Network meta-analysis: application and practical use

MSc. Fernanda S. Tonin

- International collaboration

Prof. Dr. Roberto Pontarolo

Department of Pharmacy, Federal University of Paraná (UFPR), Brazil

Prof. Dr. Fernando Fernandez-Llimos

Department of Social-Pharmacy, Faculty of Pharmacy, University of Lisbon (ULisboa), Portugal

Research Institute for Medicines (iMed.ULisboa), Lisbon, Portugal

- Research group

Evidence Synthesis and Health-Technology Assessment

- Publications

> 10 systematic reviews w/o quantitative

> 15 pairwise meta-analyses

> 10 network meta-analyses

Summary

Background

Meta-analysis and network meta-analysis

Research

Objectives and challenges

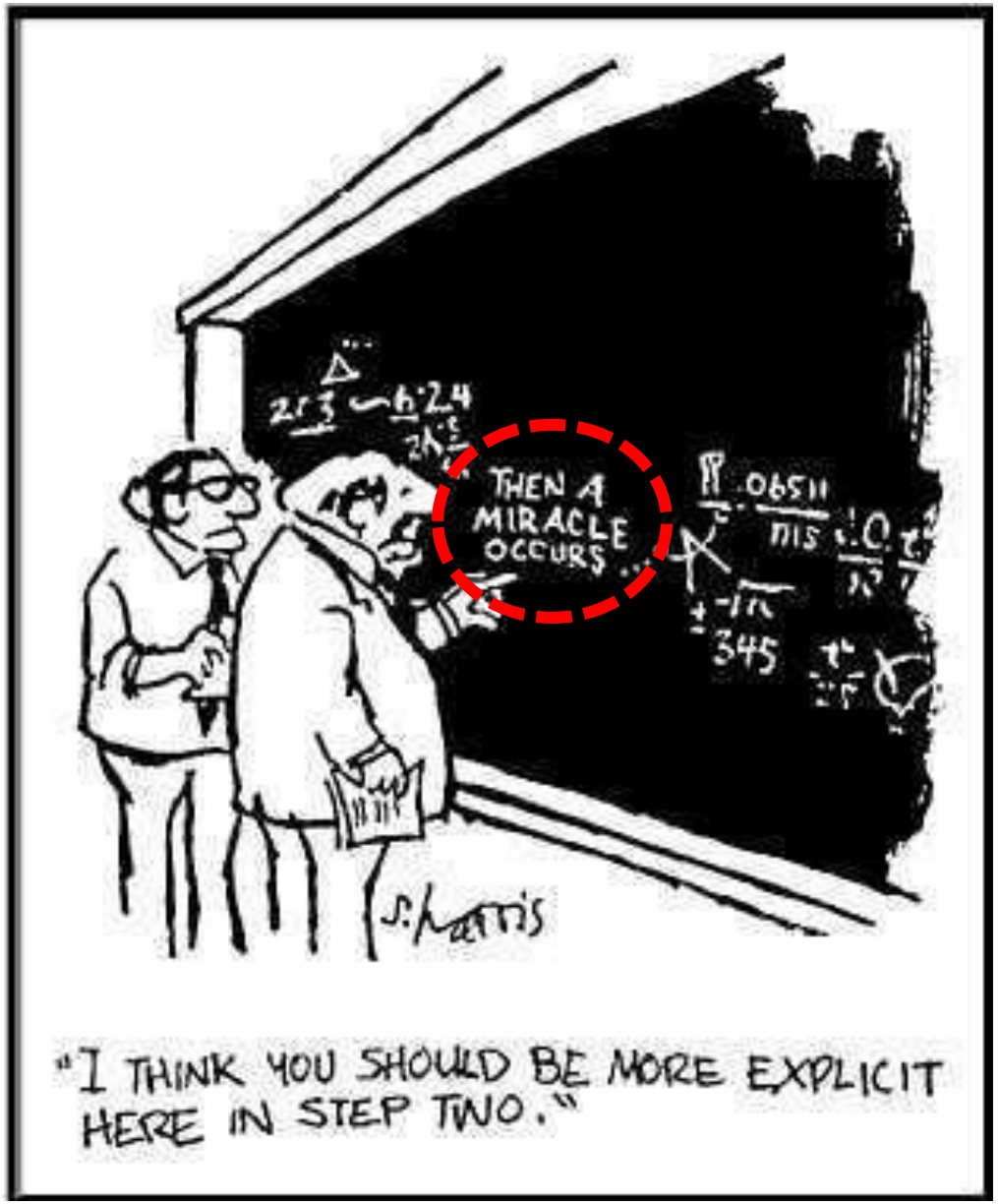
Perspectives

Application

Suboptimal research

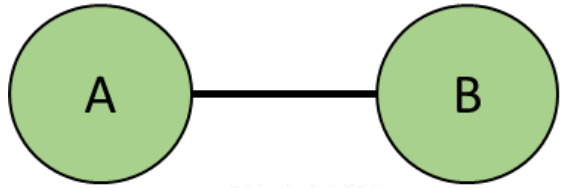
27% of publications are redundant
20% have methodological flaws
20% are unpublished
17% are decent but not useful
13% misleading conclusions

3% have a scientific meaning



Ioannidis JP. The Milbank quarterly. 2016;94(3):485-514.

Pairwise meta-analysis

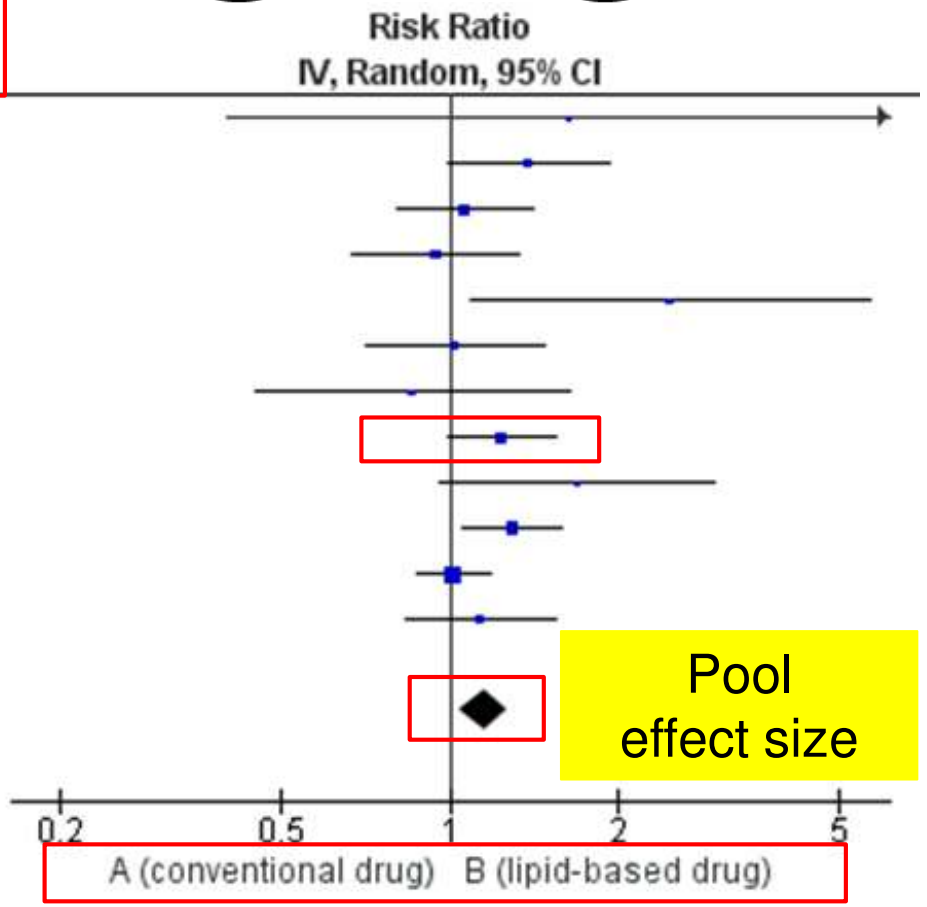


Effect size

Study or Subgroup	B Events	B Total	A Events	A Total	Weight	Risk Ratio IV, Random, 95% CI
Bowden 2002	5	88	3	86	0.5%	1.63 [0.40, 6.61]
Johnson 2002	45	51	14	22	7.7%	1.39 [1.00, 1.93]
Joly 1996	31	42	27	39	10.3%	1.07 [0.81, 1.41]
Leenders 1997	12	15	11	13	7.3%	0.95 [0.67, 1.33]
Leenders 1998	14	32	6	34	1.4%	2.48 [1.09, 5.66]
Nucci 1999	17	24	18	26	6.6%	1.02 [0.71, 1.47]
Pascual 1995	6	10	7	10	2.3%	0.86 [0.45, 1.64]
Prentice 1997	143	235	49	100	13.9%	1.24 [0.99, 1.55]
Sandler 2000	18	26	9	22	3.0%	1.69 [0.96, 2.97]
Sorkine 1996	30	30	23	30	15.8%	1.30 [1.06, 1.59]
Walsh 1999	172	343	170	344	22.5%	1.01 [0.87, 1.18]
White 1998	48	98	41	95	8.7%	1.13 [0.84, 1.54]
Total (95% CI)		**994**		**821**	**100.0%**	**1.15 [1.04, 1.28]**
Total events	541		378			

Heterogeneity: Tau² = 0.01; Chi² = 13.75, df = 11 (P = 0.25); I² = 20%

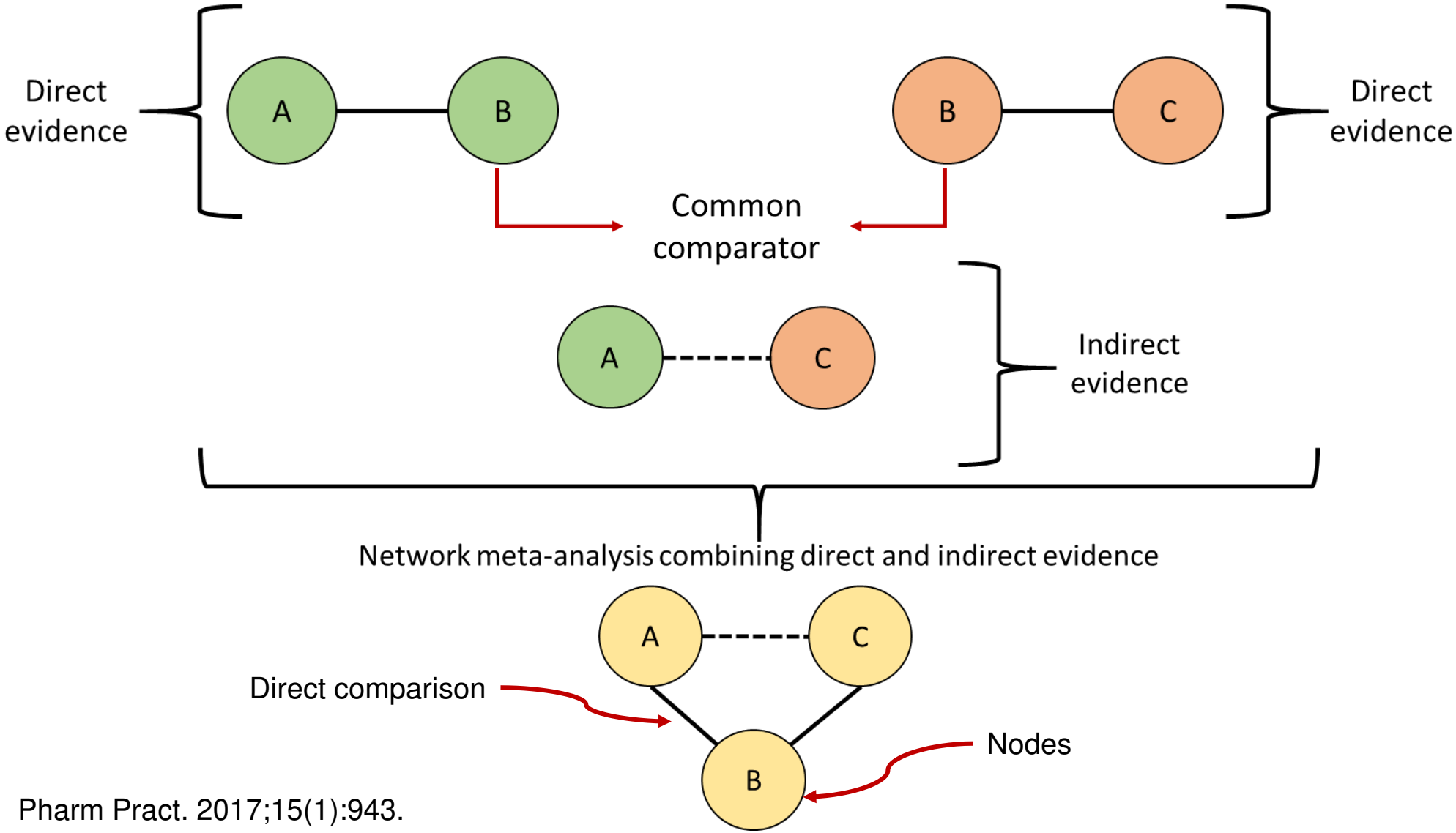
Test for overall effect: Z = 2.77 (P = 0.006)



Pool effect size

Mycoses. 2017;60(3):146-154.

Network meta-analysis



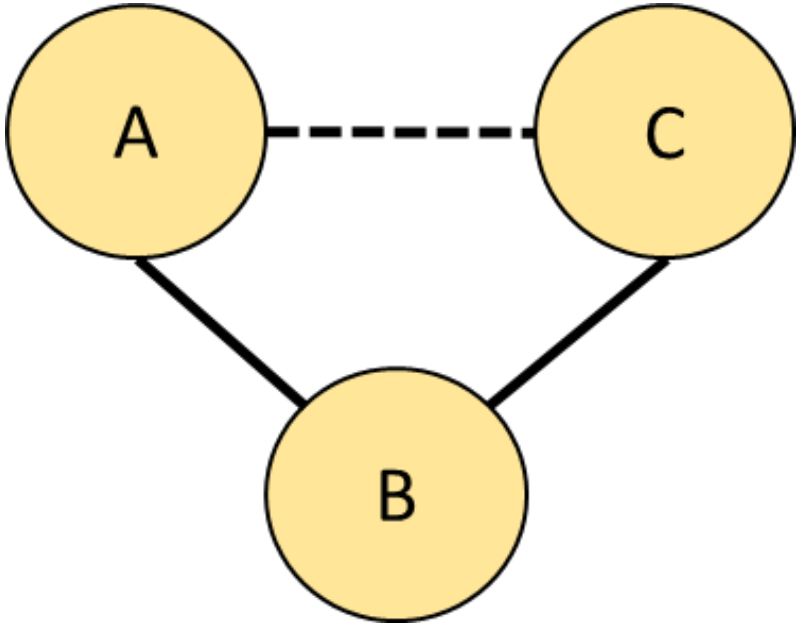
Pharm Pract. 2017;15(1):943.

Network meta-analysis

Results presentation

Pool effect sizes (95% CrI)
for each pair of comparison

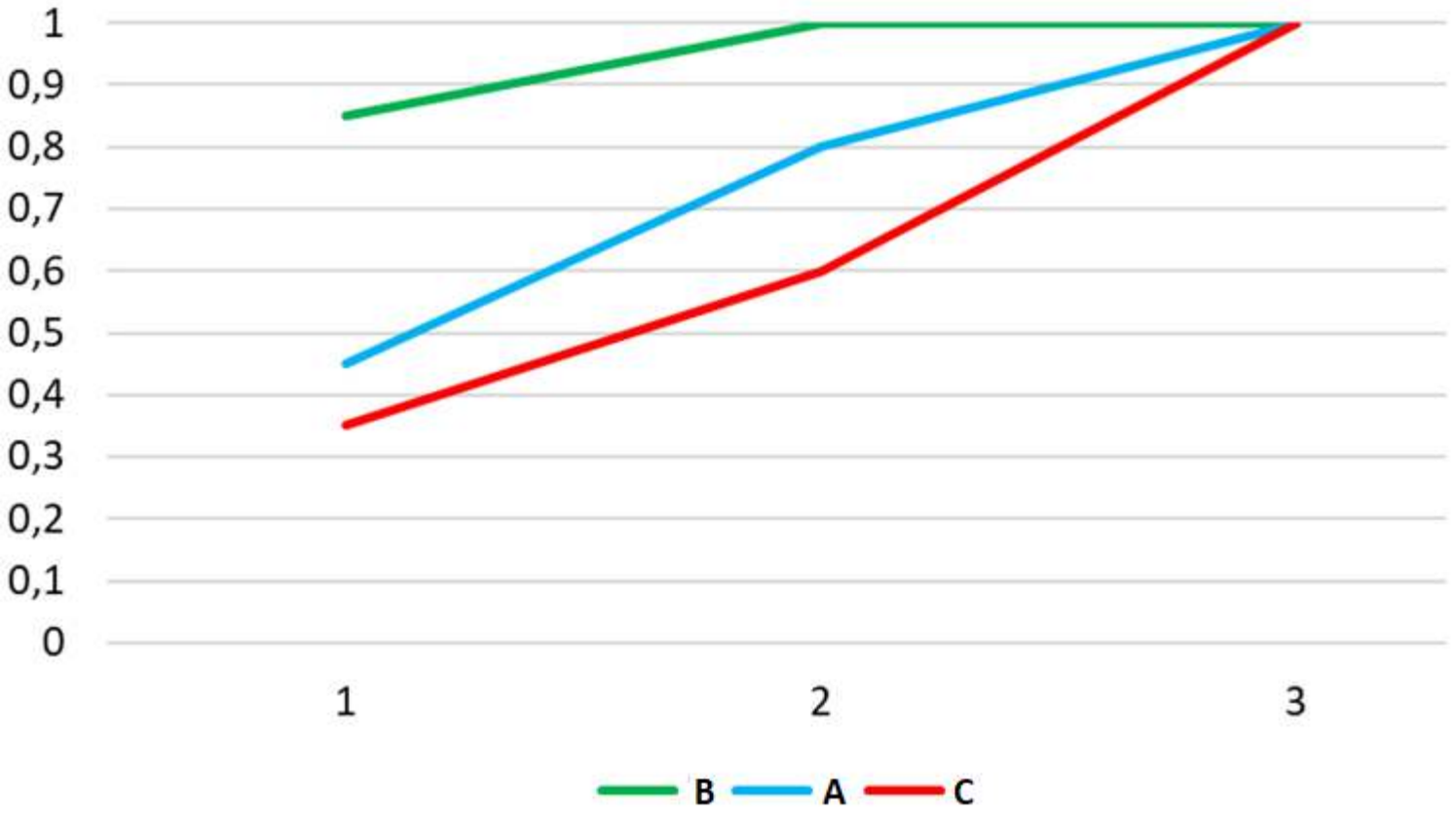
A	1.14 [1.04 - 1.28]	
	B	0.73 [0.44 – 0.93]
		C



Network meta-analysis

Rank order

Probability of each intervention to be the best, second best, and so on...



Surface under the cumulative curve analysis (SUCRA)

0% = worst option
100% = best option

A = 62%
B = 92%
C = 45%

Objectives and challenges

- Dissemination of the NMAs

Growth worlwide publications **x** redundancy

- ✓map the characteristics of published NMAs
- ✓evaluate the delay and speed of NMAs publications

- Statistical concerns

Bayesian model, consistency, software

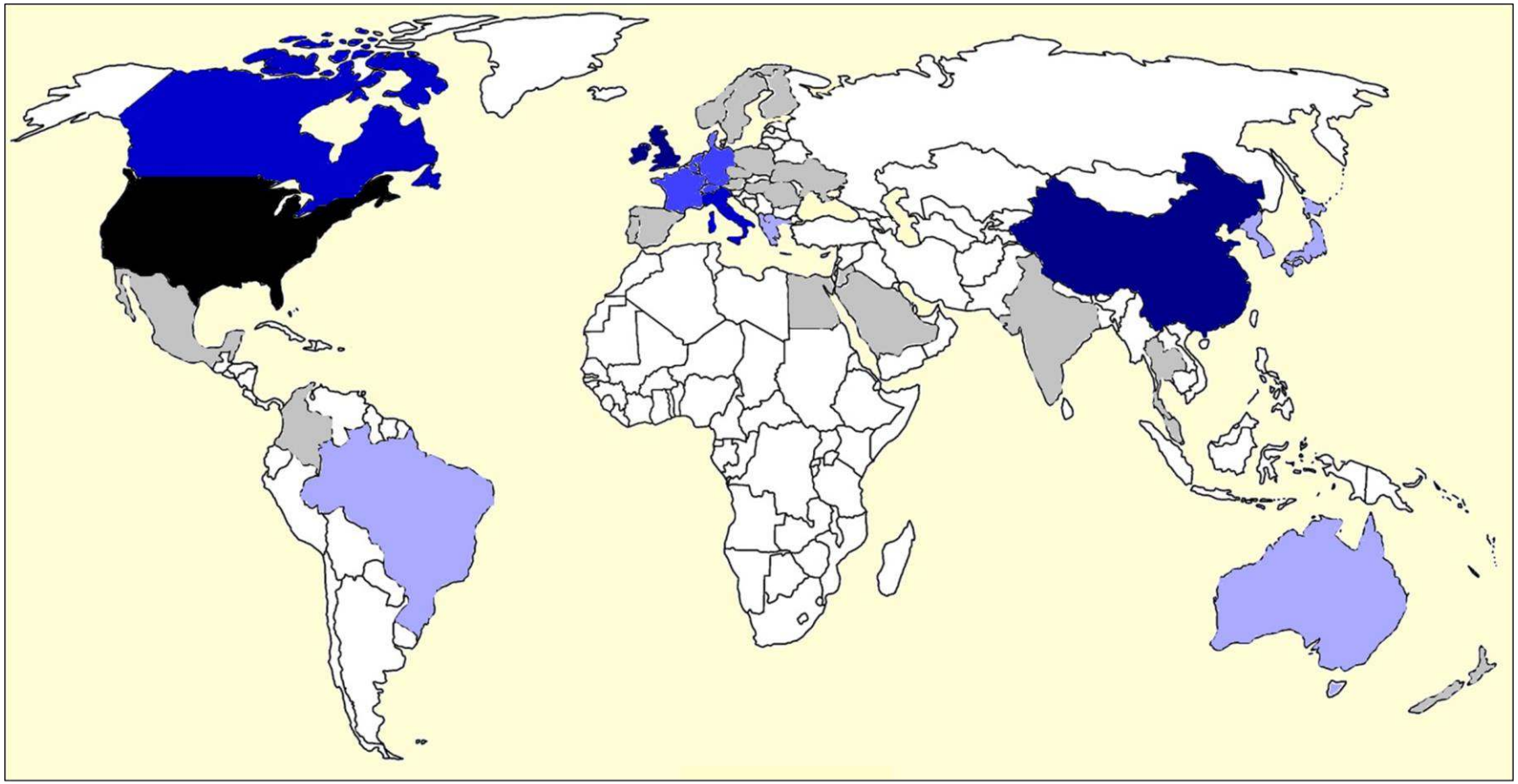
- ✓assess the sensibility of remove or add treatments in NMAs
- ✓evaluate the feasibility of using NMAs to compare different interventions
- ✓propose geometry metrics to describe NMAs

- Conduct and reporting

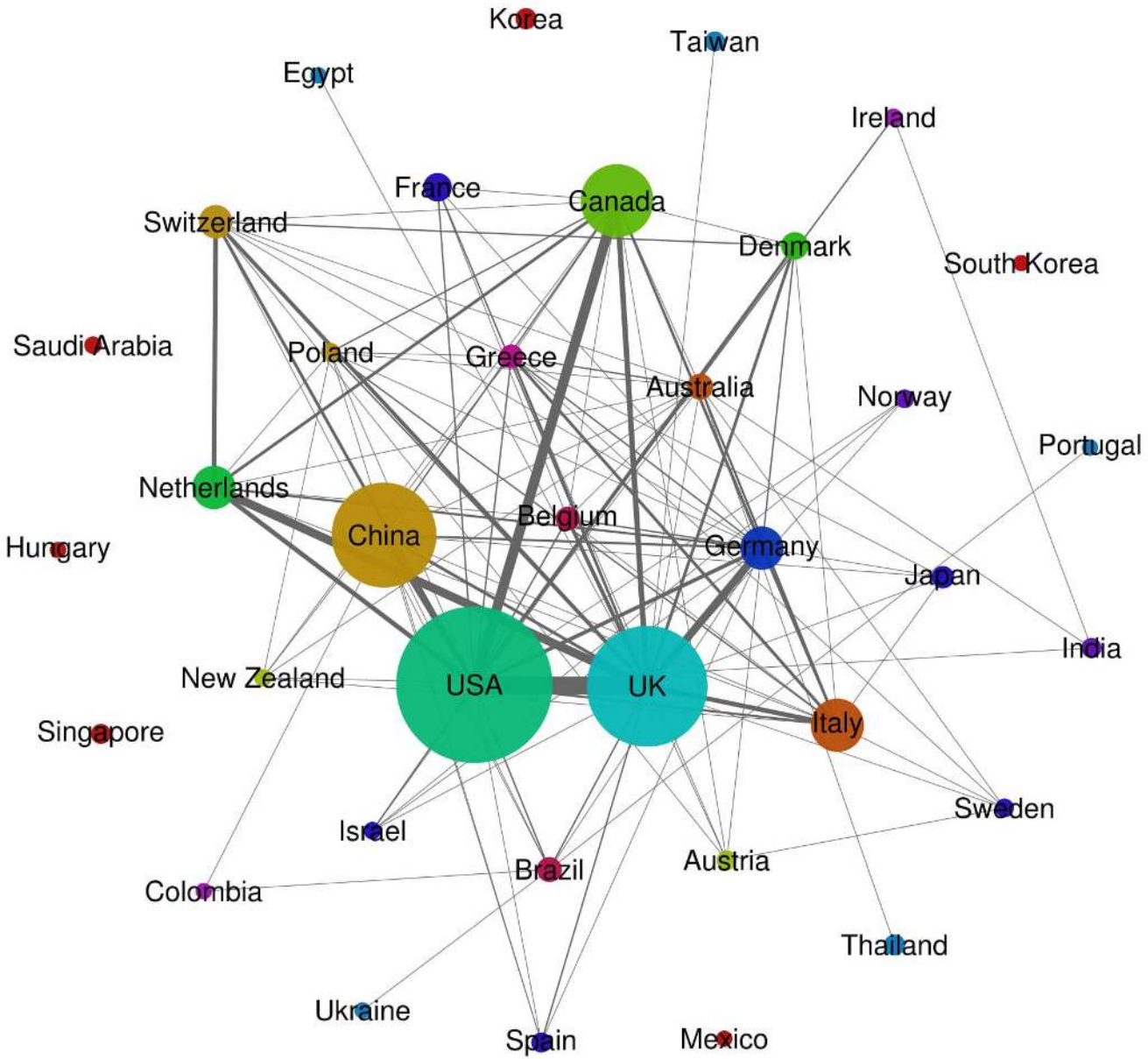
Methodological and evidence quality

- ✓map the methodological quality of NMAs publications
- ✓propose standards for reporting some parameters of NMAs

More than 500 NMAs published worldwide



PLoS One. 2018 Apr 30;13(4):e0196644.



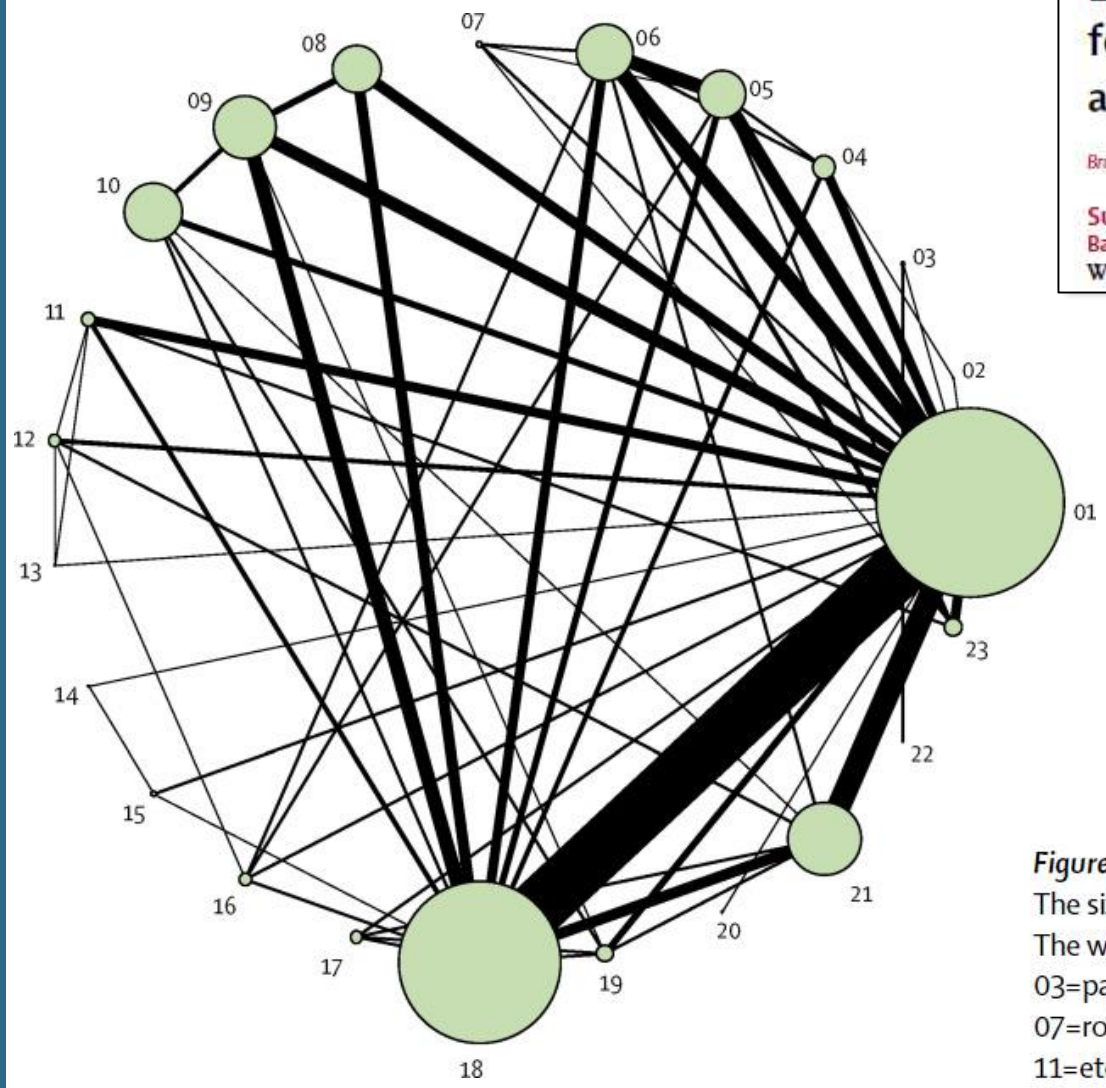
…suboptimal research:

70% do not follow reporting standards
75% lack study protocol
70% issues in literature searches
90% lack of raw data
70% flaws in statistical methods

Delay in publication = outdated evidence
> 1 year after first search to publication

PLoS One. 2018 Apr 30;13(4):e0196644.

Drugs



Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis

Bruno R da Costa*, Stephan Reichenbach*, Noah Keller, Linda Nartey, Simon Wandel, Peter Jüni, Sven Trelle

Summary

Background Non-steroidal anti-inflammatory drugs (NSAIDs) are the backbone of osteoarthritis pain management. We aimed to assess the effectiveness of different preparations and doses of NSAIDs on osteoarthritis pain in a

Lancet 2017; 390: e21–33

See Comment page 109

Network of non-steroidal anti-inflammatory drugs

76 RCTs (n=58,451 patients)
23 nodes (drugs + placebo)

Figure 1: **Network of comparisons included in the analyses**
The size of every circle is proportional to the number of randomly assigned patients and indicates the sample size. The width of the lines corresponds to the number of trials. 01=placebo. 02=paracetamol <2000 mg. 03=paracetamol 3000 mg. 04=paracetamol 3900–4000 mg. 05=rofecoxib 12·5 mg. 06=rofecoxib 25 mg. 07=rofecoxib 50 mg. 08=lumiracoxib 100 mg. 09=lumiracoxib 200 mg. 10=lumiracoxib 400 mg. 11=etoricoxib 30 mg. 12=etoricoxib 60 mg. 13=etoricoxib 90 mg. 14=diclofenac 70 mg. 15=diclofenac 100 mg. 16=diclofenac 150 mg. 17=celecoxib 100 mg. 18=celecoxib 200 mg. 19=celecoxib 400 mg. 20=naproxen 750 mg. 21=naproxen 1000 mg. 22=ibuprofen 1200 mg. 23=ibuprofen 2400 mg.

Lancet. 2017;390(10090):e21-e33.

Drugs class

Original Investigation

Comparison of Clinical Outcomes and Adverse Events Associated With Glucose-Lowering Drugs in Patients With Type 2 Diabetes

A Meta-analysis

Suetonia C. Palmer, PhD; Dimitris Mavridis, PhD; Antonio Nicolucci, MD; David W. Johnson, PhD; Marcello Tonelli, MD; Jonathan C. Craig, PhD; Jasjot Maggo, MMed; Vanessa Gray, MSc; Giorgia De Berardis, MSc; Marinella Ruospo, MSc; Patrizia Natale, MSc; Valeria Saglimbene, MSc; Sunil V. Badve, MD; Yeoungjee Cho, PhD; Annie-Claire Nadeau-Fredette, MD; Michael Burke, MD; Labib Faruque, MSc; Anita Lloyd, MSc; Nasreen Ahmad, BSc; Yuanchen Liu; Sophanny Tiv, BSc; Natasha Wiebe, MMath; Giovanni F. M. Strippoli, PhD

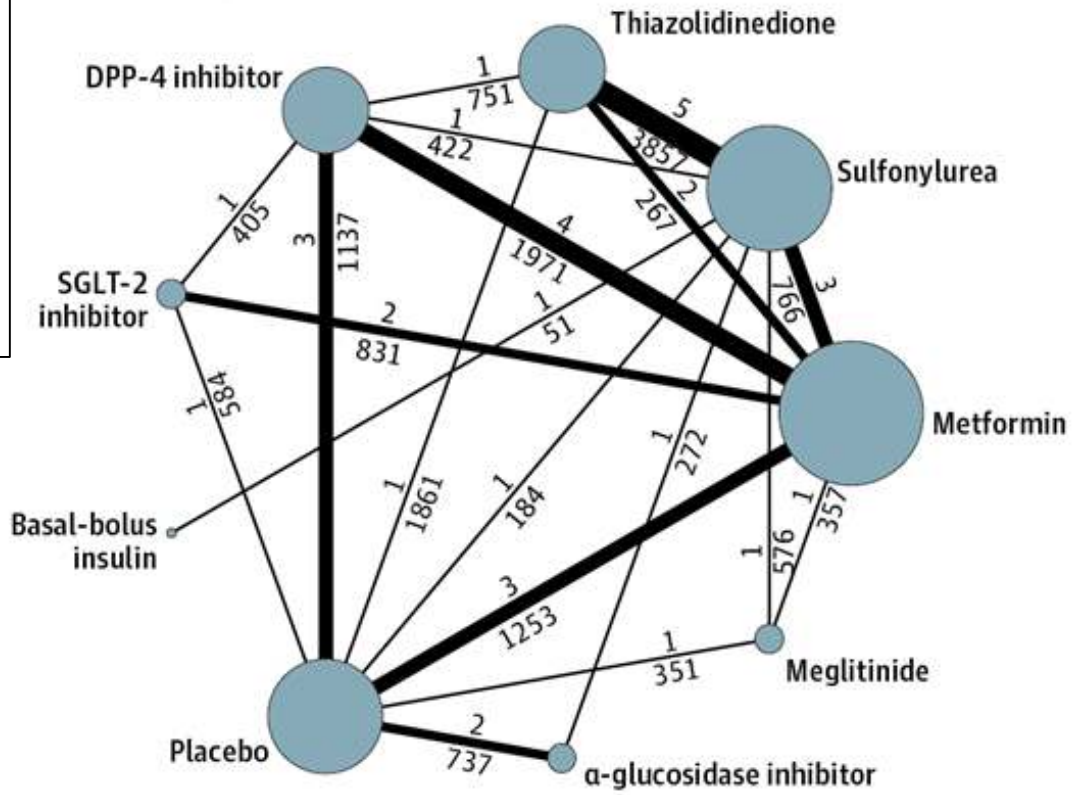
IMPORTANCE Numerous glucose-lowering drugs are used to treat type 2 diabetes.

OBJECTIVE To estimate the relative efficacy and safety associated with glucose-lowering

Supplemental content at jama.com

Network of glucose-lowering drugs

25 RCTs (n=14,477 patients)
9 nodes (8 classes + placebo)

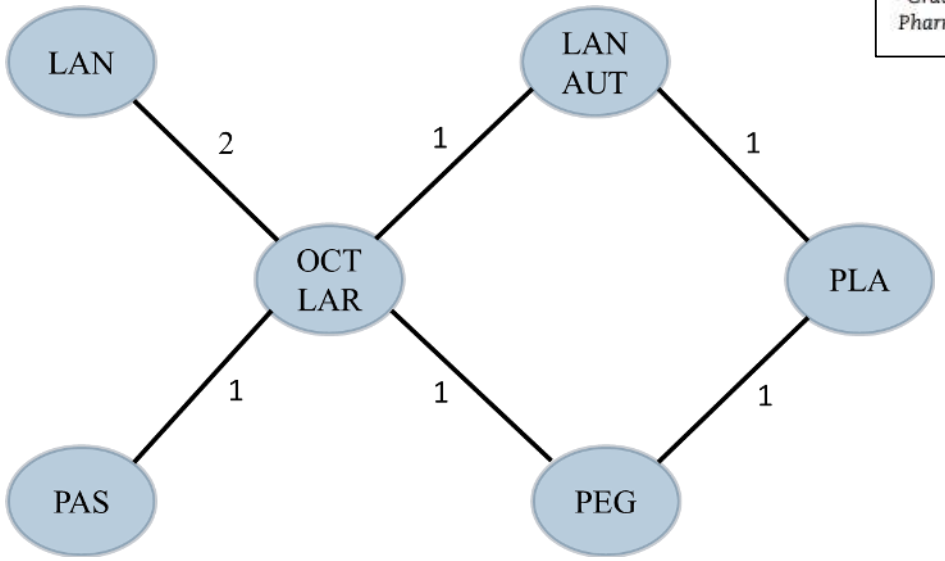


JAMA. 2016;316(3):313-24.

Orphan diseases

Network of acromegaly drugs

7 RCTs (n=801 patients)
6 nodes (5 drugs + placebo)



ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

Systematic Review

Medical Treatments for Acromegaly: A Systematic Review and Network Meta-Analysis

Letícia P. Leonart, MSc[1], Vinicius L. Ferreira, MSc[1], Fernanda S. Tonin, MSc[1], Fernando Fernandez-Llimos, PhD[2], Roberto Pontarolo, PhD[1,]*

[1]Graduate Program in Pharmaceutical Sciences, Universidade Federal do Paraná, Curitiba, Paraná, Brazil; [2]Department of Social Pharmacy, Faculty of Pharmacy, Research Institute for Medicines (iMed.ULisboa), Universidade de Lisboa, Lisbon, Portugal

LAN = lanreotide
LAN AUT = lanreotide autogel
OCTLAR = octreotide long-acting release
PEG = pegvisomant
PAS = pasireotide
PLA = placebo

Value Health. Article in press. February 7, 2018.

Drugs formulation

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Comparative safety profile of hyaluronic acid products for knee osteoarthritis: a systematic review and network meta-analysis

R.R. Bannuru*, M. Osani, E.E. Vaysbrot, T.E. McAlindon

Center for Treatment Comparison and Integrative Analysis (CTCIA), Division of Rheumatology, Tufts Medical Center, Boston, MA, USA

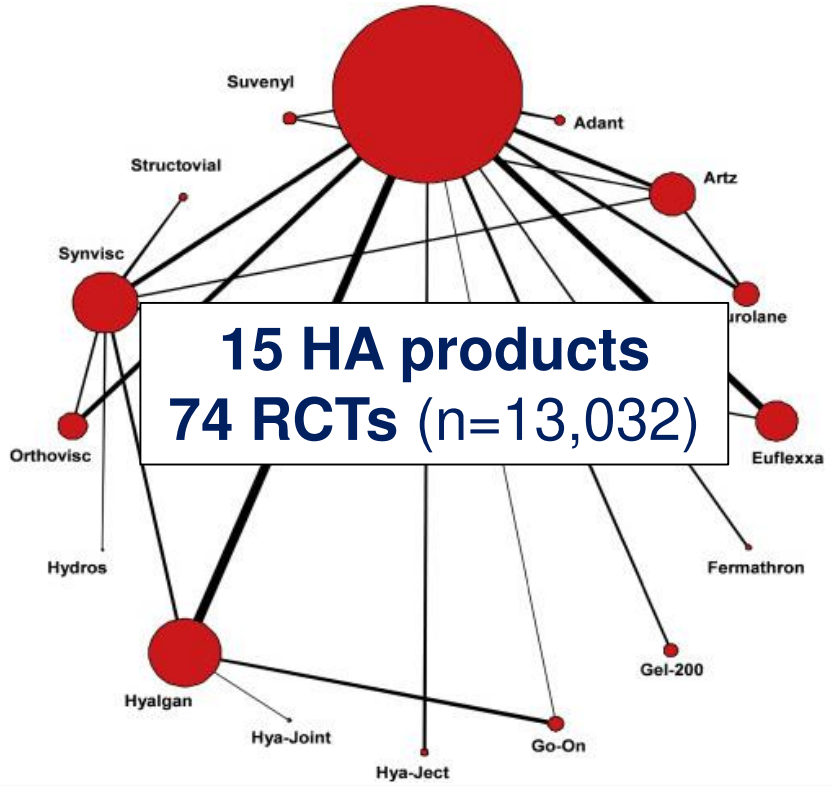
ARTICLE INFO

Article history:
Received 7 January 2016
Accepted 24 July 2016

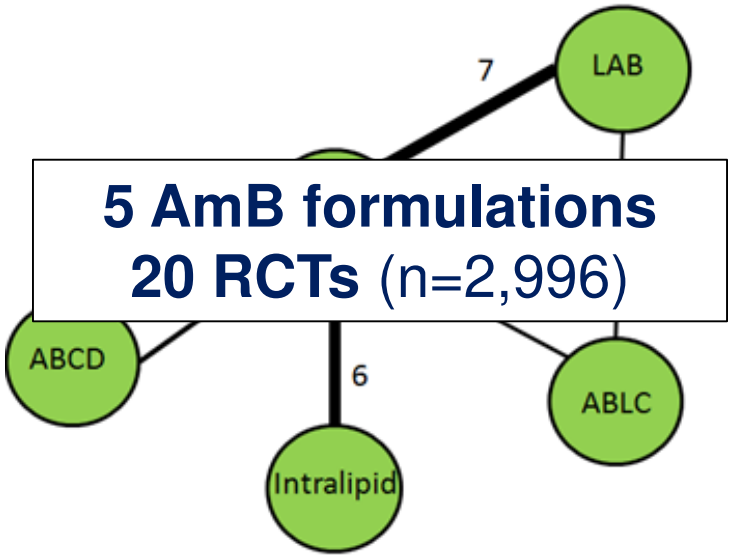
SUMMARY

Purpose: Intra-articular (IA) hyaluronic acid (HA) is considered a safer alternative to oral Non-Steroidal Antiinflammatory Drugs (NSAIDs) and opioids for knee osteoarthritis (OA). A recent review raised potential safety concerns about HA, warranting further review of safety outcomes. We examined the risks

Osteoarthritis Cartilage. 2016;24(12):2022-2041.



15 HA products
74 RCTs (n=13,032)



5 AmB formulations
20 RCTs (n=2,996)

JPP
Journal of Pharmacy
And Pharmacology

Research Paper

Efficacy and safety of amphotericin B formulations: a network meta-analysis and a multicriteria decision analysis

Fernanda S. Tonin[a], Laiza M. Steimbach[a], Helena H. Borba[a], Andreia C. Sanches[b], Astrid Wiens[c], Roberto Pontarolo[c] and Fernando Fernandez-Llimos[d]

[a]Pharmaceutical Sciences Postgraduate Program, Universidade Federal do Paraná, Curitiba, Brazil, [b]Department of Pharmacy, Universidade Estadual do Oeste do Paraná, Cascavel, Brazil, [c]Department of Pharmacy, Universidade Federal do Paraná, Curitiba, Brazil and [d]Department of Social Pharmacy, Faculty of Pharmacy, Research Institute for Medicines (iMed.ULisboa), Universidade de Lisboa, Lisbon, Portugal

J Pharm Pharmacol. 2017;69(12):1672-1683.

Drugs dose and regimen

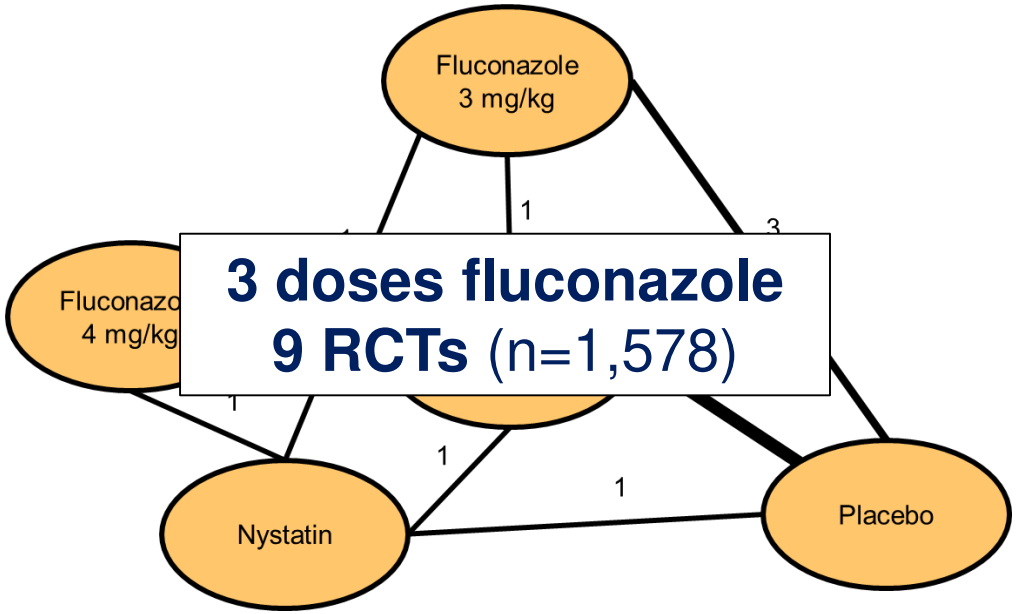
THE JOURNAL OF PEDIATRICS • www.jpeds.com

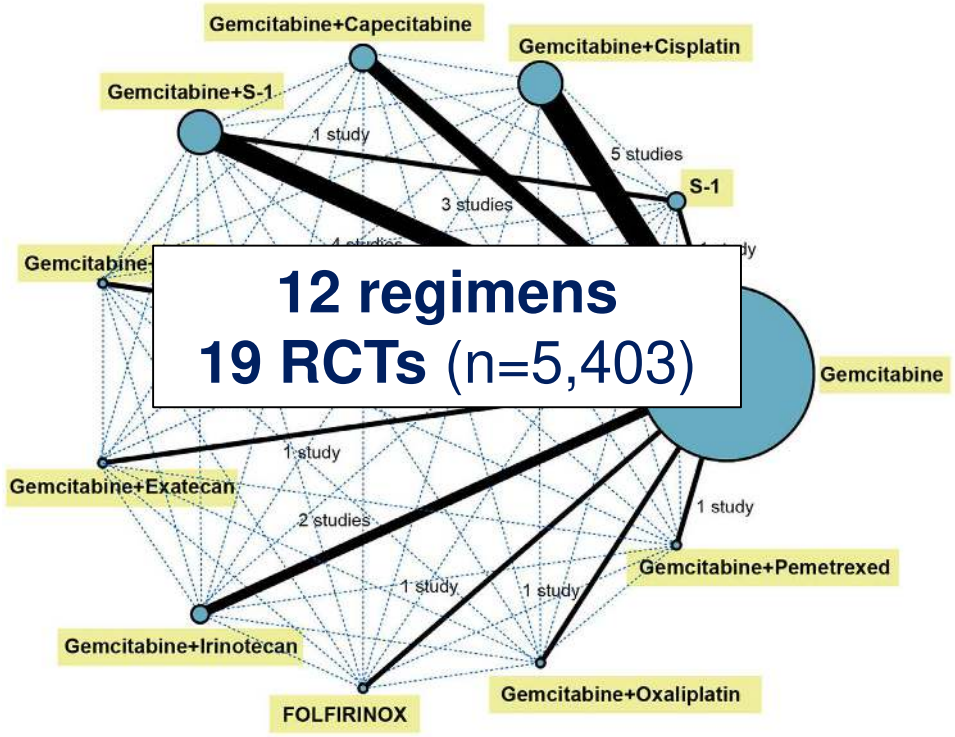
ORIGINAL ARTICLES

Fluconazole Doses Used for Prophylaxis of Invasive Fungal Infection in Neonatal Intensive Care Units: A Network Meta-Analysis

Letícia Paula Leonart, MSc[1], Fernanda Stumpf Tonin, MSc[1], Vinicius Lins Ferreira, MSc[1], Suelem Tavares da Silva Penteado, MSc[1], Fábio de Araújo Motta, PhD[2], and Roberto Pontarolo, PhD[1]

J Pediatr. 2017;185:129-135.e6





ARTICLE

Journal of Cellular Biochemistry 119:511–523 (2018)

Journal of Cellular Biochemistry

Efficacy and Toxicity of Different Chemotherapy Regimens in the Treatment of Advanced or Metastatic Pancreatic Cancer: A Network Meta-Analysis

Gui-Feng Liu,[1] Gui-Jie Li,[2] and Hang Zhao [3]*

[1]Department of Radiology, China-Japan Union Hospital of Jilin University, Changchun 130033, P.R. China

[2]Department of ENT, China-Japan Union Hospital of Jilin University, Changchun 130033, P.R. China

[3]Department of Neurosurgery, China-Japan Union Hospital of Jilin University, Changchun 130033, P.R. China

J Cell Biochem. 2018;119(1):511-523

Non-pharmacological complex interventions

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.elsevier.com/locate/rsap

An innovative and comprehensive technique to evaluate different measures of medication adherence: The network meta-analysis

Fernanda S. Tonin[a], Elyssa Wiecek[b], Andrea Torres-Robles[b], Roberto Pontarolo[c], Shalom (Charlie) I. Benrimoj[b], Fernando Fernandez-Llimos[d,*], Victoria Garcia-Cardenas[b]

[a] Pharmaceutical Sciences Postgraduate Programme, Federal University of Paraná, Curitiba, Brazil
[b] Graduate School of Health, University of Technology Sydney, Australia
[c] Department of Pharmacy, Federal University of Paraná, Curitiba, Brazil
[d] Research Institute for Medicines (iMed.ULisboa), Department of Social Pharmacy, Faculty of Pharmacy, Universidade de Lisboa, Lisbon, Portugal

Res Social Adm Pharm. 2018 May 19. S1551-7411(18)30407-8

5 measures of adherence
91 RCTs (n=42,338 patients)
10 interventions + standard of care

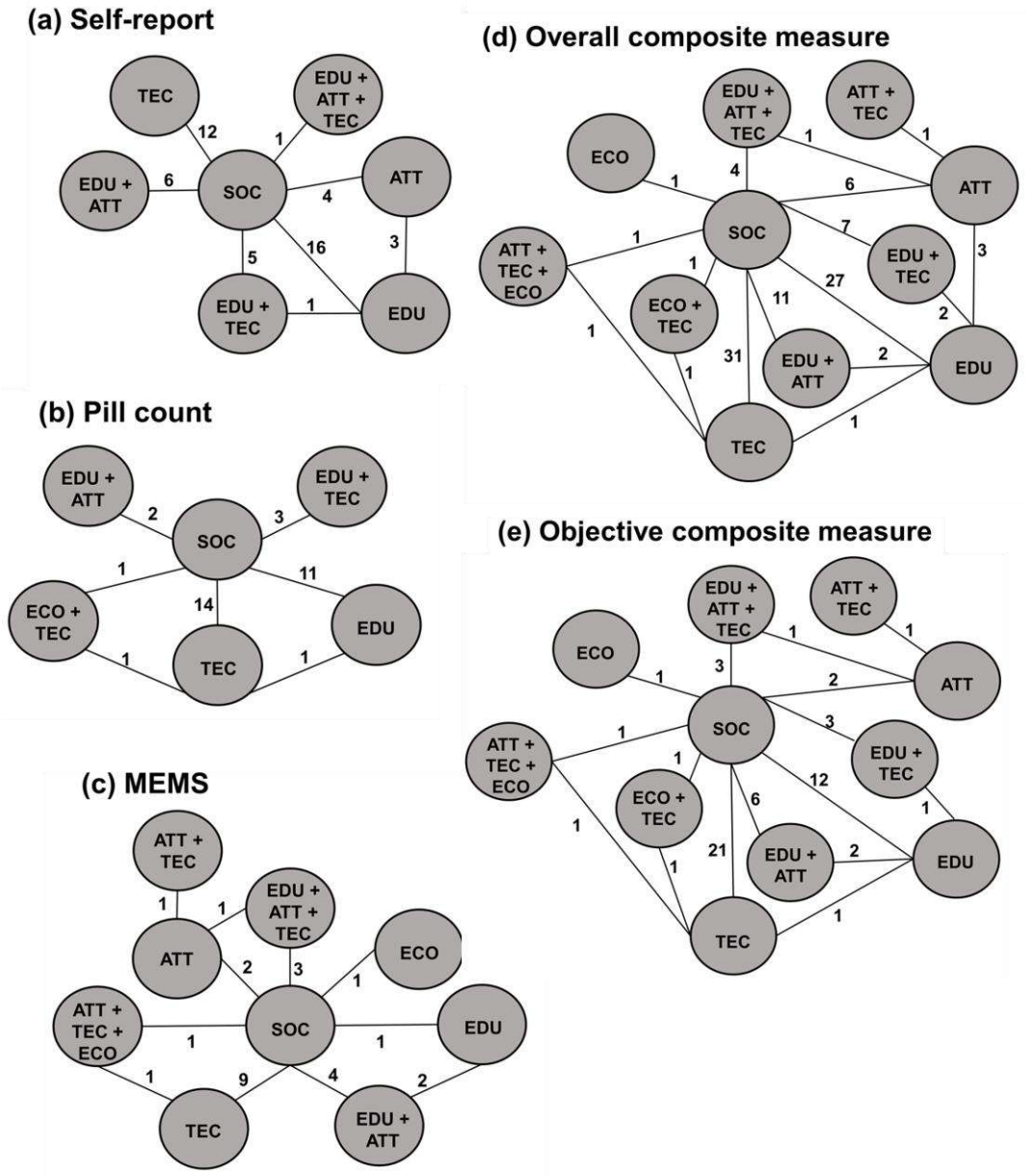


Fig. 2. Network diagrams of different measures of adherence for complex interventions.
(a) Self-report; (b) Pill count; (c) MEMS; (d) Overall composite measure; (e) Objective composite measure. Directly comparable interventions are linked with a line, the number of trials for each comparison are shown in each line. ATT: attitudinal; ECO: economic; EDU: educational; TEC: technical; SOC: standard of care.

Diagnostic methods

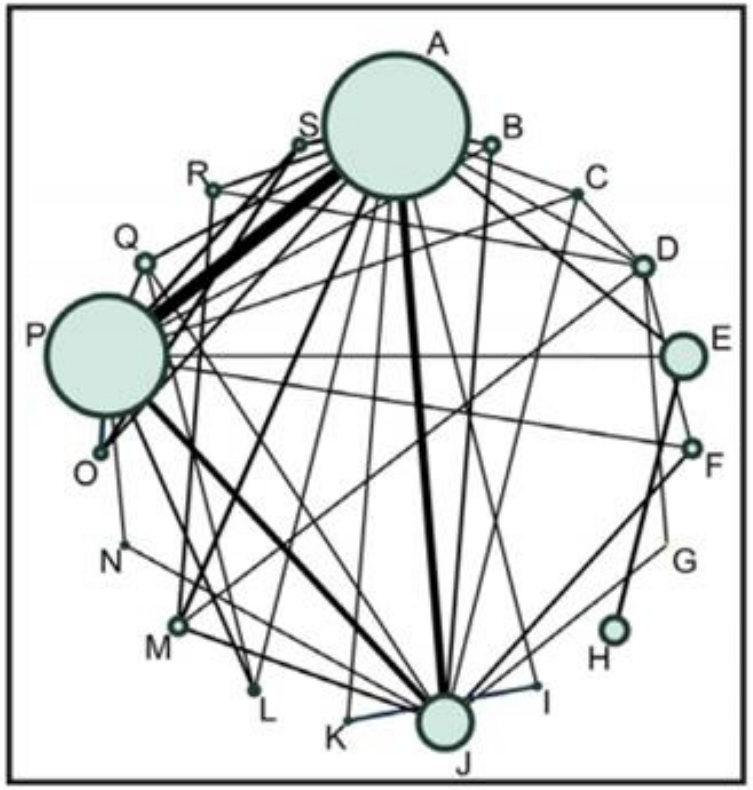


Fig. 3. Evidence network plot of diagnostic value of nineteen imaging methods for BC. Note: A = mammography (MG); B = breast-specific gamma imaging (BSGI); C = color Doppler sonography (CD); D = contrast-enhanced magnetic resonance imaging (CE-MRI); E = digital breast tomosynthesis (DBT); F = fluorodeoxyglucose positron-emission tomography/computed tomography (FDG PET/CT); G = fluorodeoxyglucose positron-emission tomography (FDG-PET); H = full field digital mammography (FFDM); I = handheld breast ultrasound (HHUS); J = magnetic resonance imaging (MRI); K = automated breast volume scanner (ABUS); L = magnetic resonance mammography (MRM); M = scintimammography (SMM); N = single photon emission computed tomography scintimammography (SPECT SMM); O = ultrasound elastography (UE); P = ultrasonography (US); Q = mammography + ultrasonography (MG + US); R = mammography + scintimammography (MG + SMM); S = ultrasound (UE + US); and BC = breast cancer.

Original Paper

Diagnostic Value of Nineteen Different Imaging Methods for Patients with Breast Cancer: a Network Meta-Analysis

Xiao-Hong Zhang Can Xiao

Department of Ultrasound, Huaihe Hospital of Henan University, Kaifeng, P.R. China

19 imaging methods
39 studies of diagnostic tests

Cell Physiol Biochem. 2018;46(5):2041-2055

Various interventions

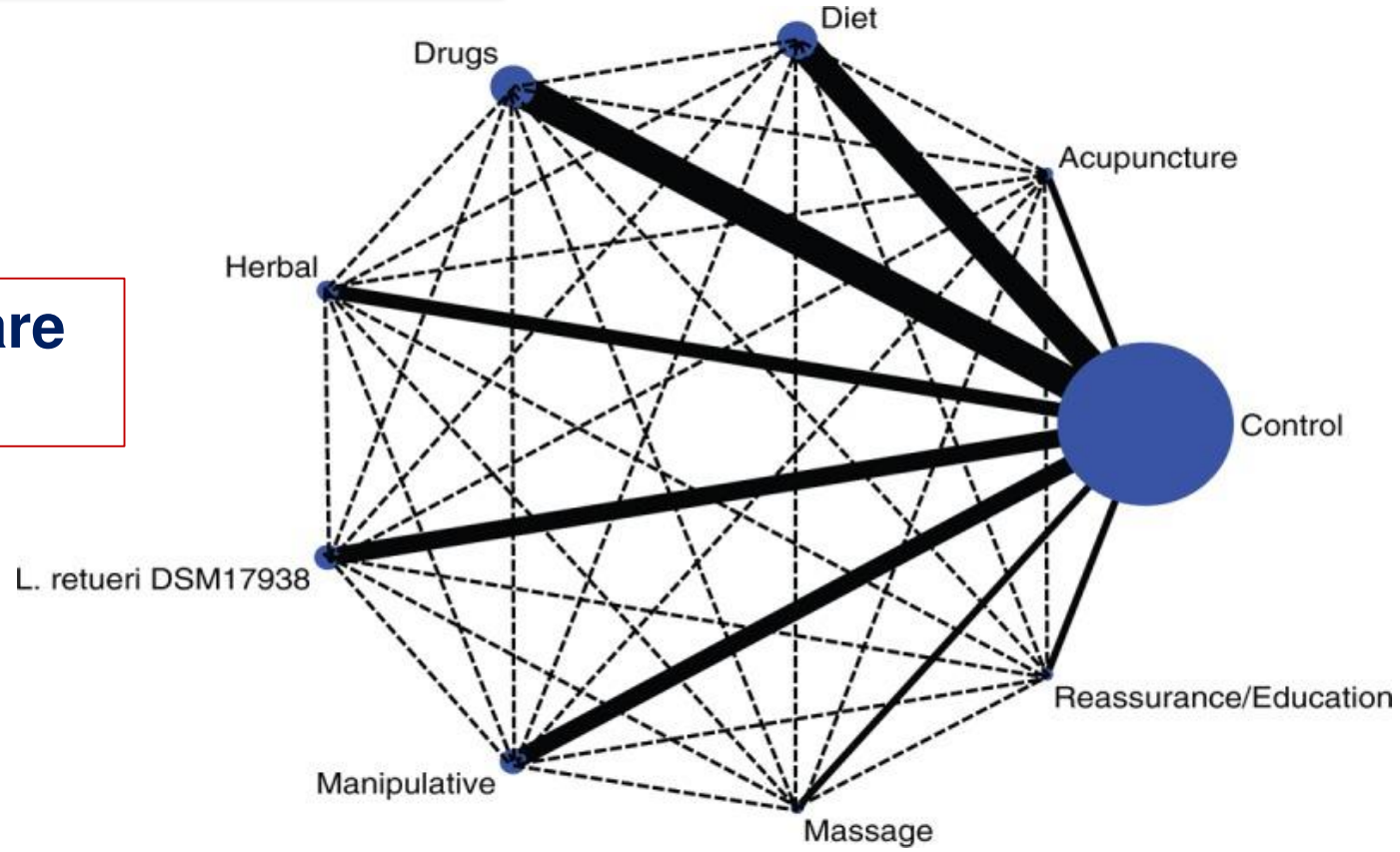
OPEN

Efficacy of *Lactobacillus reuteri* DSM 17938 for infantile colic

Systematic review with network meta-analysis

Pedro Gutiérrez-Castrellón, MD, MSc, PhD[a,*], Flavia Indrio, MD[b], Alexis Bolio-Galvis, MD, MSc[c], Carlos Jiménez-Gutiérrez, MPH, DPH[d], Irma Jimenez-Escobar, MD[e], Gabriel López-Velázquez, MSc, PhD[f]

8 interventions + standard of care
32 RCTs (n=2,242 patients)



Medicine (Baltimore). 2017;96(51):e9375

Biomarkers and genetics

Contents lists available at ScienceDirect

Gene

journal homepage: www.elsevier.com/locate/gene

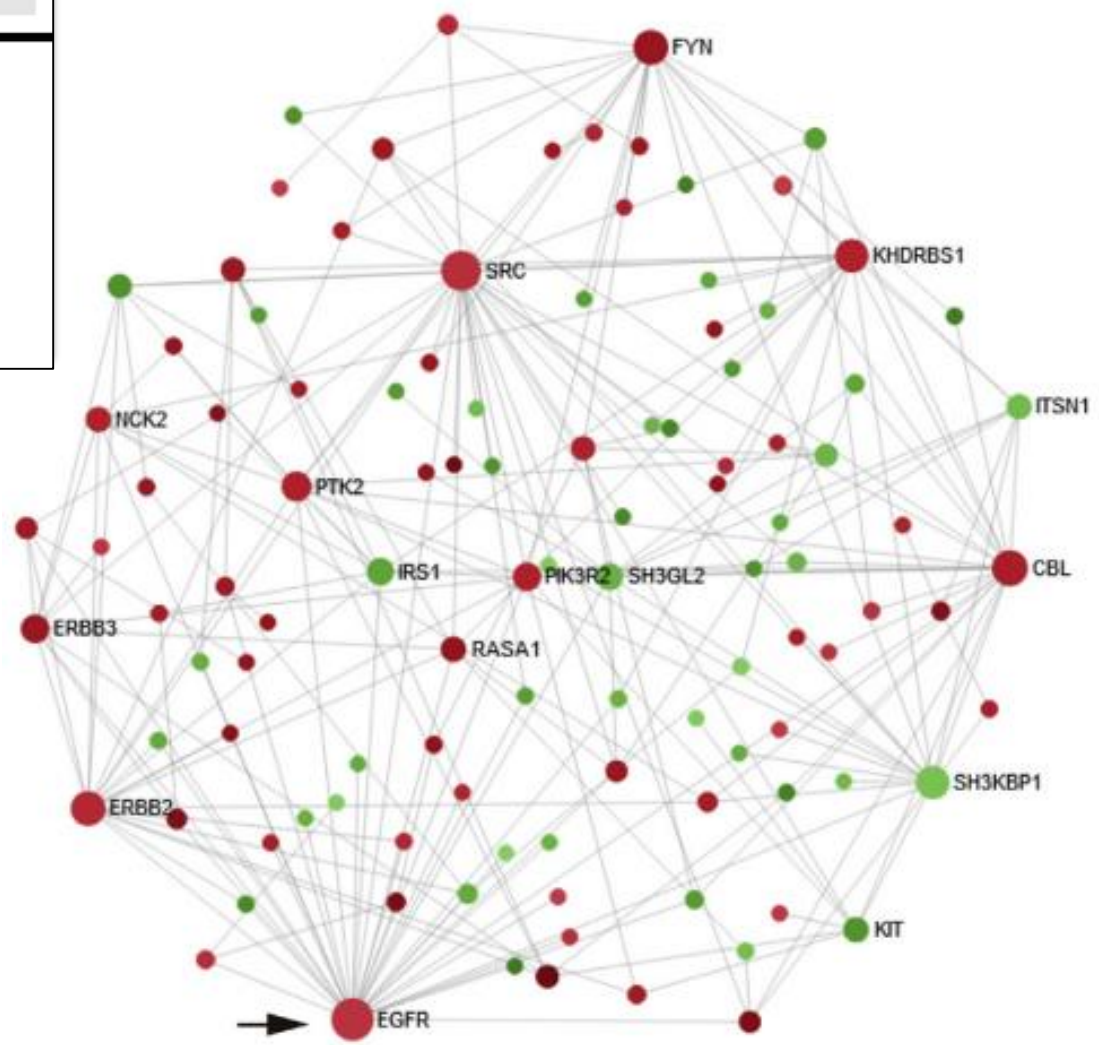
Research paper

Network-based meta-analysis in the identification of biomarkers for papillary thyroid cancer

Hengqiang Zhao[a,b,*], Hehe Li[a]

[a] Department of Pancreatic Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China
[b] Department of Breast and Thyroid Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China

5 microarray datasets with
94 carcinoma + 81 normal thyroid samples



Gene. 2018;661:160-168

…and so on…

J Neurotrauma. 2016 Feb 1;33(3):290-300. doi: 10.1089/neu.2015.4038. Epub 2016 Jan 7.

Melatonin for Spinal Cord Injury in Animal Models: A Systematic Review and Network Meta-Analysis.

Yang L[1,2], Yao M[1,2], Lan Y[1,2], Mo W[1,2], Sun YL[1,2], Wang J[1], Wang YJ[1,2], Cui XJ[1,2].

BMC Complement Altern Med. 2018 Apr 3;18(1):120. doi: 10.1186/s12906-018-2178-9.

Comparative efficacy of Chinese herbal injections for treating acute cerebral infarction: a network meta-analysis of randomized controlled trials.

Liu S[1], Wu JR[2], Zhang D[1], Wang KH[1], Zhang B[1], Zhang XM[1], Tan D[1], Duan XJ[1], Cui YY[1], Liu XK[1].

Syst Rev. 2015 Aug 27;4:114. doi: 10.1186/s13643-015-0099-y.

Comparison of physical interventions, behavioral interventions, natural health products, and pharmacologics to manage hot flashes in patients with breast or prostate cancer: protocol for a systematic review incorporating network meta-analyses.

Hutton B[1,2], Yazdi F[3], Bordeleau L[4], Morgan S[5], Cameron C[6], Kanji S[7], Fergusson D[8,9], Tricco A[10], Straus S[11], Skidmore B[12], Hersi M[13], Pratt M[14], Mazzarello S[15], Brouwers M[16], Moher D[17,18], Clemons M[19].

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Network meta-analysis **can** improve your life!
(...*research life*...)

Let's work together!

stumpf.tonin@ufpr.br

pontarolo@ufpr.br

f-llimos@ff.ul.pt