

# **Introduction to Systematic Review and Meta-analysis**

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# Session A. Introduction to Systematic Review

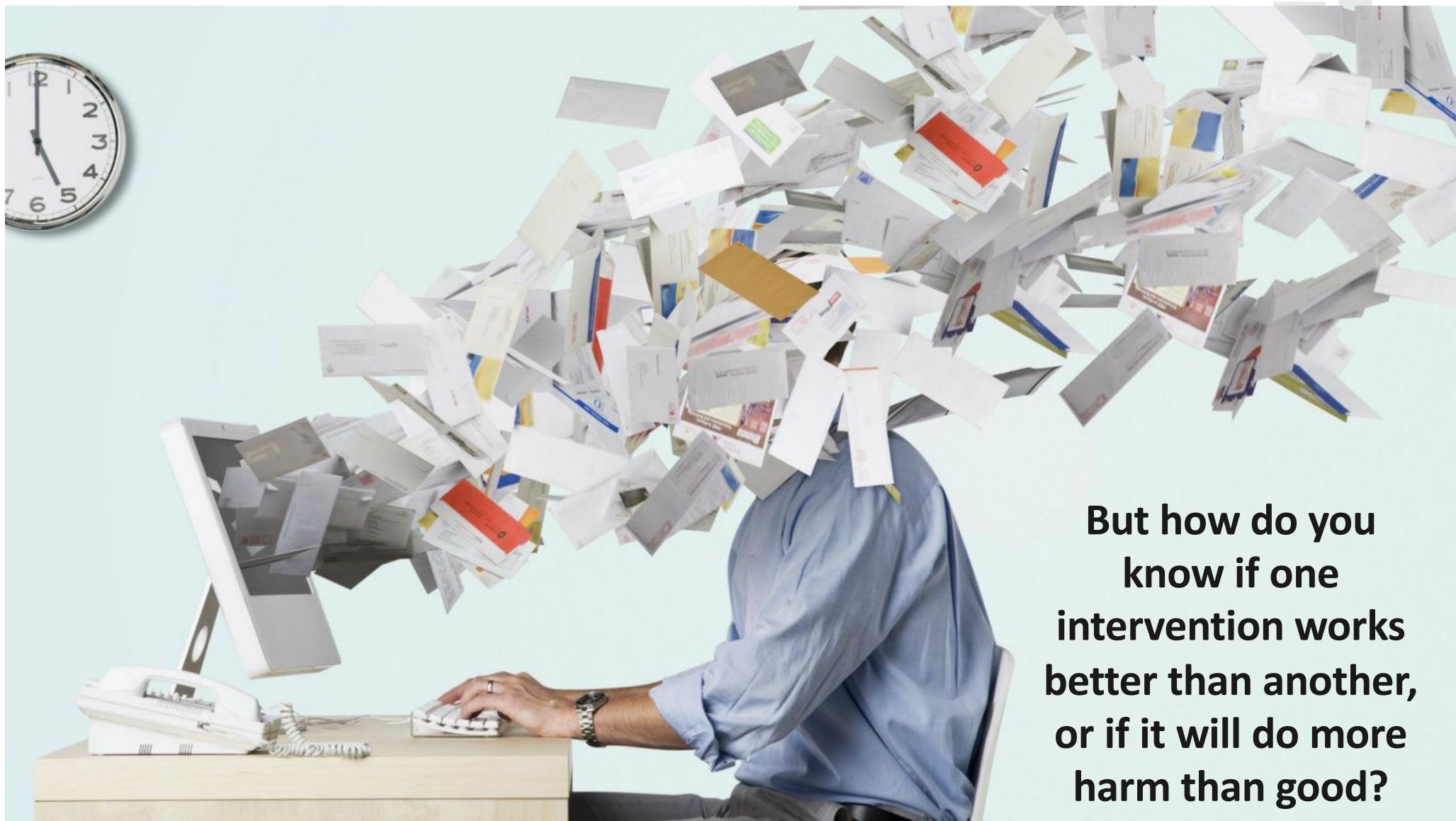


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## *Key Messages*

- Systematic review uses explicit methods to identify, select, appraise, and synthesize results from similar but separate studies.
- Meta-analysis, the statistical analysis of a collection of results from individual studies is an optional component of a systematic review.
- *The Cochrane Library*, main product of Cochrane is the single best place to find independent, high-quality evidence for healthcare decision making.

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By

UK World Business Football UK politics Environment Education **Society** Science Tech Global development Cities Obituaries**Alcohol**This article is more than **8 months old**

## No healthy level of alcohol consumption, says major study

**Governments should consider advising people to abstain entirely, say authors**

**Sarah Boseley** Health editor

Thu 23 Aug 2018 18.30 EDT



8,544



▲ The study contradicts most national guidelines which say there may be health benefits to one or two glasses of wine. Photograph: Inti St Clair/Getty Images/Blend Images

Even the occasional drink is harmful to health, according to the largest and

groups, and federal agencies, including the National Institutes of Health (NIH), has just issued new clinical guidelines aimed at preventing peanut allergy [1]. The guidelines suggest that parents should introduce most babies to peanut-containing foods around the time they begin eating other solid foods, typically 4 to 6 months of age. While early introduction is especially important for kids at particular risk for developing allergies, it is also recommended that high-risk infants—those with a history of severe eczema and/or egg allergy—undergo a blood

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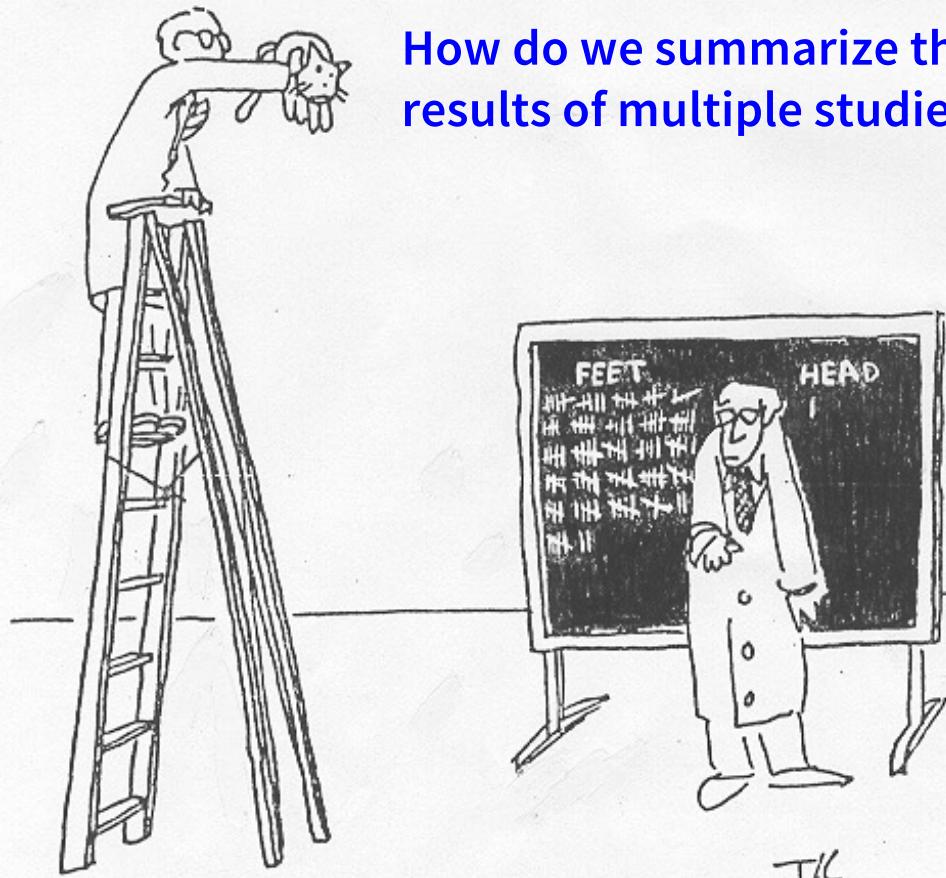


Passengers escape after plane skids off runway into river in Jacksonville, Florida



Blind date: 'He asked if I wanted "a little prick"

## How do we summarize the results of multiple studies?



“The hundreds of hours spent conducting a scientific study ultimately contribute only a piece of an enormous puzzle. **The value of any single study is derived from how it fits with and expands previous work, as well as from the study's intrinsic properties.** Through systematic review the puzzle's intricacies may be disentangled.”

- Cynthia D Mulrow, Senior Deputy Editor of Annals of Internal Medicine

## *Typical Clinical Questions*

- Is yoga effective for improving health-related quality of life, mental health, and cancer-related symptoms in women diagnosed with breast cancer?
- Is “early” epidural as effective and safe as “late” epidural for women in labor?
- Does IVF increase the risk of breast cancer?
- Does formaldehyde exposure increase the risk of leukemia?

## *Typical Questions Outside of Medicine*

- Does spending more money on schools improve educational outcomes?
- Do women or men make better leaders?
- Does sexual orientation of the parent matter?
- Are fathers more likely than mothers to treat their sons and daughters differently?
- Is job absenteeism an indicator of job dissatisfaction?



## **Yoga for women diagnosed with breast cancer**

### **What did we find?**

We found 24 studies that involved 2166 women. Our evidence is current to January 2016...

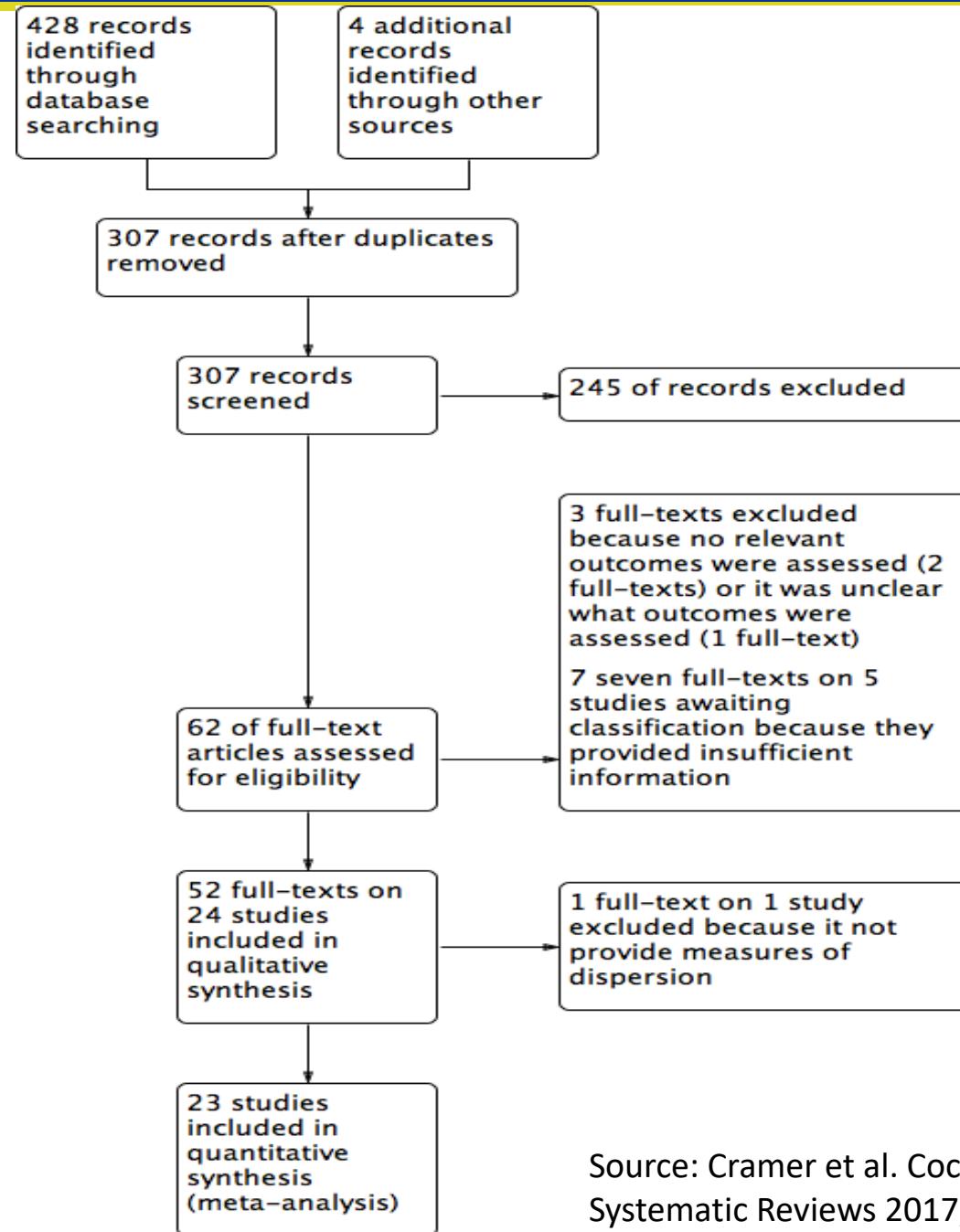
We found that yoga was more effective than no therapy in improving quality of life and reducing fatigue and sleep disturbances. We also found that yoga was better for reducing depression, anxiety and fatigue in women when compared with psychosocial or educational interventions such as counselling...Studies have poorly reported risks of yoga. However, we found no evidence of serious risks of yoga among women with a diagnosis of breast cancer.

### **What does this mean?**

Our findings indicate that women with a diagnosis of breast cancer can use yoga as supportive therapy for improving their quality of life and mental health, in addition to standard cancer treatments.

Source: Cramer et al. Cochrane Database of Systematic Reviews 2017, Issue 1.

# *Yoga for Women Diagnosed With Breast Cancer*



Source: Cramer et al. Cochrane Database of Systematic Reviews 2017, Issue 1.

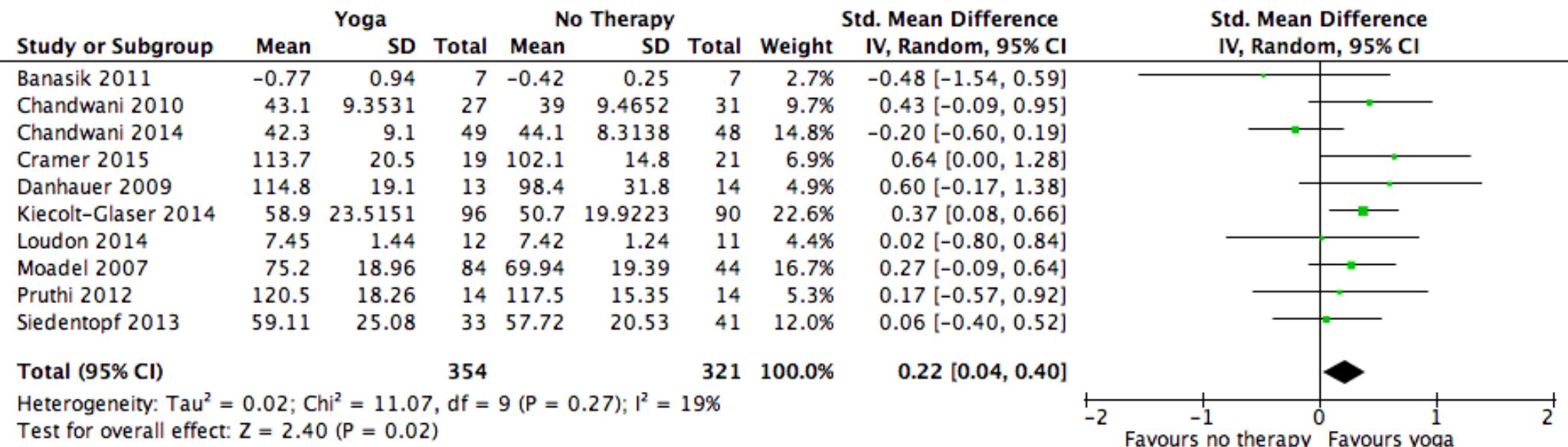
# *Yoga for Women Diagnosed With Breast Cancer*

	Banasik 2011	Banerjee 2007	Bernardi 2013	Bower 2012	Carson 2009	Chakrabarty 2015	Chandwani 2010	Cramer 2015	Danhauer 2009	Kiecolt-Glaser 2014	Kovacic 2013	Littman 2012	Lötzke 2016	Loudon 2014	Moadel 2007	Mustian 2013	Pruthi 2012	Raghavendra 2007	Siedentopf 2013	Taso 2014	Vadiraja 2009	Vardar Yağılı 2015	Wang 2014	
Random sequence generation (selection bias)	?	+	+	+	+	?	?	?	?	+	+	+	?	?	+	+	+	+	+	+	+	+	?	?
Allocation concealment (selection bias)	-	+	+	+	+	-	?	-	?	+	+	+	?	?	+	+	+	+	+	+	+	+	+	?
Blinding of participants and personnel (performance bias)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
Blinding of outcome assessment (detection bias)	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
Incomplete outcome data (attrition bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Selective reporting (reporting bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Other bias	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Source: Cramer et al. Cochrane Database of Systematic Reviews 2017, Issue 1.

# *Yoga for Women Diagnosed With Breast Cancer*

Forest plot of comparison: yoga versus no therapy, outcome: health-related quality of life short-term



Source: Cramer et al. Cochrane Database of Systematic Reviews 2017, Issue 1.

# *Yoga for Women Diagnosed With Breast Cancer*

## **Yoga versus no therapy for women with diagnosed breast cancer**

**Patient or population:** women with diagnosed breast cancer

**Settings:** inpatient and outpatient facilities

**Intervention:** yoga

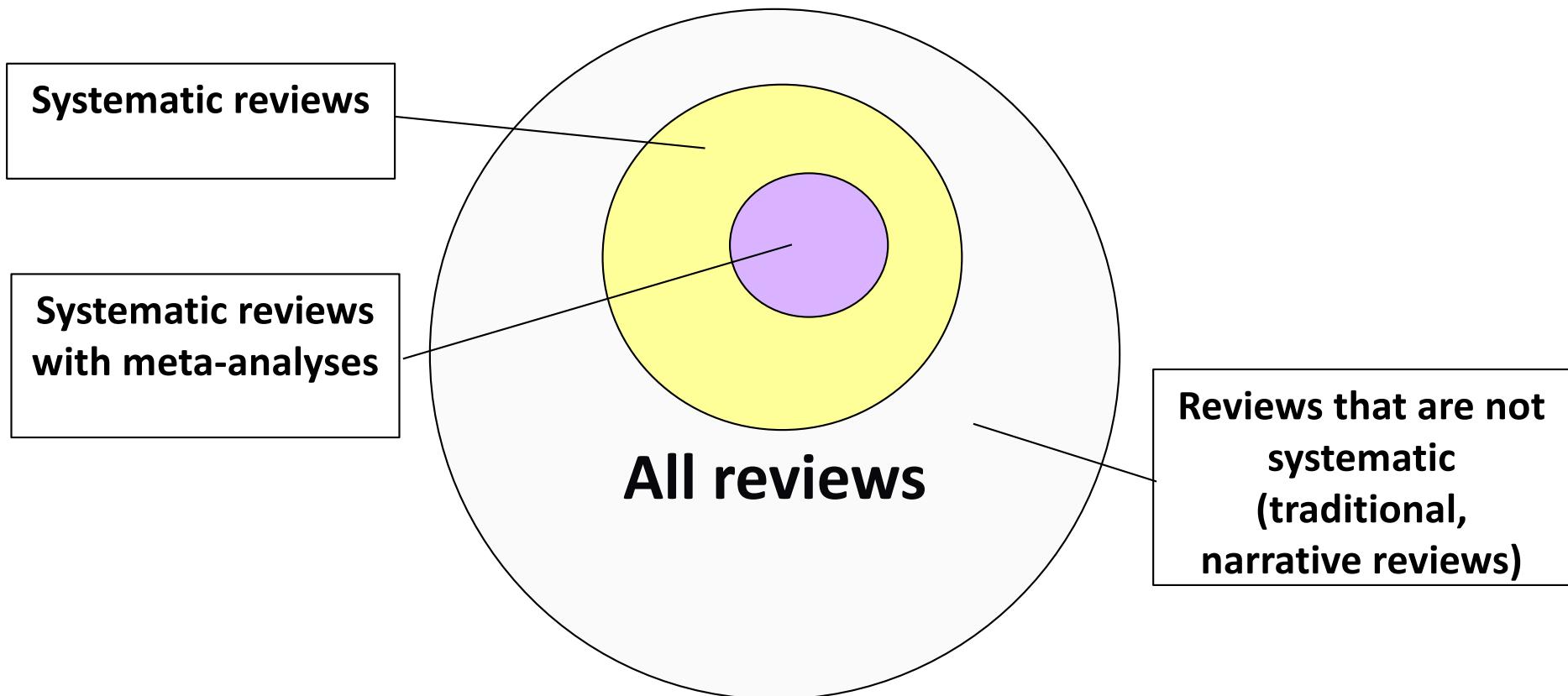
**Comparison:** no therapy

Outcomes	Illustrative comparative risks* (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Corresponding risk			
	<b>Yoga vs no therapy</b>			
<b>Health-related quality of life (short-term)</b> Self-assessed questionnaires Follow-up: 5-12 weeks	Mean health-related quality of life in intervention groups was <b>0.22 standard deviations higher</b> (0.06 to 0.38 higher)	675 (10 studies)	⊕⊕⊕⊖ <b>Moderate<sup>a</sup></b>	SMD 0.22 (95% CI 0.04 to 0.40)
<b>Health-related quality of life (medium-term)</b> Self-assessed questionnaires Follow-up: 30-48 weeks	Mean health-related quality of life in intervention groups was <b>0.10 standard deviations higher</b> (0.23 lower to 0.42 higher)	146 (2 studies)	⊕⊕⊕⊖ <b>Low<sup>b,c</sup></b>	SMD 0.10 (95% CI -0.23 to 0.42)
<b>Depression (short-term)</b> Self-assessed questionnaires Follow-up: 6-12 weeks	Mean depression in intervention groups was <b>0.13 standard deviations lower</b> (0.31 lower to 0.05 higher)	496 (7 studies)	⊕⊕⊕⊖ <b>Low<sup>b</sup></b>	SMD -0.13 (95% CI -0.31 to 0.05)
<b>Anxiety (short-term)</b>	Mean anxiety in intervention groups was	346	⊕⊕⊕⊖	SMD -0.53 (95% CI -1.10 to

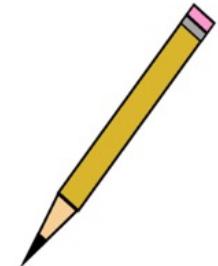
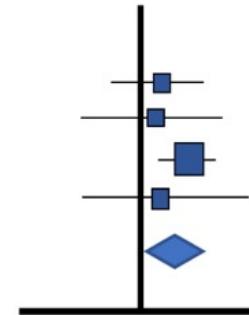
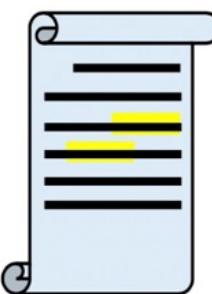
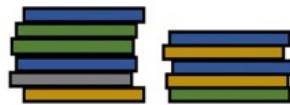
Summary of findings for the main comparison. Yoga versus no therapy for women with diagnosed breast cancer

# *What is a Systematic Review?*

- Focuses on a specific question
- Uses explicit, pre-planned scientific methods to ***identify, select, appraise, and summarize*** similar but separate studies



# *Steps in Completing a Systematic Review*



## **PREPARE TOPIC**

- Formulate research question(s)
- Develop analytic framework

## **SEARCH FOR STUDIES**

- Define eligibility criteria
- Search for relevant studies

## **SCREEN STUDIES**

- Screen studies for inclusion

## **ABSTRACT DATA**

- Abstract data from included studies
- Assess risk of bias
- Construct evidence tables

## **ANALYZE AND SYNTHESIZE DATA**

- Conduct qualitative synthesis
- Conduct quantitative synthesis (ie, meta-analysis) if appropriate
- Assess the strength of evidence

## **REPORT FINDINGS**

# Why Systematic Reviews Important?

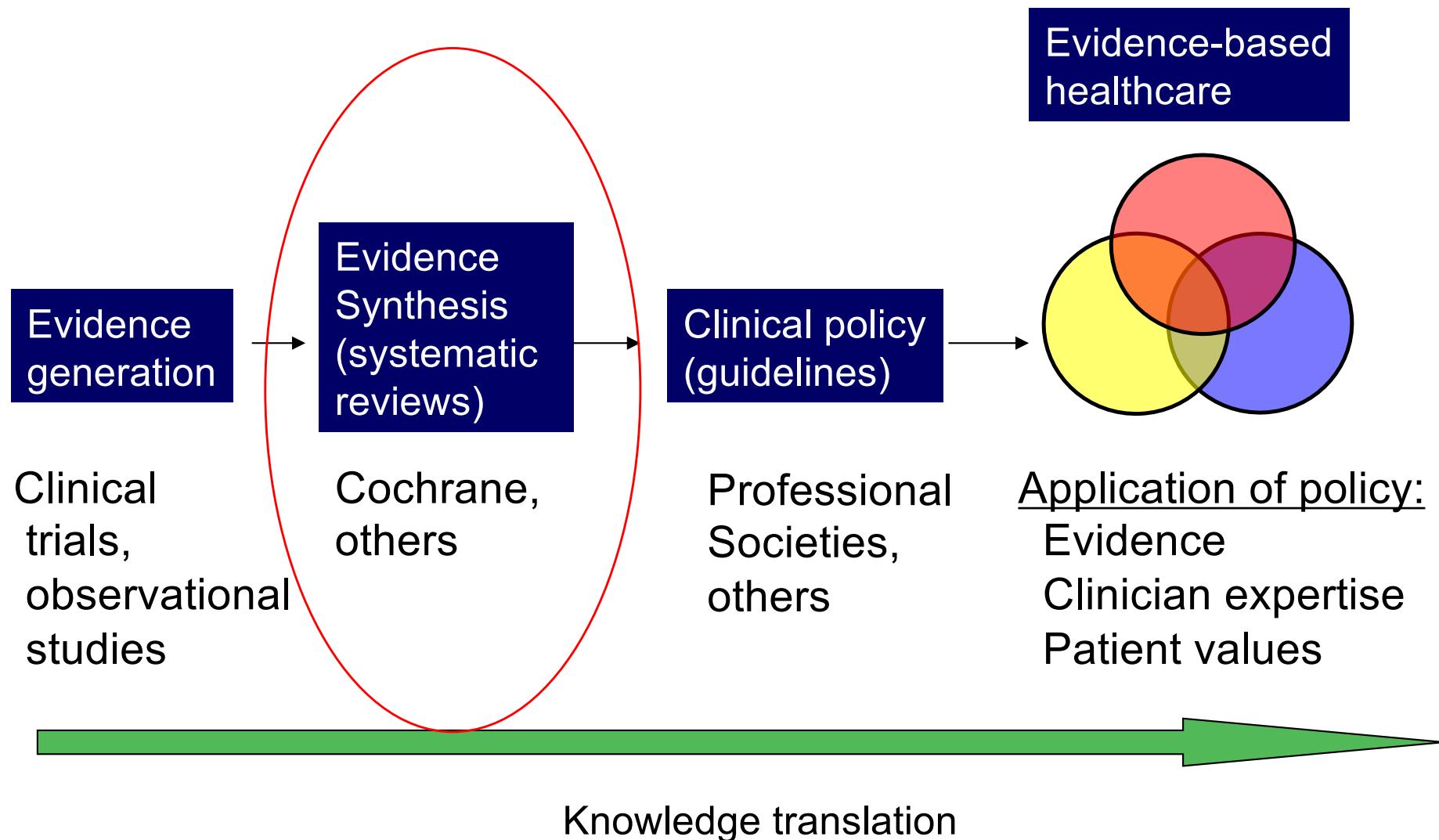
- Aim to capture all the relevant high quality evidence (comprehensive search)
- May provide a pooled estimate of effect from all studies (increase power and precision)
- Analyse the risk of bias of included studies and the certainty of the evidence
- The basis for most credible guidelines



The Concept of a Systematic Review



# Knowledge Translation: From Clinical Research to Practice Decisions





## Session B. Introduction to Meta-analysis

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# *What is a Meta-analysis?*

An ***optional*** component of a systematic review

Definition:

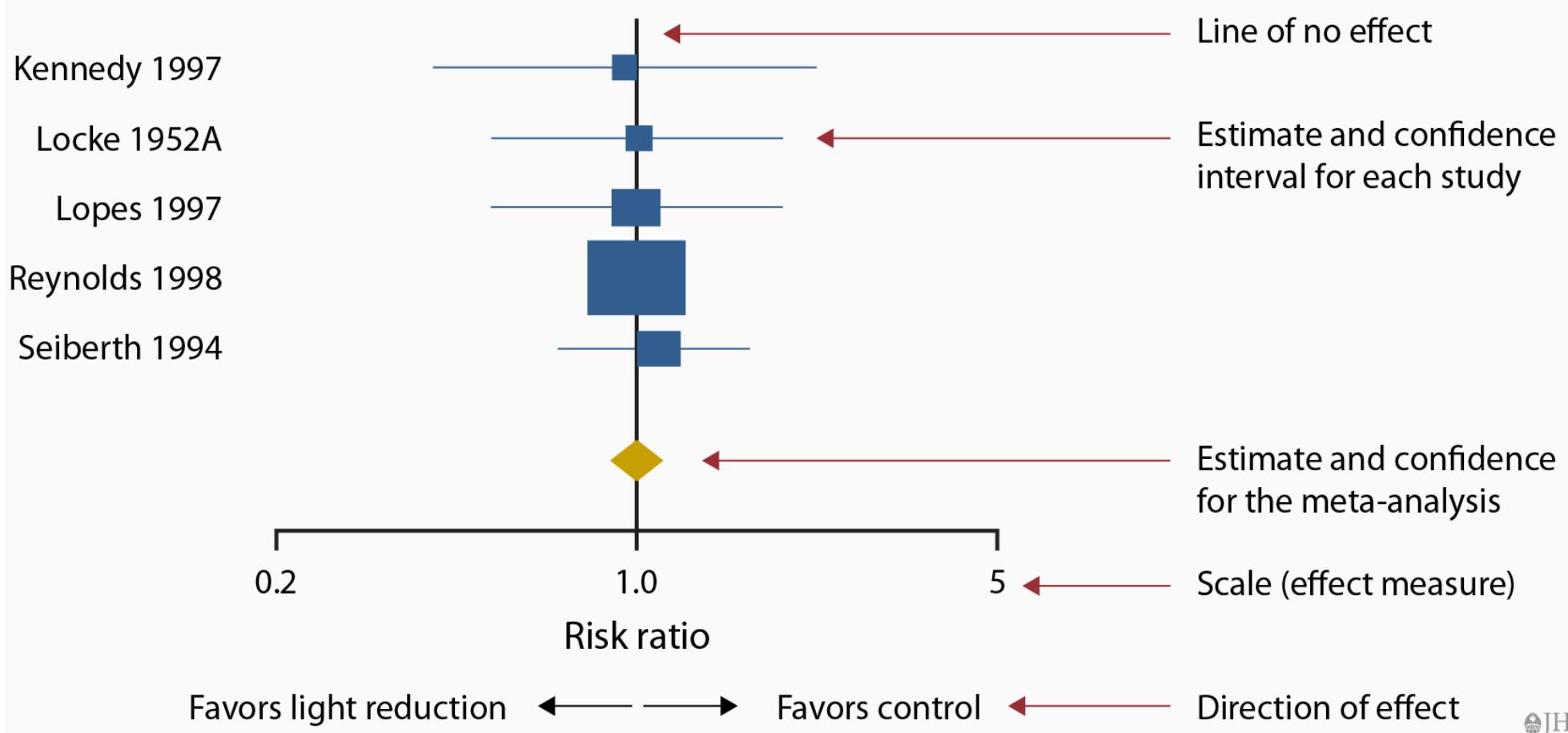
“The statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings.” (Glass 1976)

Alternative definition:

“A statistical analysis which combines the results of several independent studies considered by the analyst to be ‘combinable’ ” (Huque 1988)

# Meta-analysis Presentation: The Forest Plot

Estimates with 95% Confidence Intervals



## A General Framework for Synthesis

- What is the ***direction*** of effect (association)?
- What is the ***size*** of effect?
- Is the effect ***consistent*** across studies?
- What is the ***strength*** of evidence for the effect?\*

\* Relies additionally on judgments based on assessments of study design and risk of bias, as well as statistical measures of uncertainty

## *What Meta-Analysis Can Help You Do?*

- ▶ Assess strength of evidence
  - To determine whether an effect exists in a particular direction
- ▶ Combine results quantitatively
  - To obtain a single summary result
- ▶ Investigate heterogeneity
  - To examine reasons for different results among studies

# *Combining Results in a Meta-analysis*

- Justification for combining results:
  - Studies are estimating – in whole or in part –a common effect
  - Studies are addressing the same fundamental biological/clinical/mechanistic question.

# *Addressing Same Question?*

- What is the effectiveness of face masks in reducing the spread of respiratory viruses?
  - Different types of masks: N95, surgical masks, cloth masks
  - Different types of participants: healthcare workers, patients who are infected, vulnerable population, healthy individuals
  - Different types of settings: laboratory, hospital, community, during outbreak
  - Different types of respiratory viruses
  - Different types of design: RCTs vs. non-RCTs, animal studies, mechanistic studies

## **Poll Question 1.**

**How many studies do you need for a meta-analysis?**

- 2
- A few
- It depends
- I don't know

## *When to Do a Meta-analysis*

- When more than one study has estimated a treatment effect or association
- When the differences in the study characteristics are unlikely to affect the treatment effect (or when investigating specific differences)
- When the treatment effect have been measured and reported in similar ways (or when the data are available)

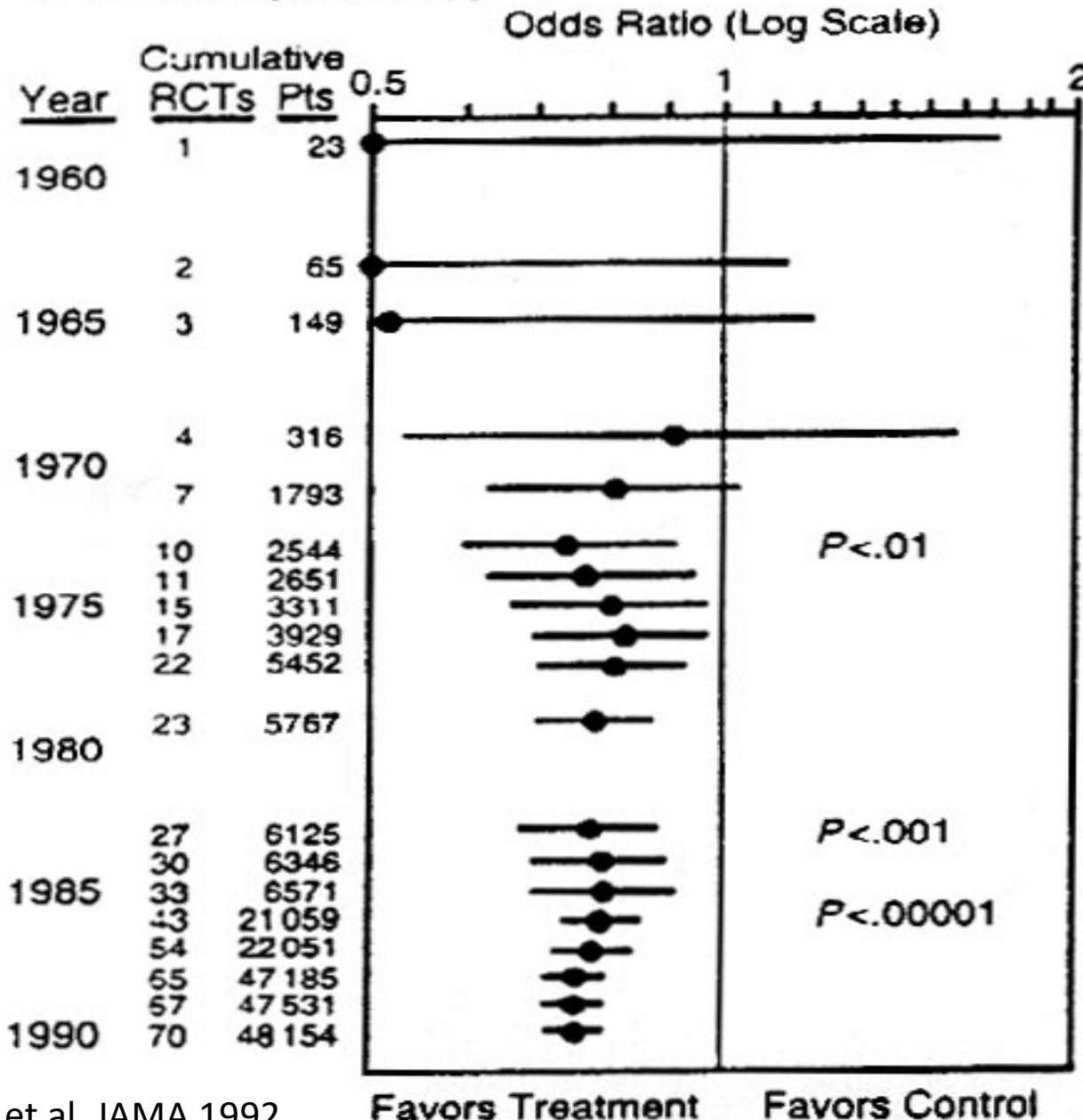
# *When Not to Do a Meta-analysis?*

- “Garbage in - garbage out”
  - A meta-analysis is only as good as the studies in it
  - Narrower confidence interval around combination of biased studies worse than the biased studies on their own
  - Beware of reporting biases
- “Mixing apples with oranges”
  - Not useful for learning about apples, although useful for learning about fruit!
  - Studies must address the same question
    - Though the question can, *and usually must*, be broader

Slide courtesy of Julian Higgins

# Importance of Synthesizing What We Know in an Ongoing Fashion

## A. Thrombolytic Therapy



## Textbook/Review Recommendations

Route	Specific	Rare/Never	Experimental	Not Mentioned
				21
				5
			1	10
			1	2
			2	8
				7
				8
M		1		12
M	1		8	4
M	1		7	3
M	5	2	2	1
M	15	8		1
M	6	1		



## Session C. How Systematic Reviews Can Improve Decisions



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# *Systematic Reviews and Guidelines*



- American Academy of Ophthalmology (AAO) publishes 23 preferred practice patterns (PPPs) on specialty topics; PPPs updated every 5 years
- Cochrane Eyes and Vision US Project
  - Identify potentially relevant systematic reviews
  - Assess reliability of relevant systematic reviews
  - Share reliable relevant systematic reviews with AAO to inform guideline recommendations



# Systematic Reviews and Guidelines (cont'd)

## Select Types

- Clinical Statements
- Compendium
- Complementary Therapy Assessments
- Ophthalmic Technology Assessments
- Patient Safety Statements
- Preferred Practice Patterns
- Guidelines
- Clinical Questions

### Dry Eye Syndrome PPP - 2018

NOV 2018 from AAO PPP Cornea/External Disease Committee, Hoskins Center for Quality Eye Care

Evidence-based update using Cochrane Eyes and Vision Group-identified systematic reviews detailing recommendations for the initial evaluation and treatment of a patient with dry eye and a detailed discussion of diagnostic tests.

Preferred Practice Pattern Guideline

Comments 0

Views 2181

### Blepharitis PPP-2018

NOV 2018 from AAO PPP Cornea/External Disease Committee, Hoskins Center for Quality Eye Care

Evidence-based update using Cochrane Eyes and Vision Group-identified systematic reviews detailing recommendations for the initial evaluation of a patient with presumed blepharitis, and for diagnostic tests and treatment.

Comments 0

Views 2098

Altogether, Cochrane Eyes and Vision US Project has supported the update of 19/23 PPPs since 2015.

## Most Commented

1. Can You Guess January's Mystery Condition?
2. Pressure-Based Method to Move Vitreous
3. Displacing a Large Submacular Hemorrhage

### Conjunctivitis PPP - 2018

NOV 2018 from AAO PPP Cornea/External Disease Committee, Hoskins Center for Quality Eye Care

Evidence-based update using Cochrane Eyes and Vision Group-identified systematic reviews for the initial evaluation of conjunctivitis patients and discussion of associated or predisposing factors, the natural history of each type of conjunctivitis and treatment recommendatio...

Preferred Practice Pattern Guideline

Comments 0

Views 1653

### Corneal Edema and Opacification PPP - 2018

NOV 2018 from AAO PPP Cornea/External Disease Committee, Hoskins Center for Quality Eye Care

Evidence-based update using Cochrane Eyes and Vision Group-identified systematic reviews for the initial evaluation and diagnosis of corneal edema and corneal opacification. Management approaches for edema and opacification, including surgical approaches, are discussed separ...

Preferred Practice Pattern Guideline

Comments 0

Views 1278

## Most Viewed

1. FDA approves Rocklatan for open-angle glaucoma, ocular hypertension
2. Displacing a Large Submacular Hemorrhage
3. Steroids for NAION

### Bacterial Keratitis PPP - 2018

NOV 2018 from AAO PPP Cornea/External Disease Committee, Hoskins Center for Quality Eye Care

Evidence-based update using Cochrane Eyes and Vision Group-identified systematic reviews on the diagnosis and management of bacterial keratitis. It contains detailed recommendations for the initial evaluation of a patient with presumed bacterial keratitis, and for diagnostic...

Preferred Practice Pattern Guideline

Comments 0

Views 1597

# Identification and Description of Reliable Evidence for 2016 American Academy of Ophthalmology Preferred Practice Pattern Guidelines for Cataract in the Adult Eye

Mayo-Wilson et al. *BMC Ophthalmology* (2017) 17:164  
DOI 10.1186/s12886-017-0561-9

JAMA Ophthalmology | Original Investigation

JAMA Ophthalmology | Original Investigation

dressing Treatment

## Evaluation of Systematic Reviews of Interventions for Retina and Vitreous Conditions

IEWS

Jimmy T. Le, MA, ScD; Riaz Qureshi, MSc; Claire Twose, MLIS; Lori Rosman, MLS; Genie Han, MS; Kolade Fapohunda, BS;  
Ian J. Saldanha, MBBS, MPH, PhD; Roberta W. Scherer, PhD; Flora Lum, MD; Ali Al-Rajhi, PhD, MPH; David C. Musch, PhD, MPH;  
Barbara S. Hawkins, PhD; Kay Dickersin, MA, PhD; Tianjing Li, MD, MHS, PhD

D;

**IMPORTANCE** Patient care and clinical practice guidelines should be informed by evidence from reliable systematic reviews. The reliability of systematic reviews related to forthcoming guidelines for retina and vitreous conditions is unknown.

**OBJECTIVES** To summarize the reliability of systematic reviews on interventions for 7 retina and vitreous conditions, describe characteristics of reliable and unreliable systematic reviews, and examine the primary area in which they appeared to be lacking.

**DESIGN, SETTING, AND PARTICIPANTS** A cross-sectional study of systematic reviews was conducted. Systematic reviews of interventions for retina- and vitreous-related conditions in a database maintained by the Cochrane Eyes and Vision United States Satellite were identified. Databases that the reviewers searched, whether any date or language restrictions were applied, and bibliographic information, such as year and journal of publication, were documented. The initial search was conducted in March 2007, and the final update was performed in July 2018. The conditions of interest were age-related macular degeneration; diabetic retinopathy; idiopathic epiretinal membrane and vitreomacular traction; idiopathic macular hole; posterior vitreous detachment; retinal breaks; and lattice degeneration; retinal

+ Supplement practice guidelines, which in turn views. The American Academy of PPs) for the management of the conjunctivitis, corneal ectasia,

matic reviews addressing

abase.

ews from 1997 to 2017 (median, was searched for systematic / corneal disease, combining eyes validated search filter.

+ Suppl

# Cochrane Evidence Informs Guidelines

In 2016, close to 90% of WHO guidelines used Cochrane Systematic Reviews.



***“Cochrane is a major player at a global level to synthesize, analyze and disseminate health evidence.”***

Marie Paule Kieny, Former Assistant Director-General, WHO



## Session D. Producers and Users of Systematic Reviews



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# *Who is Doing Systematic Reviews?*

- Independent authors
- Cochrane
- Groups interested in policy (professional societies, governments, payers)
  - ▶ United States: Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Centers (EPCs), US Preventive Services Task Force (USPSTF)
  - ▶ United Kingdom: National Institute for Health and Care Excellence (NICE), Health Technology Assessments
  - ▶ Germany: Institute for Quality and Efficiency in Health Care (IQWiG)
- Businesses: Hayes, ECRI

## **Poll Question 2.**

### **Who is Archie Cochrane?**

- A medical doctor who founded the Cochrane Collaboration.
- A British epidemiologist who called for a system of producing up-to-date summaries of reliable healthcare evidence.
- The father of modern epidemiology.


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**Systemic pharmacological treatments for chronic plaque psoriasis**

 Emilie Sbidian, Anna Chaimani, Ignacio Garcia-Doval, Liz Doney, Co  
Naldi, Sivem Afach, Laurence Le Cleach

23 May 2022

**Signs and symptoms to determine if a patient presenting in primary care has COVID-19**

 Thomas Struyf, Jonathan J Deeks, Jacqueline Dinnis, Yemisi Takwo  
Spijker, Lotty Hooft, Devy Emperador, Julie Domen, Anouk Tans, Sté  
Lannoy, Sebastiaan R A Horn, Ann Van den Bruel, Cochrane COVID-19

20 May 2022

**Ocrelizumab for multiple sclerosis**

Mengbing Lin, Jian Zhang, Yueling Zhang, Jiefeng Luo, Shengliang S

18 May 2022

**Physiotherapy for pain and disability in adults with complex regional pain syndrome**

Keith M Smart, Michael C Ferraro, Benedict M Wand, Neil E O'Conno

17 May 2022

**Thoracic imaging tests for the diagnosis of COVID-19**

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6

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# Systematic Reviews of Interventions

SECOND EDITION

Edited by

Julian P. T. Higgins

James Thomas

Associate Editors

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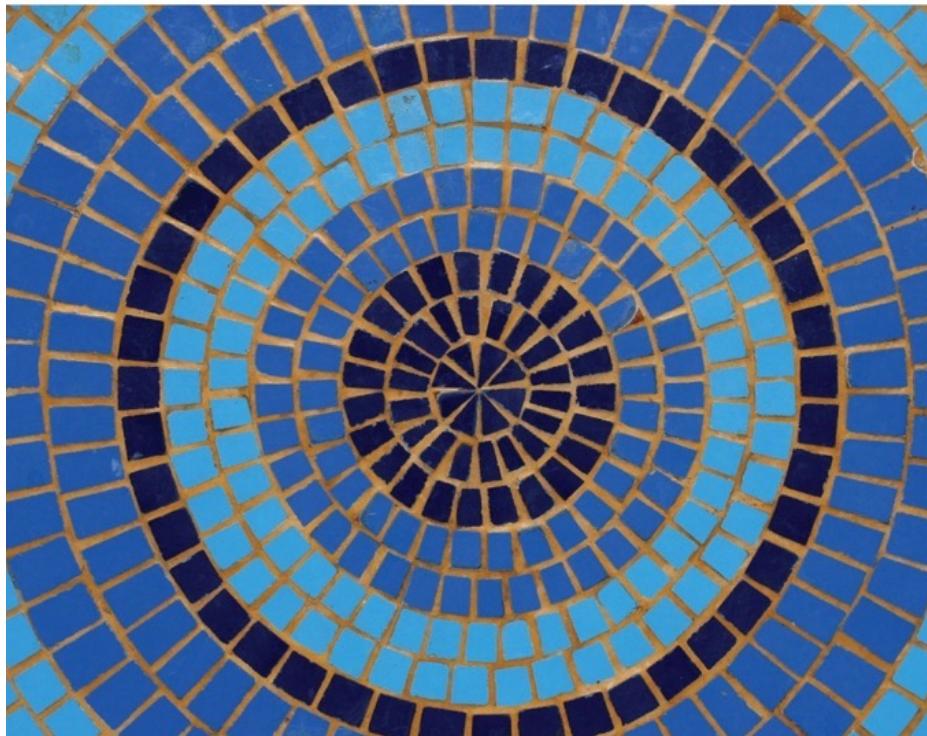
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# FINDING WHAT WORKS IN HEALTH CARE

## STANDARDS FOR SYSTEMATIC REVIEWS



Available at: <https://www.nap.edu/catalog/13059/finding-what-works-in-health-care-standards-for-systematic-reviews>

# Methodological Expectations of Cochrane Intervention Reviews (MECIR)

Version February 2022

**Standards for the conduct and reporting of new Cochrane Intervention Reviews, reporting of protocols and the planning, conduct and reporting of updates**

**Julian Higgins<sup>1</sup>, Toby Lasserson<sup>2</sup>, Jackie Chandler<sup>3</sup>, David Tovey<sup>4</sup>, James Thomas<sup>5</sup>, Ella Flenyng<sup>2</sup>, Rachel Churchill<sup>6</sup>**

<sup>1</sup> Professor of Evidence Synthesis, University of Bristol, Bristol, UK

<sup>2</sup> Cochrane Evidence Production and Methods Directorate, Cochrane, London, UK

<sup>3</sup>Evaluation Programme Manager, Wessex Academic Health Science Network, Southampton, UK

<sup>4</sup> Editor in Chief (2009-2019), Cochrane Library, UK

<sup>5</sup>Professor of Social Research and Policy, University College London, London, UK

<sup>6</sup> Centre for Reviews and Dissemination, University of York, York, UK

These MECIR Standards present a guide to the conduct and reporting of Cochrane Intervention Reviews. Each set of Standards includes links to Cochrane Training resources, the [\*Cochrane Handbook for Systematic Reviews of Interventions\*](#) (the *Handbook*) and other available resources.

This online version will be kept up to date. A PDF of each section can be generated. All substantive changes will be noted [here](#).

- MECIR Standards link to the most up-to-date version of the *Handbook* chapters.
- Where links to external resources are included [\*Cochrane Interactive Learning\*](#) is referred to as '**CIL**'.
- We welcome your feedback on MECIR, or if you have any general queries related to the MECIR Standards, please contact [support@cochrane.org](mailto:support@cochrane.org).

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- Meta-analysis, the statistical analysis of a collection of results from individual studies is an optional component of a systematic review.
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