0.15
Variance is -0.27 to -0.03

استفاده از مقایسه مستقیم و غیر مستقیم:



Indirect and mixed effects:

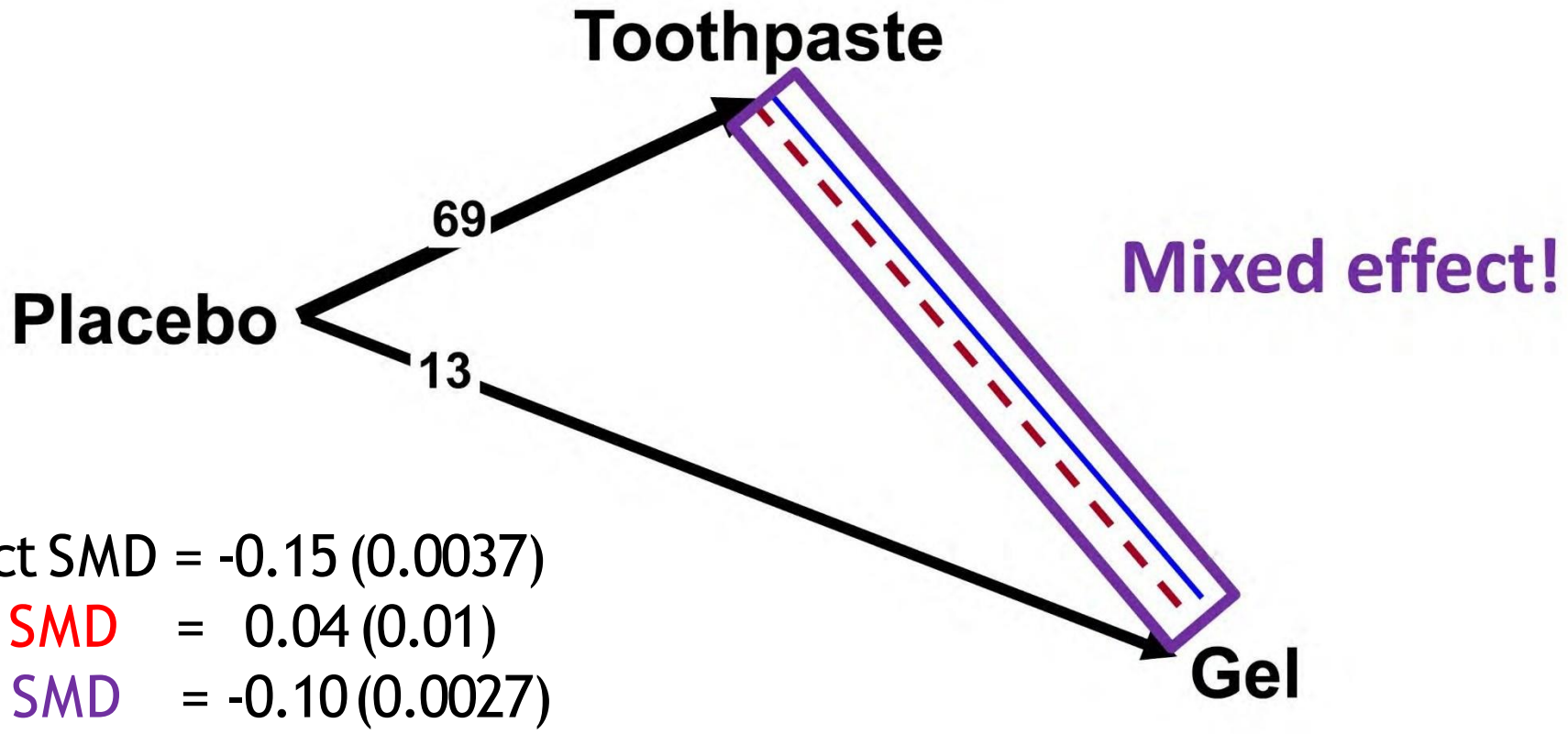


Indirect effect

Direct effect

Mixed effect

اثر ترکیبی (مستقیم + غیر مستقیم) : دقت برآورد بالا



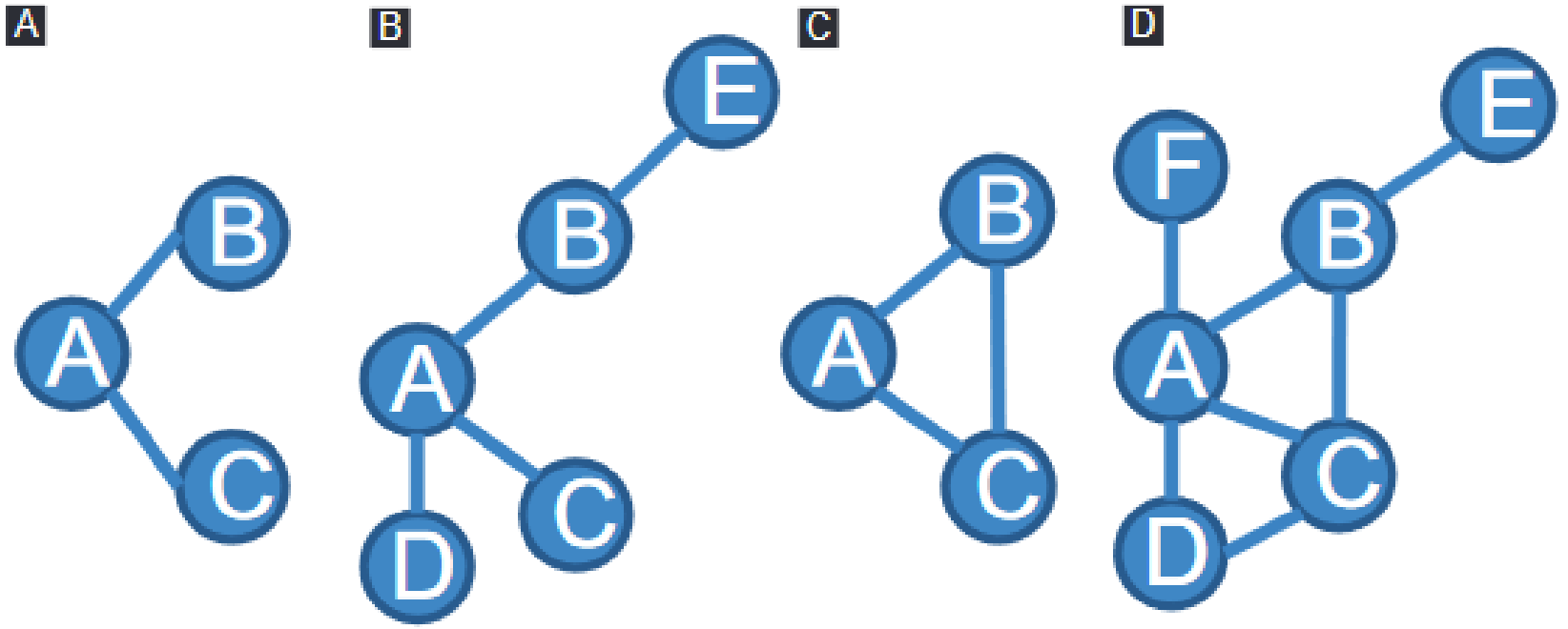
Indirect SMD = -0.15 (0.0037)
Direct SMD = 0.04 (0.01)
Mixed SMD = -0.10 (0.0027)

فرمول محاسبه مقدار mixed و ورایانس

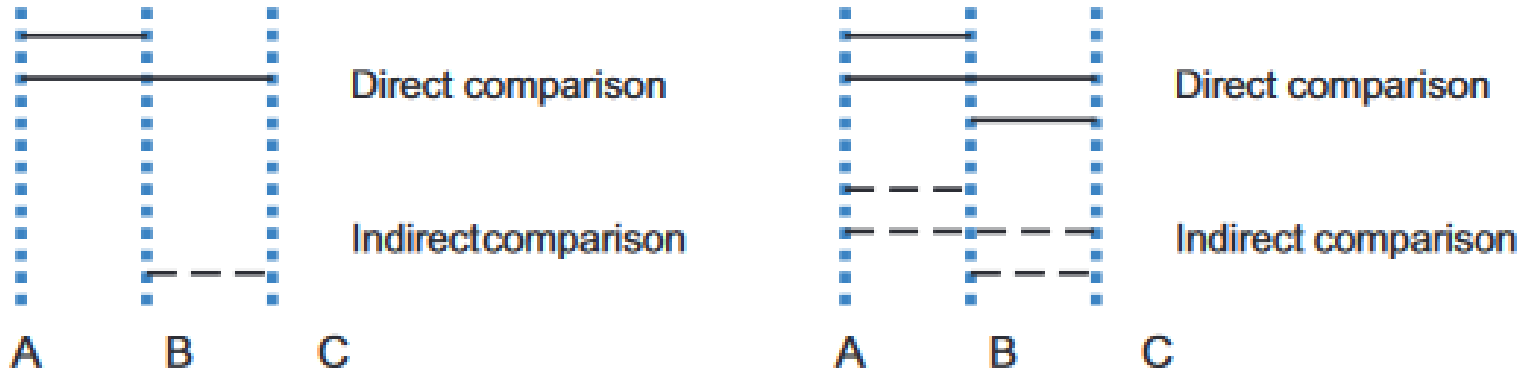
$$\text{Mixed SMD} = \frac{\frac{SMD_{Direct}}{var(SMD_{Direct})} + \frac{SMD_{Indirect}}{var(SMD_{Indirect})}}{\frac{1}{var(SMD_{Direct})} + \frac{1}{var(SMD_{Indirect})}}$$

$$var(\text{Mixed SMD}) = \frac{1}{\frac{1}{var(SMD_{Direct})} + \frac{1}{var(SMD_{Indirect})}}$$

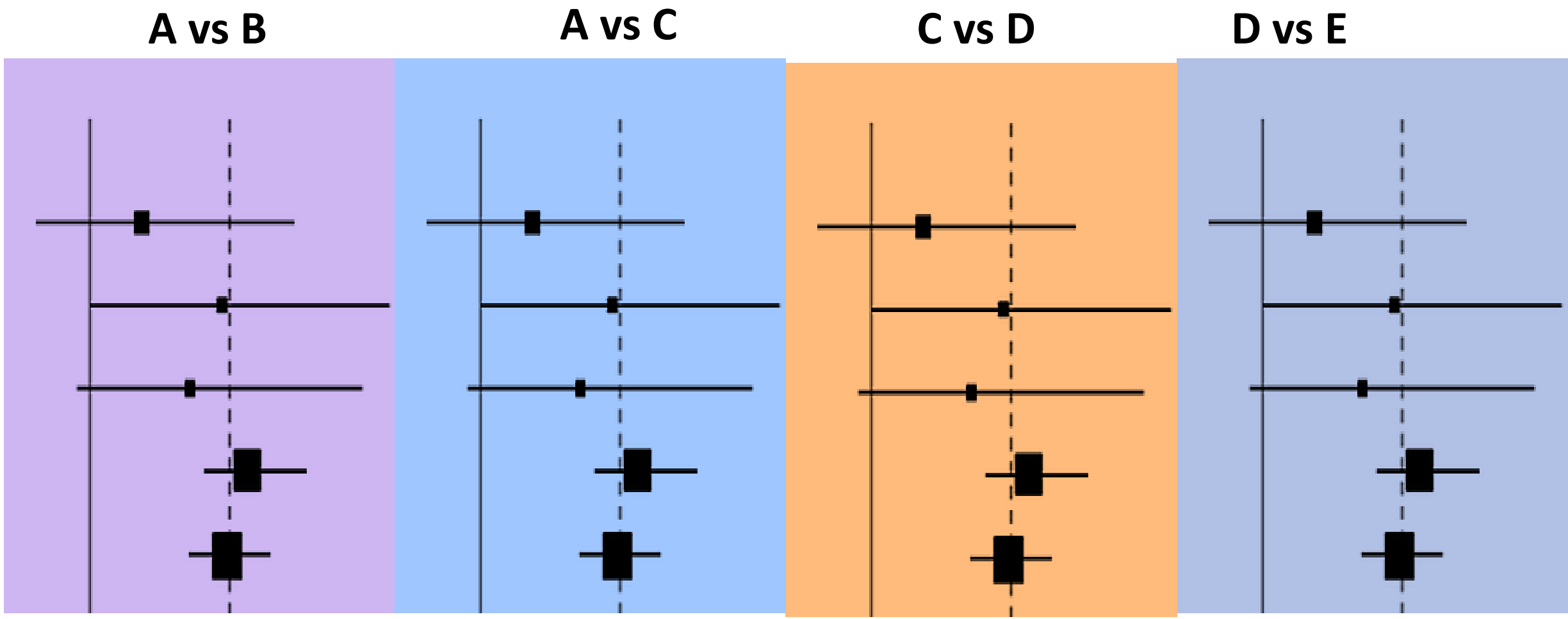
لوپ بسته

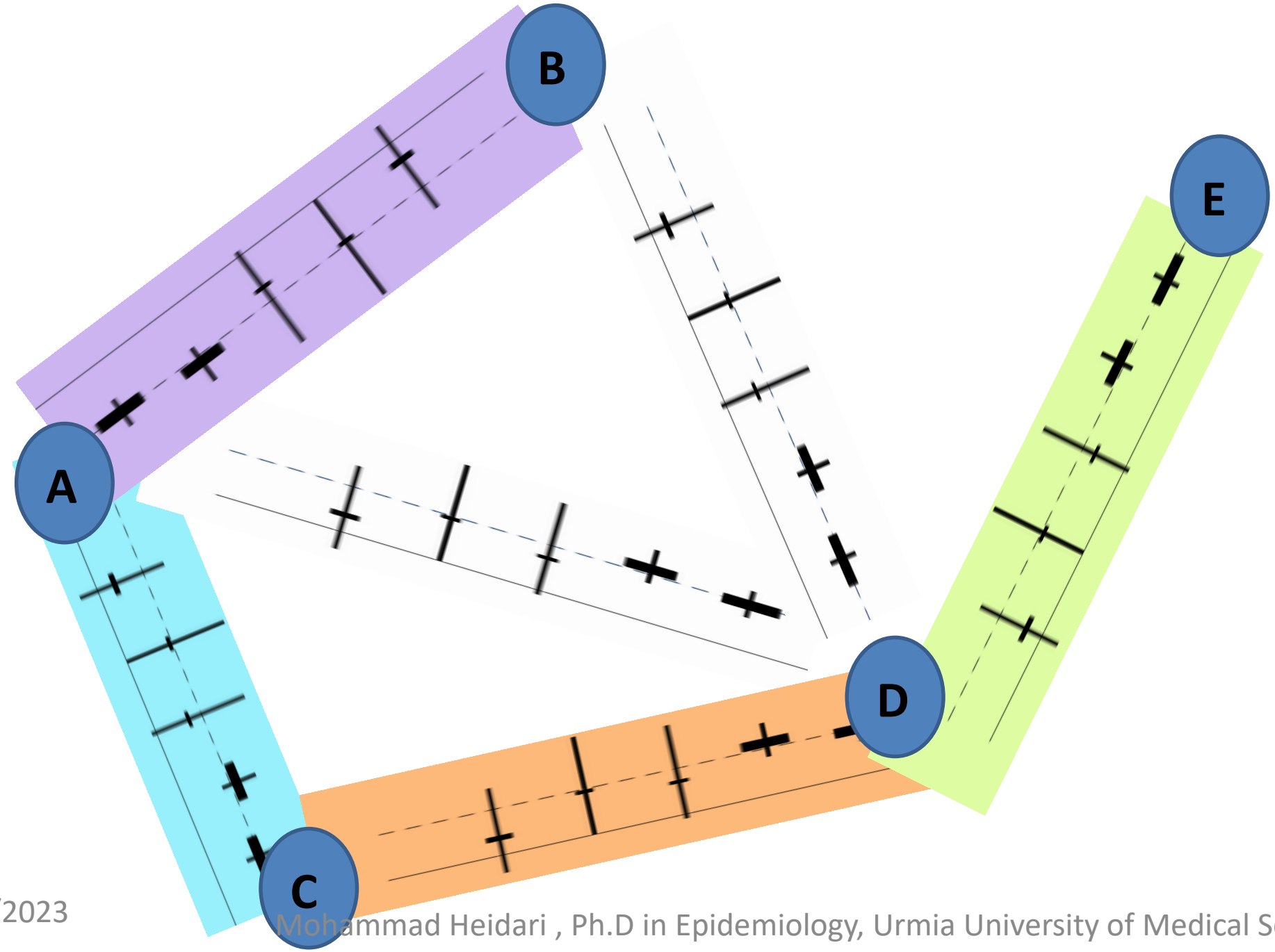


Indirect treatment comparison Open loop	Mixed treatment comparison Closed loop



متاآنالیز شبکه ای : ترکیب متاآنالیزهای دو به دو

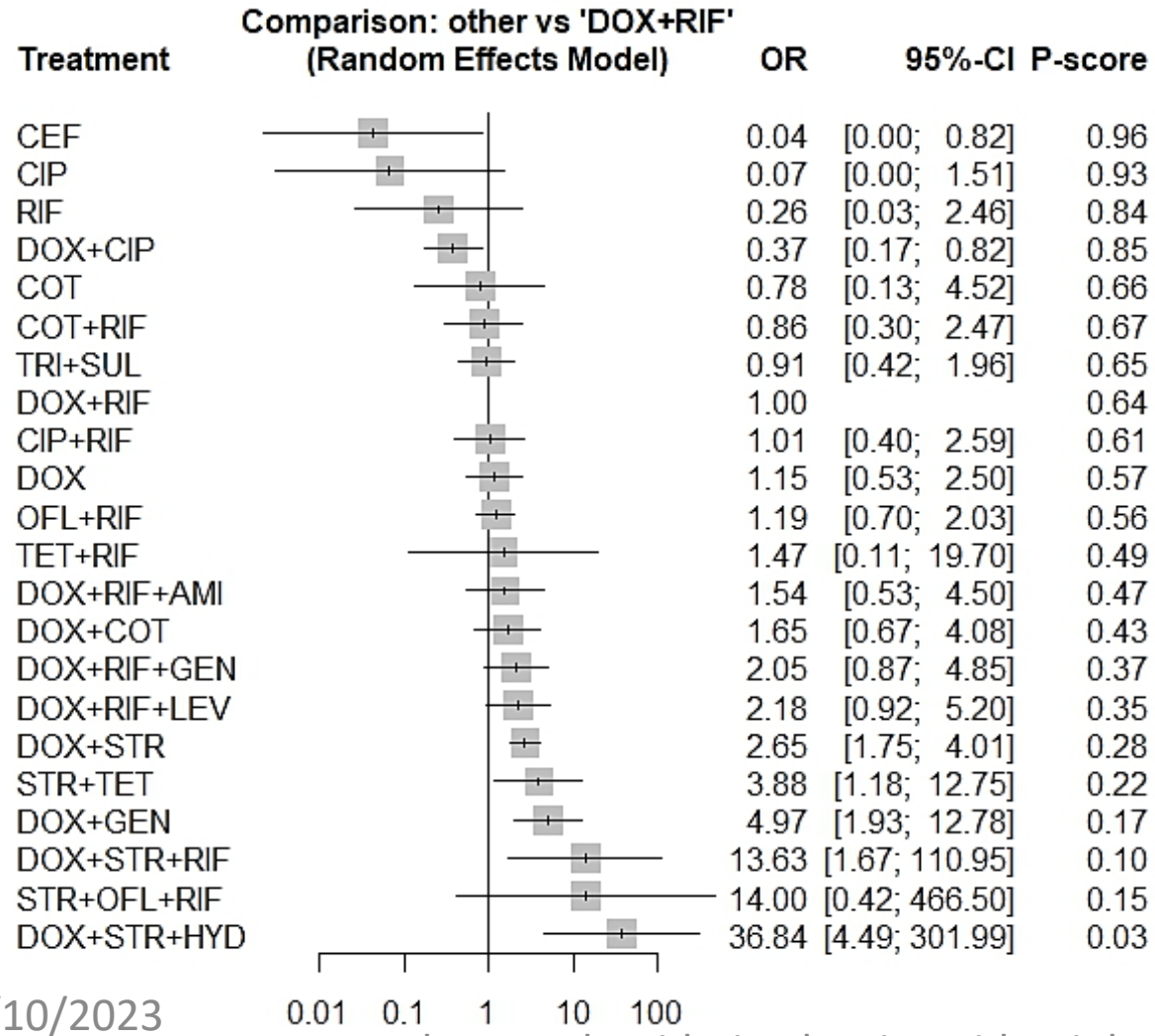



B
A
E
D
C

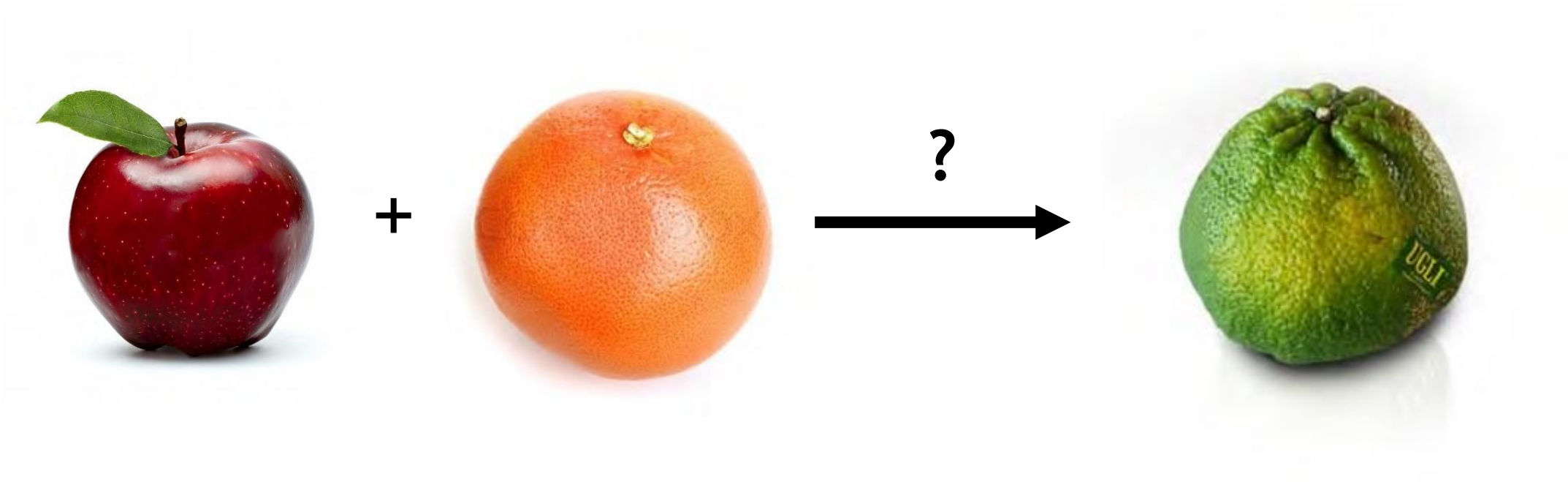
مدل آماری متاآنالیز شبکه ای:

- Meta-analysis : a weighted regression with no covariates
- Network meta-analysis : a weighted regression with dummy variables for the treatments
- You should take into account **correlations** in multi-arm trials

رتبه بندی مداخلات:



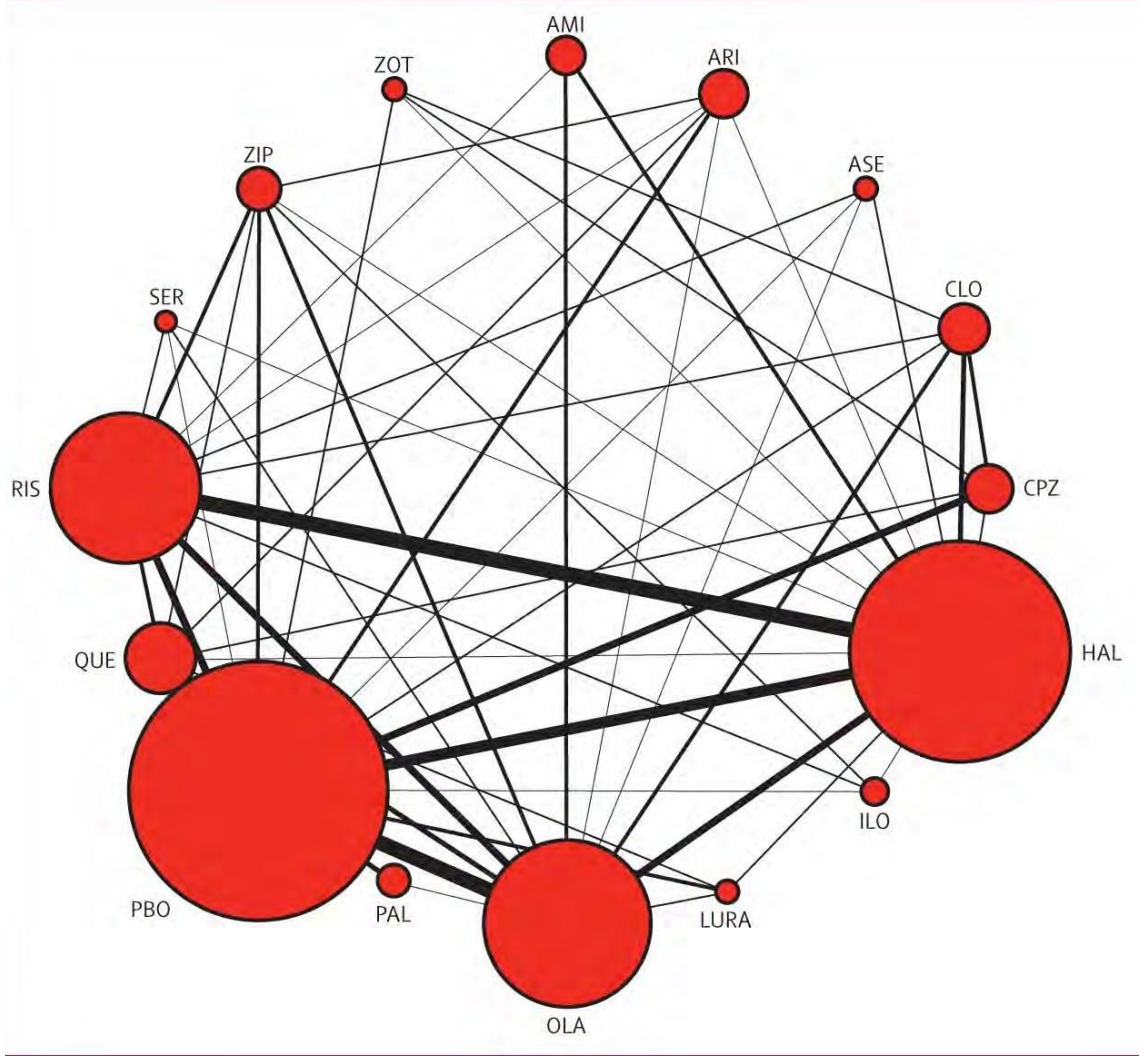
مشکل معروف ترکیب سیب و پرتقال در متاآنالیز



سه پیش فرض مهم:

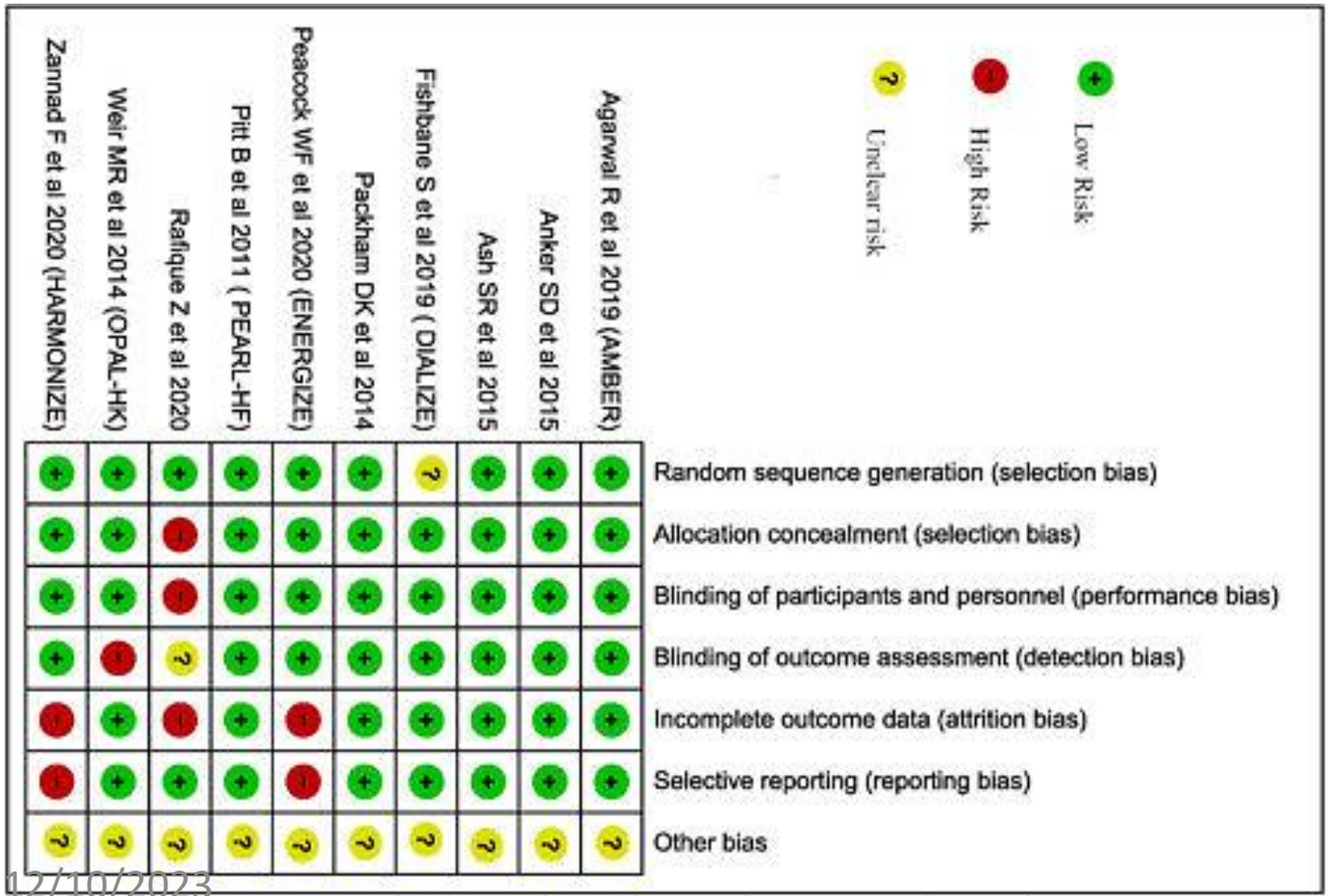
- **Homogeneity** : فرض عدم ناهمگنی در مقایسه های مستقیم دو به دو
  - Heterogeneity in Direct Comparison….. (Cochrane Q & I^2)
- **Transitivity (similarity)** : شرایط ایدآل کارآزمایی های بزرگ است که تمام مداخلات ممکن تصادفی اجرا شوند . مشکل برآورد های مستقیم و غیر مستقیم
  - Clinical experts
- **Consistency (Coherence)** : برابری برآورد مستقیم و غیر مستقیم
  - (Loop Specific & Cochrane Q for Total Network)

مشاهده هندسه مطالعات :



سنجش کیفیت شواهد :

Cochrane RoB 2.0 :Bias summary of included Randomized Controlled Trials



NMA certainty in evidence

Elements of a GRADE SoF table

Probiotics compared to no probiotics in INFANTS for the prevention of allergies

Patient or population: INFANTS for the prevention of allergies
Setting: outpatient
Intervention: probiotics
Comparison: no probiotics

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no probiotics	Risk with probiotics			
Asthma / wheezing - infants follow up: range 6 to 24 months to	121 per 1,000	**126 per 1,000** (76 to 206)	**RR 1.04** (0.63 to 1.70)	412 (3 RCTs)	⨁◯◯◯ VERY LOW a,b,c
Adverse effects follow up: range 6 to 24 months to	532 per 1,000	**676 per 1,000** (271 to 1,000)	**RR 1.27** (0.51 to 3.18)	187 (2 RCTs)	⨁◯◯◯ VERY LOW b,c,d

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **SMD:** Standardised mean difference

نکات کلی:

- وجود چندین مداخله برای یک پیامد/ یا چند پیامد
- بسیاری از متاآنالیزهای شبکه ای با همان روش دو به دو تحلیل شده اند
- تحلیل زیر گروه وجود ندارد اما می توان شبکه های مختلف در تحلیل داشت (subset)
- تحلیل زیر گروها ابزار قدرتمند متاآنالیز برای کشف علل هتروژنیتی است
- نرم افزارهای مختلف خروجی های گاها متفاوت دارند
- با متاآنالیز شبکه ای ضرورت انجام متاآنالیزهای کلاسیک دو به دو کمتر می شود
- ضرورت انجام مطالعات مختلف با سوال مشترک جهت سنجش اعتبار نتایج

دو محقق برجسته در زمینه متاآنالیز شبکه ای:

Prof. Dr. Georgia Salanti

Head of Research Group, Institute of Social and Preventive Medicine (ISPM)

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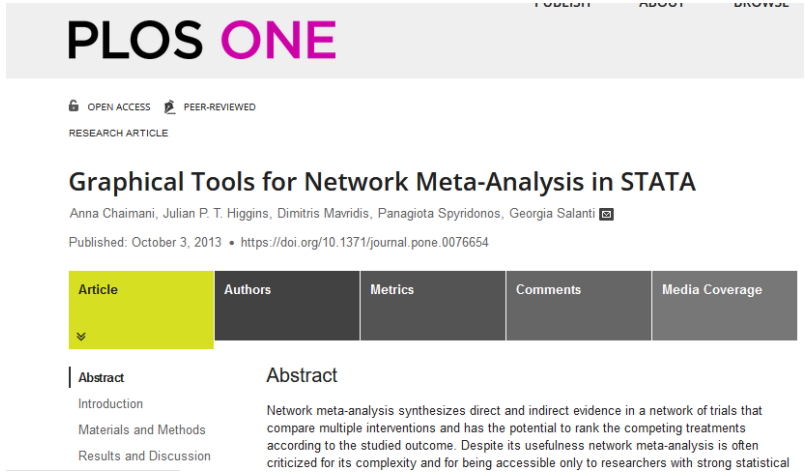

PLOS ONE

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Graphical Tools for Network Meta-Analysis in STATA

Anna Chaimani, Julian P. T. Higgins, Dimitris Mavridis, Panagiota Spyridonos, Georgia Salanti

Published: October 3, 2013 • https://doi.org/10.1371/journal.pone.0076654

Article | Authors | Metrics | Comments | Media Coverage

Abstract

Introduction

Materials and Methods

Results and Discussion

Abstract

Network meta-analysis synthesizes direct and indirect evidence in a network of trials that compare multiple interventions and has the potential to rank the competing treatments according to the studied outcome. Despite its usefulness network meta-analysis is often criticized for its complexity and for being accessible only to researchers with strong statistical

Guido Schwarzer

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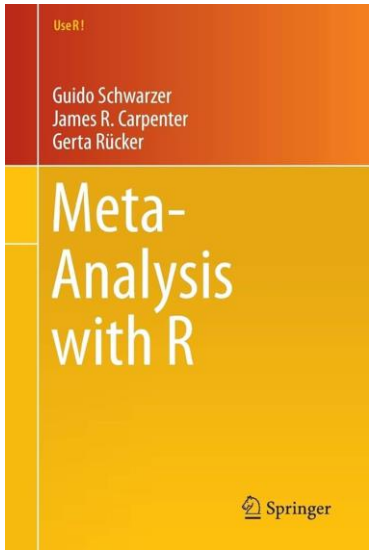
Germany



ابزار های آنلاین:

CRSU Software Suite (http://www.nihrcrsu.org/guidance/apps/#d.en.581059)

• MetaInsight : https://crsu.shinyapps.io/metainsightc/

Apps for carrying out network meta-analysis

Owen, RK, Bradbury, N, Xin, Y, Cooper, N, Sutton, A. MetaInsight: An interactive web-based tool for analyzing, interrogating, and visualizing network meta-analyses using R-shiny and netmeta. Res Syn Meth. 2019; 1- 13. https://doi.org/10.1002/jrsm.1373

• MetaDTA : https://crsu.shinyapps.io/dta_ma/

App for carrying out diagnostic test accuracy meta-analysis

Freeman SC, Kerby CR, Patel A, Cooper NJ, Quinn T, Sutton AJ. Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA. BMC Medical Research Methodology 2019; 19: 81 https://doi.org/10.1186/s12874-019-0724-x

• Primers on diagnostic test evaluation methods: https://crsu.shinyapps.io/diagprimer/

& https://vigorous-hawking-f95f83.netlify.com/

ممنون از توجه شما