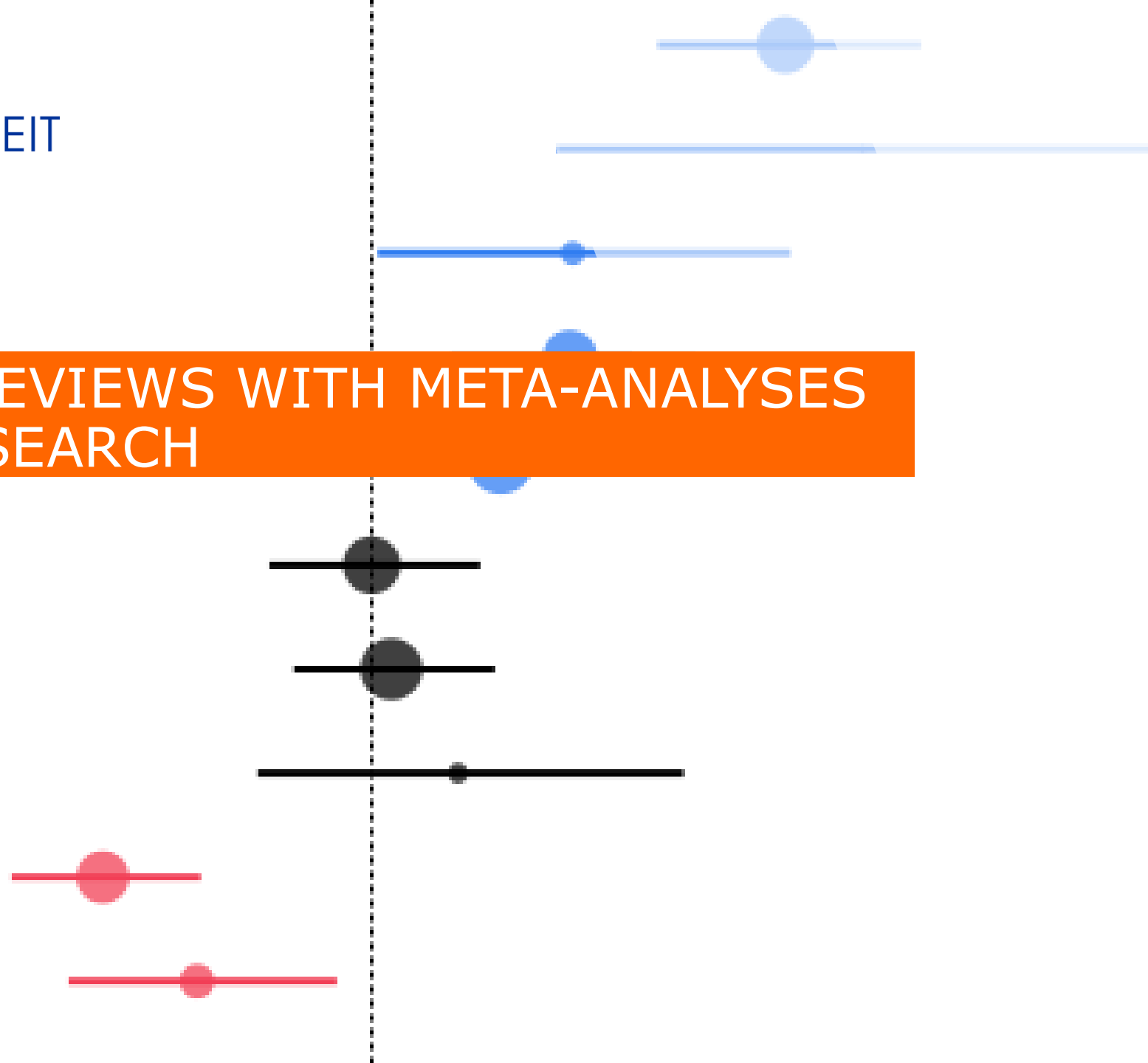


# SYSTEMATIC REVIEWS WITH META-ANALYSES IN HEALTH RESEARCH

Nils Runge



# CONTENT

1. Initial considerations
2. Components of Systematic Reviews
3. Meta-Analyses
4. The Forest Plot

# INITIAL CONSIDERATIONS

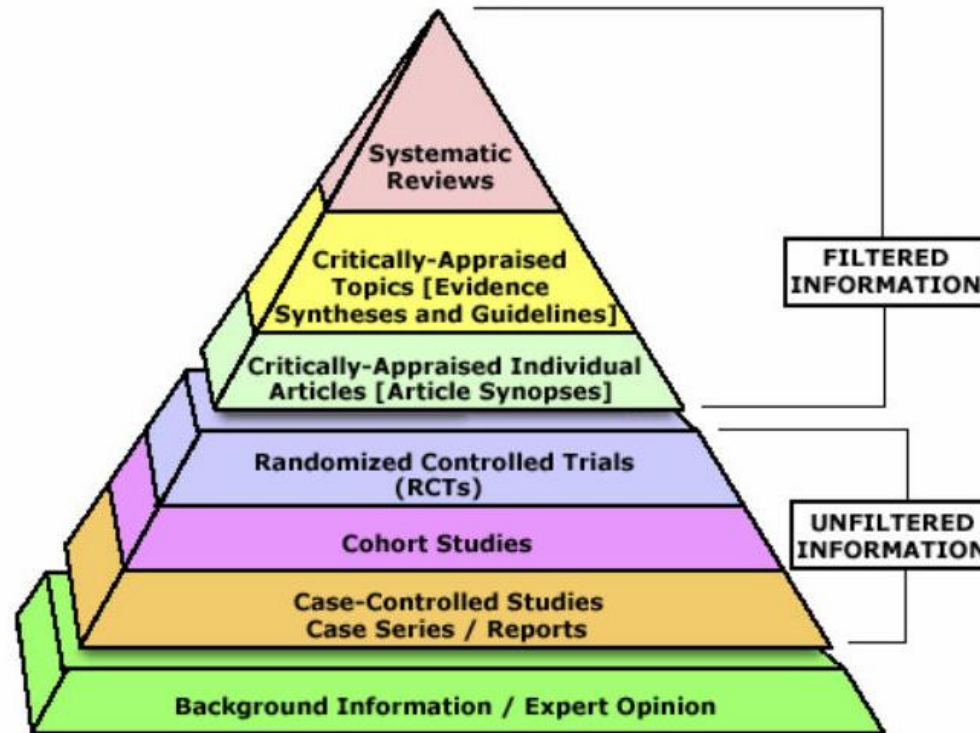
# WHAT IS A SYSTEMATIC REVIEW?

“A systematic review attempts to identify, appraise and synthesize **all the empirical evidence** that meets **pre-specified eligibility criteria** to answer a **specific research question**.”

“Researchers conducting systematic reviews use **explicit, systematic methods** that are selected with a view aimed at **minimizing bias**, to produce more reliable findings to **inform decision making**.”

(Cochrane 2024)

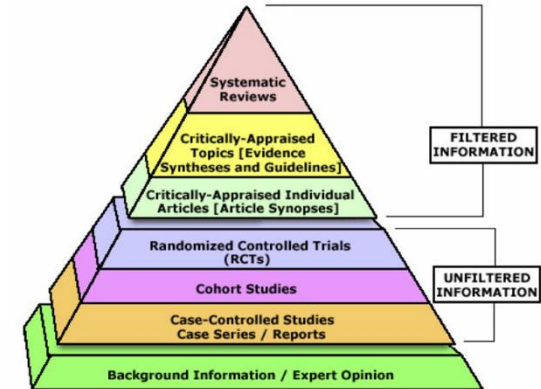
# WHY ARE SYSTEMATIC REVIEWS RELEVANT?



<https://s4be.cochrane.org/blog/2014/04/29/the-evidence-based-medicine-pyramid/>

# WHY ARE SYSTEMATIC REVIEWS RELEVANT?

- **Comprehensive Analysis**
- **Identifying Research Gaps (or the lack of gaps)**
- **Synthesizing Conflicting Evidence**
- **Quality Assessment**
- **Transparency and Reproducibility**
- **Evidence-Based Decision Making (Policy and Practice Impact)**



<https://s4be.cochrane.org/blog/2014/04/29/the-evidence-based-medicine-pyramid/>

# TYPES OF REVIEWS

## SYSTEMATIC, SCOPING AND NARRATIVE REVIEWS

	Systematic Review	Scoping Review	Narrative Review
Purpose	To <b>systematically synthesize</b> and <b>analyze</b> all available evidence on a <b>specific research question</b> or topic.	To <b>map and summarize</b> existing literature, often to identify gaps in research or clarify concepts.	To provide a (comprehensive) <b>overview</b> of a topic by synthesizing evidence and expert opinions in a narrative form.
Research Question	Typically focused on specific question	May have broader research questions and aims	Often very general
Methodology	Rigorous and structured methodology	Less stringent methodology (?) but still systematic	No strict methodology

# TYPES OF REVIEWS

## SYSTEMATIC, SCOPING AND NARRATIVE REVIEWS

	Systematic Review	Scoping Review	Narrative Review
<b>Synthesis of Evidence</b>	Quantitative synthesis (meta-analysis) or qualitative synthesis	Focus on summarizing and mapping the literature	Relies on narrative synthesis
<b>Reporting Standards</b>	Adheres to established reporting guidelines such as PRISMA	Adheres to established reporting guidelines such as PRISMA	Reporting standards vary
<b>Impact and Use</b>	Often used to inform evidence-based practice, policy-making, and further research.	Identifies gaps in literature, informs research priorities (e.g. for systematic reviews).	Provides a broad overview of a topic (often for other researchers or clinicians)



# SYSTEMATIC REVIEW AND META-ANALYSES

“If the results of the **individual studies are combined** to produce an overall **statistic**, this is usually called a meta-analysis”

(Cochrane 2024)

# SYSTEMATIC REVIEW AND META-ANALYSES

“If the results of the **individual studies are combined** to produce an overall **statistic**, this is usually called a meta-analysis”

“Not every systematic review contains a meta-analysis. **This might not be appropriate** if the designs of the studies are too different, if the outcomes measured are not sufficiently similar, or if there are concerns about the quality of the studies, for an average result across the studies to be meaningful.”

(Cochrane 2024)



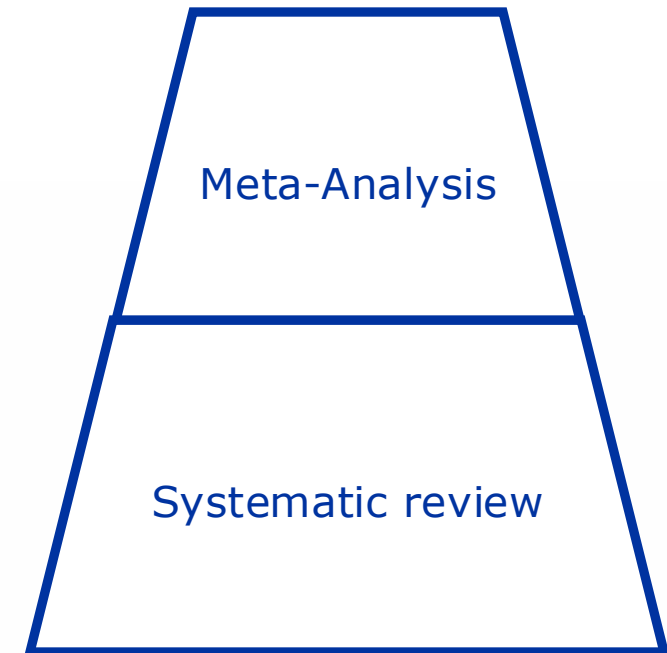
Systematic review

# SYSTEMATIC REVIEW AND META-ANALYSES

“If the results of the **individual studies are combined** to produce an overall **statistic**, this is usually called a meta-analysis”

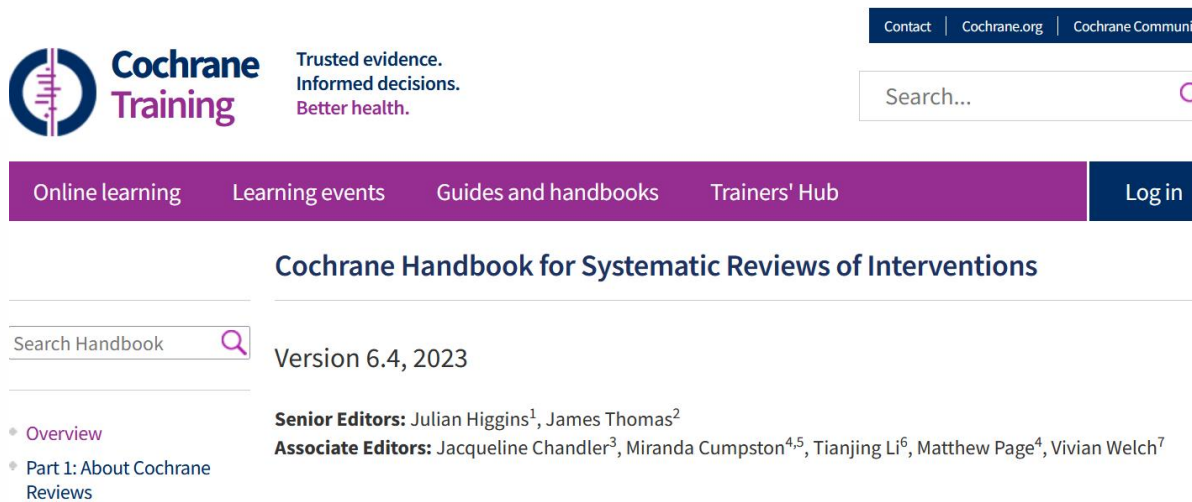
“Not every systematic review contains a meta-analysis. **This might not be appropriate** if the designs of the studies are too different, if the outcomes measured are not sufficiently similar, or if there are concerns about the quality of the studies, for an average result across the studies to be meaningful.”

(Cochrane 2024)



# IMPORTANT RESOURCES

## Cochrane Handbook



The screenshot shows the Cochrane Training Handbook website. At the top left is the Cochrane Training logo with the tagline "Trusted evidence. Informed decisions. Better health." To the right are links for "Contact", "Cochrane.org", and "Cochrane Community". Below these is a search bar. A purple navigation bar contains links for "Online learning", "Learning events", "Guides and handbooks", "Trainers' Hub", and a "Log in" button. The main heading is "Cochrane Handbook for Systematic Reviews of Interventions". Below this is a "Search Handbook" bar and the text "Version 6.4, 2023". A list of editors is provided: "Senior Editors: Julian Higgins<sup>1</sup>, James Thomas<sup>2</sup>" and "Associate Editors: Jacqueline Chandler<sup>3</sup>, Miranda Cumpston<sup>4,5</sup>, Tianjing Li<sup>6</sup>, Matthew Page<sup>4</sup>, Vivian Welch<sup>7</sup>". A sidebar on the left lists "Overview" and "Part 1: About Cochrane Reviews".

**Cochrane Training**  
Trusted evidence.  
Informed decisions.  
Better health.

Contact | Cochrane.org | Cochrane Community

Search...

Online learning | Learning events | Guides and handbooks | Trainers' Hub | Log in

### Cochrane Handbook for Systematic Reviews of Interventions

Search Handbook

Version 6.4, 2023

**Senior Editors:** Julian Higgins<sup>1</sup>, James Thomas<sup>2</sup>  
**Associate Editors:** Jacqueline Chandler<sup>3</sup>, Miranda Cumpston<sup>4,5</sup>, Tianjing Li<sup>6</sup>, Matthew Page<sup>4</sup>, Vivian Welch<sup>7</sup>

- Overview
- Part 1: About Cochrane Reviews

<https://training.cochrane.org/handbook>

# IMPORTANT RESOURCES

## PRISMA guidelines

thebmj

covid-19 Research ▾ Education ▾ News & Views ▾ Campaigns ▾ Jobs ▾

### The PRISMA 2020 statement: an updated guideline for reporting systematic reviews

BMJ 2021 ; 372 doi: <https://doi.org/10.1136/bmj.n71> (Published 29 March 2021)

Cite this as: BMJ 2021;372:n71

#### Linked RMR

PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews


Article

Related content

Metrics

Responses

Peer review

Matthew J Page , senior research fellow<sup>1</sup>, Joanne E McKenzie, associate professor<sup>1</sup>, Patrick M Bossuyt, professor<sup>2</sup>, Isabelle Boutron, professor<sup>3</sup>, Tammy C Hoffmann, professor<sup>4</sup>, Cynthia D Mulrow, professor<sup>5</sup>, Larissa Shamseer, doctoral student<sup>6</sup>, Jennifer M Tetzlaff, research product specialist<sup>7</sup>, Elie A Akl, professor<sup>8</sup>, Sue E Brennan, senior research fellow<sup>1</sup>, Roger Chou, professor<sup>9</sup>, Julie Glanville, associate director<sup>10</sup>, Jeremy M Grimshaw, professor<sup>11</sup>, Asbjørn Hróbjartsson, professor<sup>12</sup>, Manoj M Lalu, associate scientist and assistant professor<sup>13</sup>, Tianjing Li, associate professor<sup>14</sup>, Elizabeth W Loder, professor<sup>15</sup>, Evan Mayo-Wilson, associate professor<sup>16</sup>, Steve McDonald, senior research fellow<sup>1</sup>, Luke A McGuinness, research associate<sup>17</sup>, Lesley A Stewart, professor and director<sup>18</sup>, James Thomas, professor<sup>19</sup>, Andrea C Tricco, scientist and associate professor<sup>20</sup>, Vivian A Welch, associate professor<sup>21</sup>, Penny Whiting, associate professor<sup>17</sup>, David Moher, director and professor<sup>22</sup>

<https://www.prisma-statement.org/>



Trusted evidence.  
Informed decisions.  
Better health.

Contact | Cochrane.org

Search...

Online learning

Learning events

Guides and handbooks

Trainers' Hub

### Cochrane Handbook for Systematic Reviews of Interventions

Search Handbook

Version 6.4, 2023

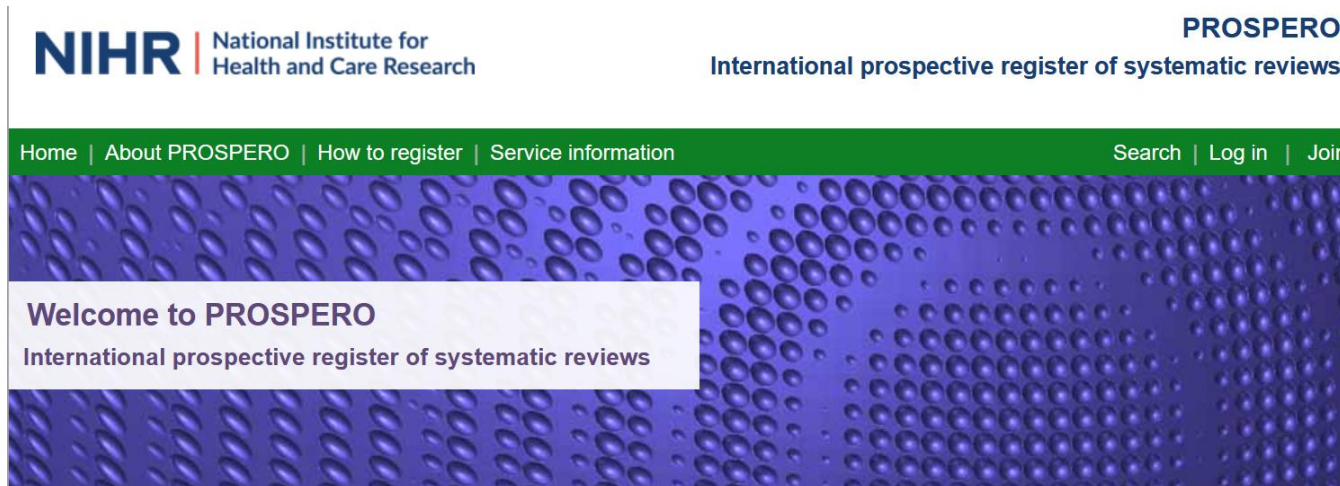
- Overview
- Part 1: About Cochrane Reviews

**Senior Editors:** Julian Higgins<sup>1</sup>, James Thomas<sup>2</sup>

**Associate Editors:** Jacqueline Chandler<sup>3</sup>, Miranda Cumpston<sup>4,5</sup>, Tianjing Li<sup>6</sup>, Matthew Page<sup>4</sup>, Viv

# IMPORTANT RESOURCES

## PROSPERO



The image shows the top section of the PROSPERO website. On the left is the NIHR logo (National Institute for Health and Care Research). To its right is the text 'PROSPERO International prospective register of systematic reviews'. Below this is a green navigation bar with links: Home, About PROSPERO, How to register, Service information, Search, Log in, and Join. Below the navigation bar is a large blue banner with a pattern of white circles. A white box on the left side of the banner contains the text 'Welcome to PROSPERO International prospective register of systematic reviews'.

<https://www.crd.york.ac.uk/prospero/>

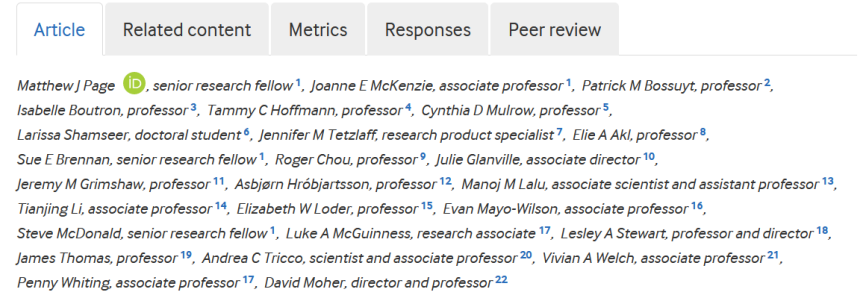
### The PRISMA 2020 statement: an updated guideline for reporting systematic reviews

BMJ 2021 ; 372 doi: <https://doi.org/10.1136/bmj.n71> (Published 29 March 2021)

Cite this as: BMJ 2021;372:n71

#### Linked RMR

PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews



The image shows the article navigation and content for the PRISMA 2020 statement. At the top are tabs for Article, Related content, Metrics, Responses, and Peer review. Below the tabs is a list of authors and their affiliations, numbered 1 through 22. The authors are: Matthew J Page, Joanne E McKenzie, Patrick M Bossuyt, Isabelle Boutron, Tammy C Hoffmann, Cynthia D Mulrow, Larissa Shamseer, Jennifer M Tetzlaff, Elie A Akl, Sue E Brennan, Roger Chou, Julie Glanville, Jeremy M Grimshaw, Asbjørn Hróbjartsson, Manoj M Lalu, Tianjing Li, Elizabeth W Loder, Evan Mayo-Wilson, Steve McDonald, Luke A McGuinness, Lesley A Stewart, James Thomas, Andrea C Tricco, Vivian A Welch, and Penny Whiting.



Trusted evidence.  
Informed decisions.  
Better health.

Contact | [Cochrane.org](https://www.cochrane.org)

Search...

Online learning | Learning events | Guides and handbooks | Trainers' Hub

### Cochrane Handbook for Systematic Reviews of Interventions

Search Handbook

Version 6.4, 2023

Overview

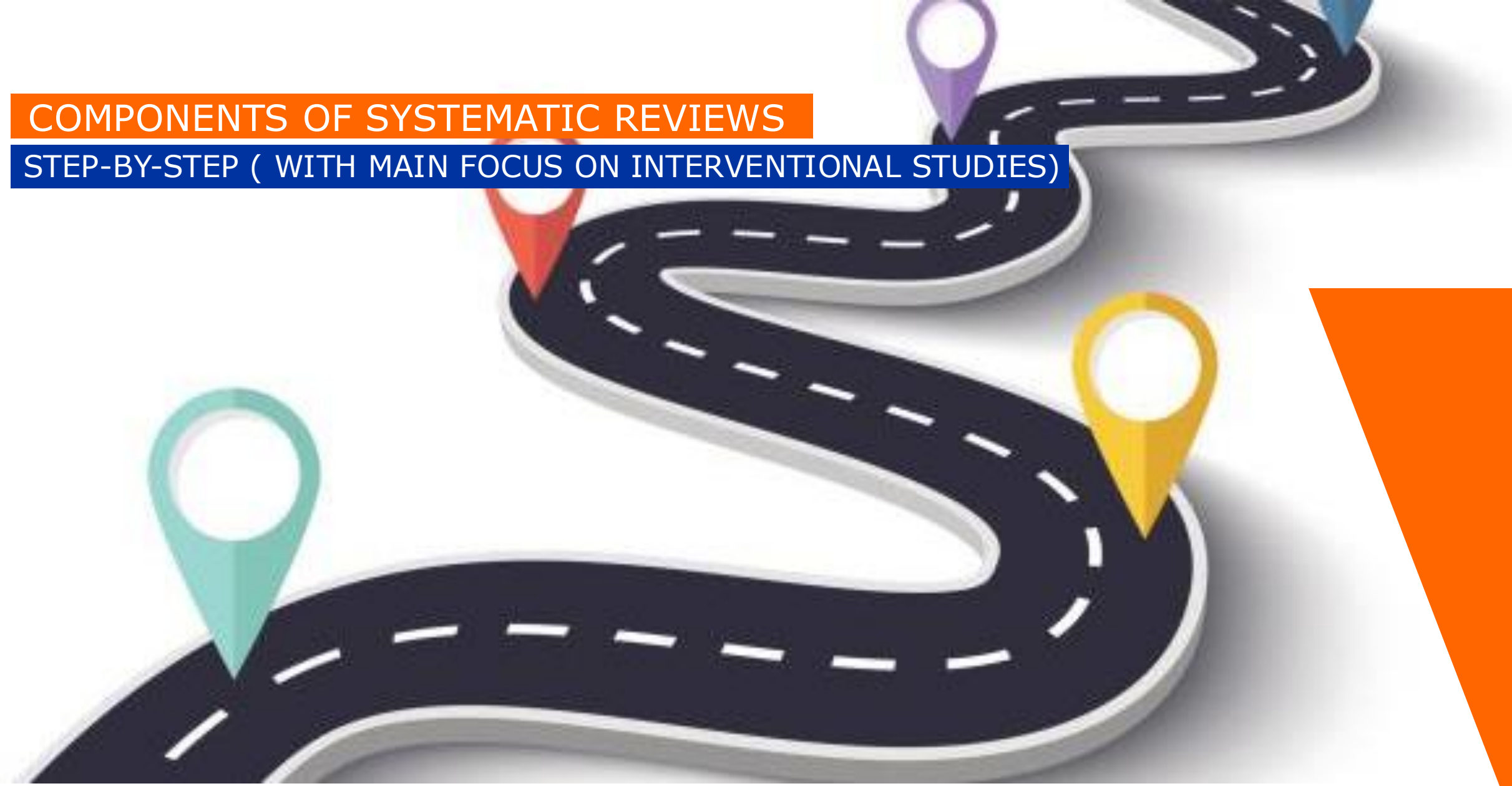
Part 1: About Cochrane Reviews

Senior Editors: Julian Higgins<sup>1</sup>, James Thomas<sup>2</sup>

Associate Editors: Jacqueline Chandler<sup>3</sup>, Miranda Cumpston<sup>4,5</sup>, Tianjing Li<sup>6</sup>, Matthew Page<sup>4</sup>, Vih

# COMPONENTS OF SYSTEMATIC REVIEWS

## STEP-BY-STEP ( WITH MAIN FOCUS ON INTERVENTIONAL STUDIES)



# COMPONENTS OF SYSTEMATIC REVIEWS

## RESEARCH QUESTION

- PICO(S)

Population – Intervention – Comparator –  
Outcome – (Setting/Study design)

What is the the effectiveness of *CBT-I*  
compared to *inactive control* on *pain* in *patients*  
*with comorbid insomnia and chronic non-*  
*cancer pain (in a community setting)?*



# COMPONENTS OF SYSTEMATIC REVIEWS

## RESEARCH QUESTION

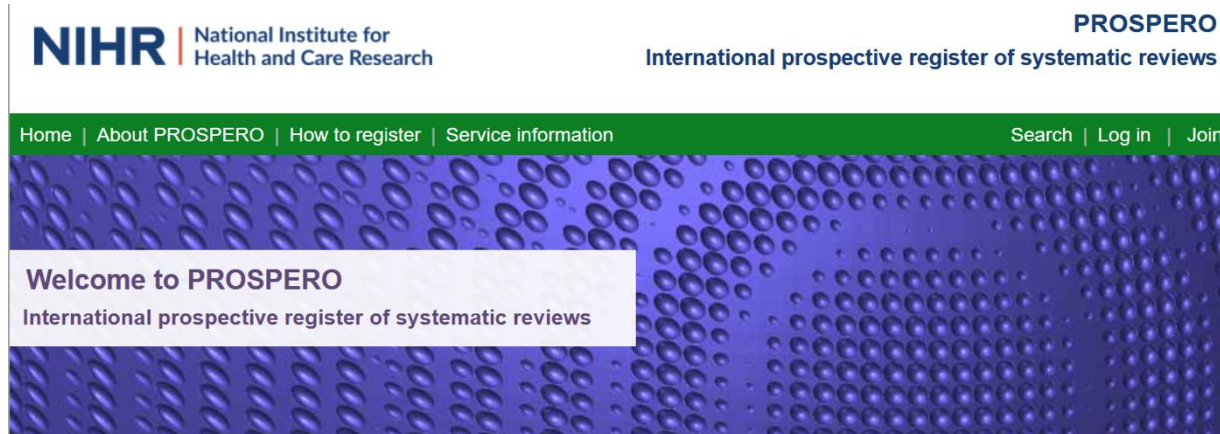
### ■ PEO(S)

Population – Exposure – Outcome – (Study design/Setting)

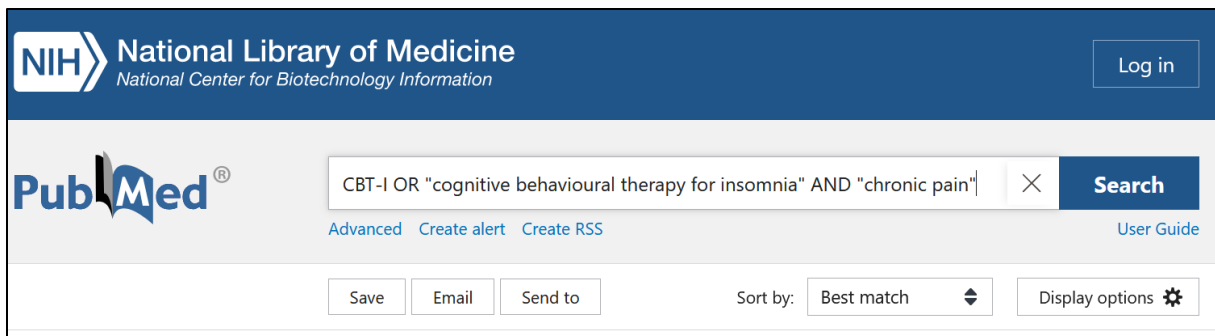
*Are sleep problems/disorders at baseline associated with an increased risk for the development of chronic musculoskeletal pain in people without pain at baseline?*

# COMPONENTS OF SYSTEMATIC REVIEWS

## PREVIOUS REVIEWS AND PROTOCOLS



PROSPERO



PubMed

# COMPONENTS OF SYSTEMATIC REVIEWS

## ELIGIBILITY CRITERIA

- Based on research question (PICO/PEO)
- As specific as possible for all components of PICO
  - How to define the **population** (E.g. people with insomnia and chronic pain?)
  - What counts as the **intervention** (E.g. How is CBT-I defined?)
  - Which **control** interventions are allowed? (E.g. only waitlist or also active controls like medication)
  - Which **outcomes** and how were they measured? (E.g. pain)
  - Other aspects like language, study type...
- Need to be pre-registered!

# COMPONENTS OF SYSTEMATIC REVIEWS

## PROTOCOL PRE-REGISTRATION

### Why pre-registration?

- Helps planning
- Reduces publication bias/waste
- Increases transparency
- Increases review quality (e.g. reporting bias)
- Part of PRISMA
- Eases publication of paper



# COMPONENTS OF SYSTEMATIC REVIEWS

## PROTOCOL PRE-REGISTRATION

### What should I pre-register?

- Follow the PROSPERO form (use it to check your preparations)
- More detail is better

### Can I make any changes afterwards?

- Yes. But be open about it.
- Consider sensitivity analyses



# COMPONENTS OF SYSTEMATIC REVIEWS

## SYSTEMATIC SEARCH (1)

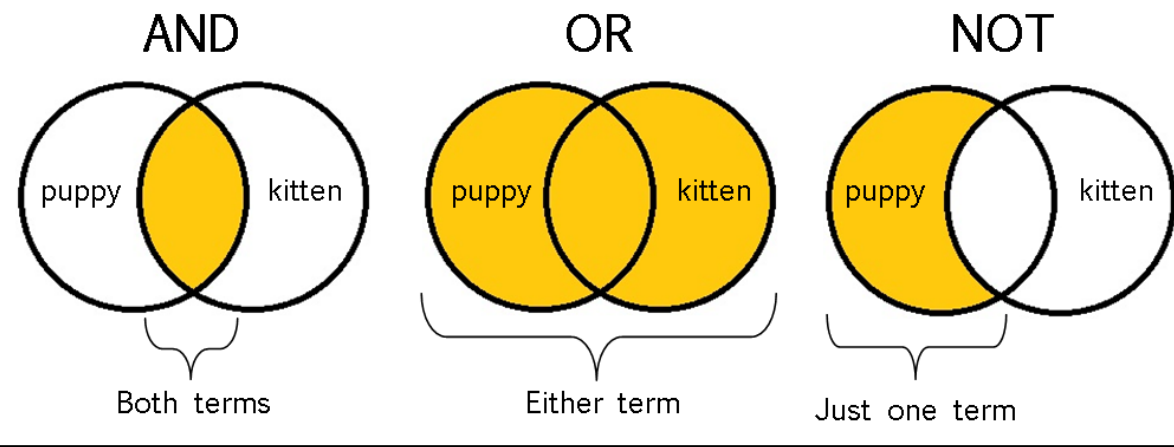
### Which databases should I search?

- MEDLINE (via pubmed)
- EMBASE
- Cochrane Central
- PsycInfo
- .... (depending on research field)
- Grey literature and protocols (Think publication bias)

# COMPONENTS OF SYSTEMATIC REVIEWS

## SYSTEMATIC SEARCH (2)

### Boolean Logic



<https://historyinformationliteracy.wordpress.com/class-1-boolean-logic-and-searching/>

# COMPONENTS OF SYSTEMATIC REVIEWS

## SYSTEMATIC SEARCH (3)

Boolean Logic - **OR**

P – “Chronic pain” **OR** Pain **OR** “persistent pain”

I – CBT-I **OR** “Cognitive behavioural therapy for insomnia” **OR** “Cognitive behavioral therapy for insomnia”

...



# COMPONENTS OF SYSTEMATIC REVIEWS

## SYSTEMATIC SEARCH (3)

Boolean Logic - **AND**

(Population terms with OR)

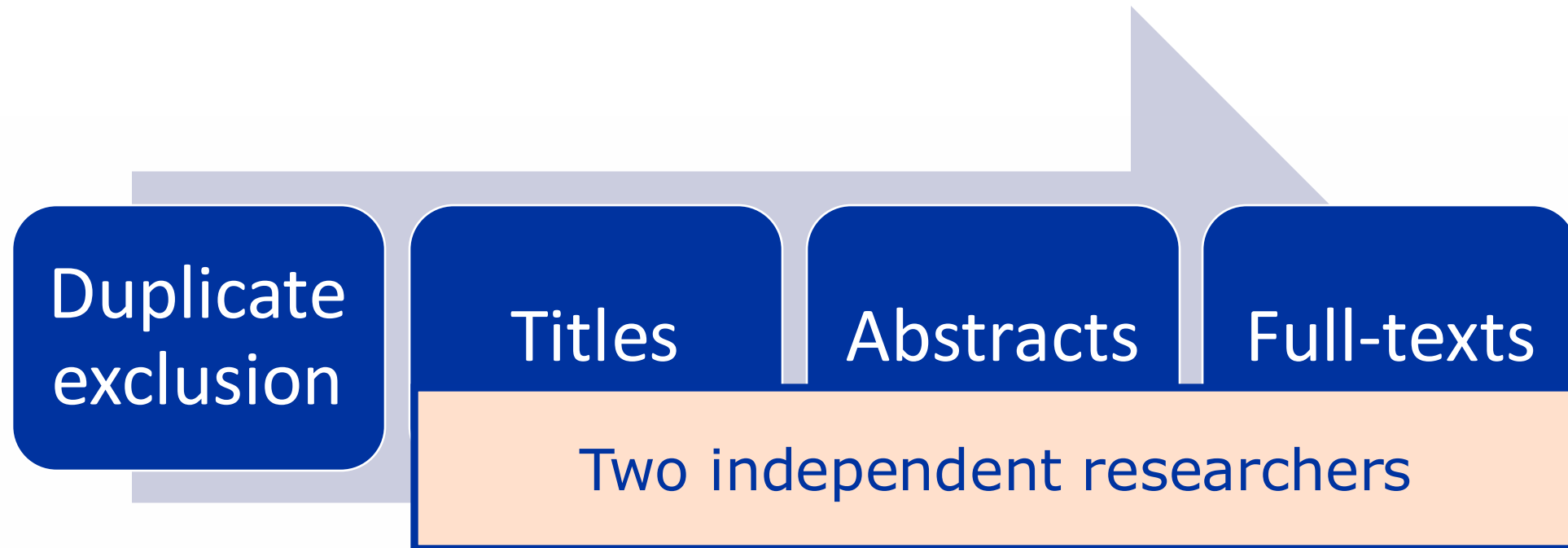
AND (Intervention terms with OR)

AND (Comparator terms with OR)

AND (Outcome terms with OR)

# COMPONENTS OF SYSTEMATIC REVIEWS

## STUDY SELECTION (1)



<https://blogs.lshtm.ac.uk/library/2018/12/07/removing-duplicates-from-an-endnote-library/>

# COMPONENTS OF SYSTEMATIC REVIEWS

## STUDY SELECTION (2)

Inclusion decisions	
Undecided	0
Maybe	95
Included	232
Excluded	421
Conflict	0

Decision by	
Mr. Nils Runge	
Ms. Julya Perea	

Minimum collaborator decisions	
At least 1	724
At least 2	653

The all new Rayyan is here with major enhancements and new features! [Click](#) to switch now.

### 2024-02-22: Scoping review FT screening

**Blind OFF**

Detect duplicates Compute ratings Export Copy New search All reviews

Showing 1 to 4 of 748 unique entries

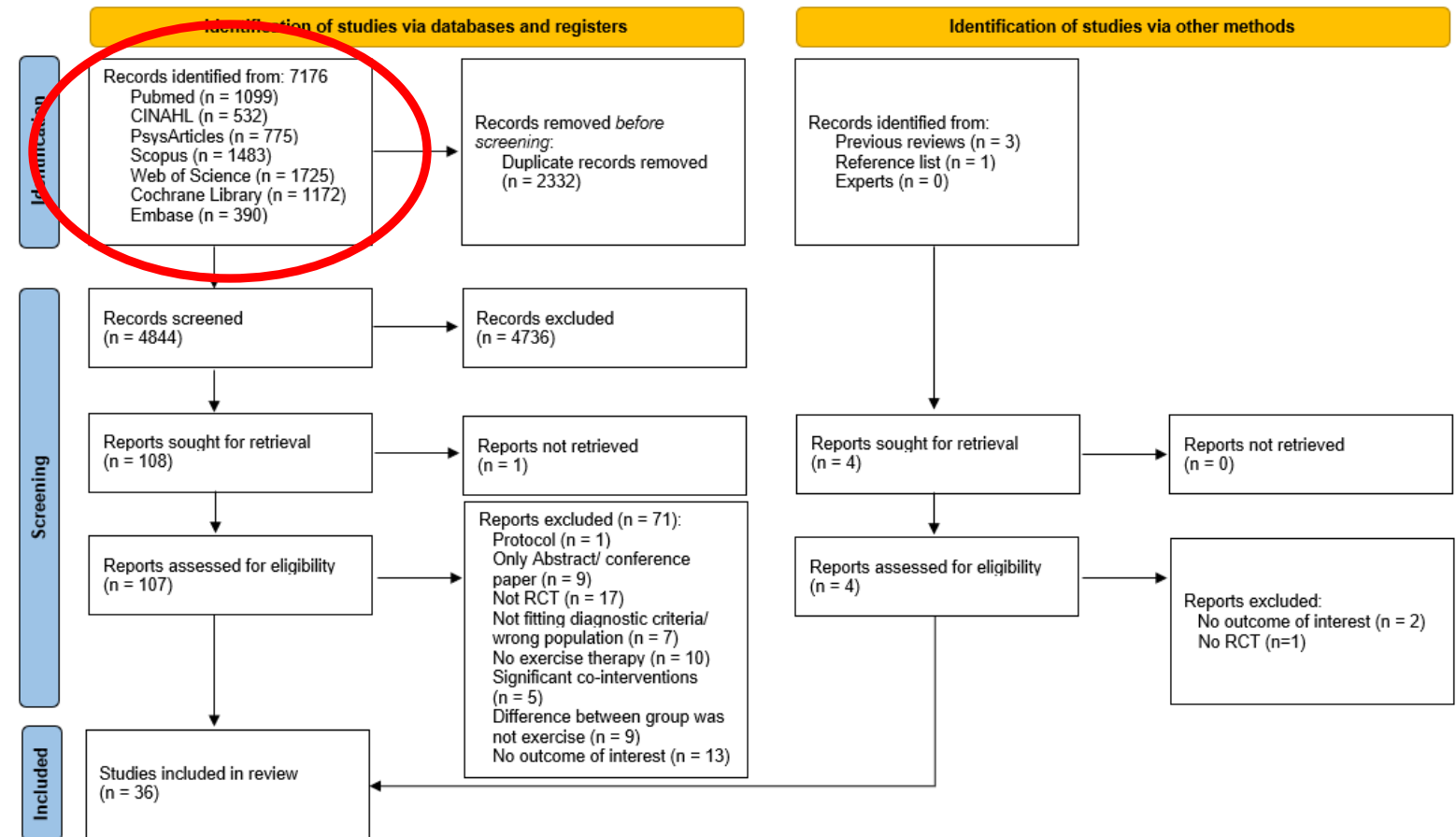
Search:

Date		Title	Authors	Rating
2022-08-01	Nils Julya	Does sleep quality modify the relationship between co...	Barazzetti, L.; Garcez, A.; Fr...	
2020-03-01	Nils Julya	Preliminary study of the association of ...	Gamal, R. M.; Mohamed, M. ...	Preliminary study
2023-06-06	Nils Julya	Sleep quality and predictors of...	Guaracha-Basáñez, G. A.; C...	Not assessed sleep problem

<https://rayyan.ai/>

# COMPONENTS OF SYSTEMATIC REVIEWS

## STUDY SELECTION (3)



Runge et al. 2023

# COMPONENTS OF SYSTEMATIC REVIEWS

## DATA EXTRACTION

- Standardized data extraction sheets
- Two independent reviewers
- Extract all relevant study and statistical data
- Contact authors for missing/unclear data

# COMPONENTS OF SYSTEMATIC REVIEWS

## RISK OF BIAS ASSESSMENT

- Assessment on outcome level rather than study level
- Different tools for different study types
- Different domains (Cochrane RoB tool 2):
  - *Bias arising from the randomization process*
  - *Bias due to deviations from intended interventions*
  - *Bias due to missing outcome data*
  - *Bias in measurement of the outcome*
  - *Bias in selection of the reported result*

Sterne et al.2019

# COMPONENTS OF SYSTEMATIC REVIEWS

## RISK OF BIAS ASSESSMENT

Study ID	Outcome	D1	D2	D3	D4	D5	Overall	
Azeez 2020	GFI	!	-	-	!	!	-	+ Low risk
Bachmair 2022	FSS	+	+	!	!	+	!	! Some concerns
Bachmair 2022	CFS	+	+	!	!	+	!	- High risk
Bestas 2022	PSQI	!	+	+	!	!	!	D1 Randomisation process
Bestas 2022	FSS	!	+	+	!	!	!	D2 Deviations from the intended interventions
Bilberg 2005	SF-36 Vitality	!	!	+	!	!	!	D3 Missing outcome data
Casilda-Lopez 2017	VAS Fatigue	+	+	+	!	-	-	D4 Measurement of the outcome
Cheung 2014	PSQI	+	+	+	!	+	!	D5 Selection of the reported result

Runge et al. 2023

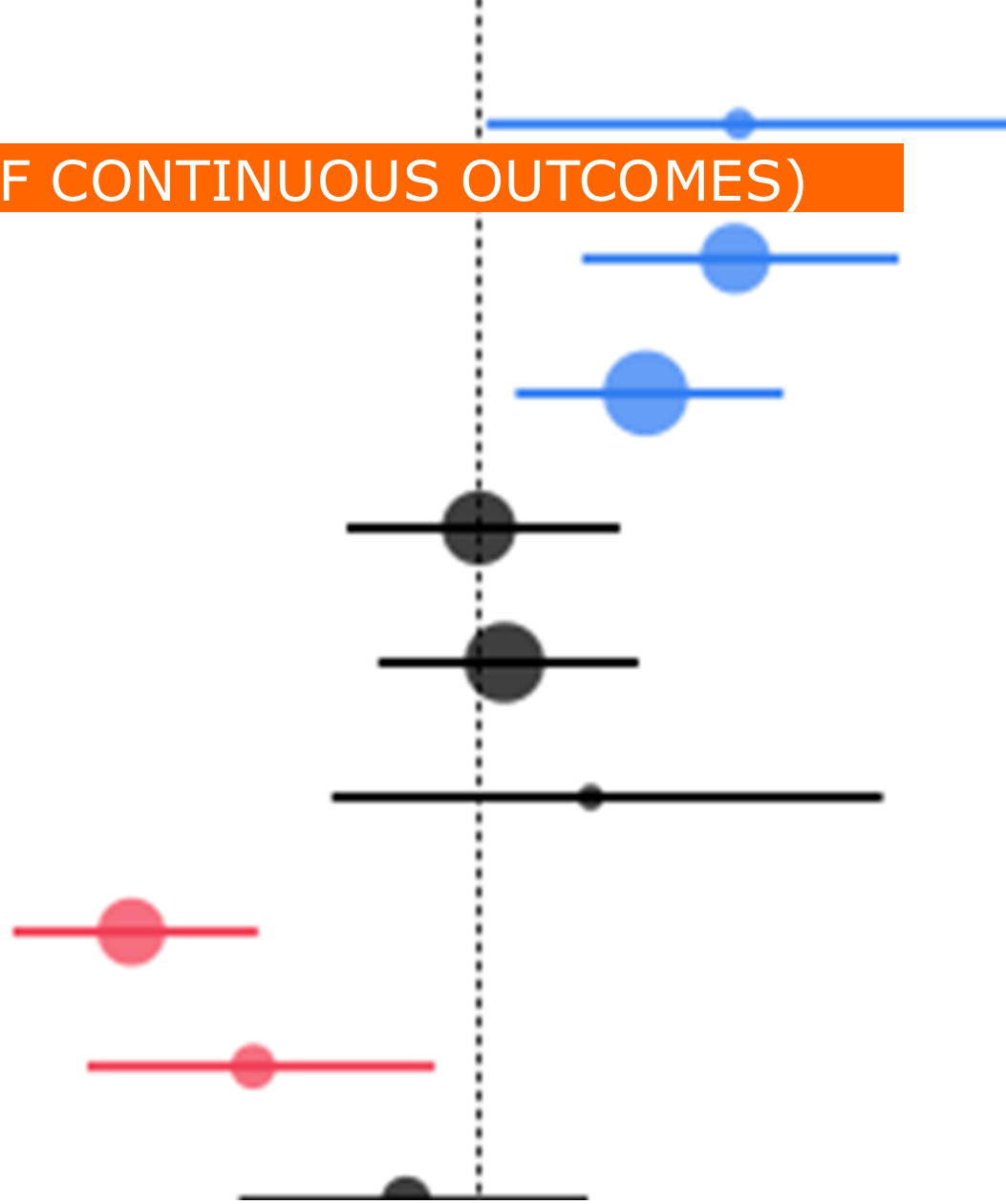
# COMPONENTS OF SYSTEMATIC REVIEWS

## DATA SYNTHESIS (QUALITATIVE)

- Descriptive summary of included studies
- Consider:
  - PICO domains
  - Used methods
  - Funding sources
  - Results within the paper
  - ...



# META-ANALYSIS (OF CONTINUOUS OUTCOMES)



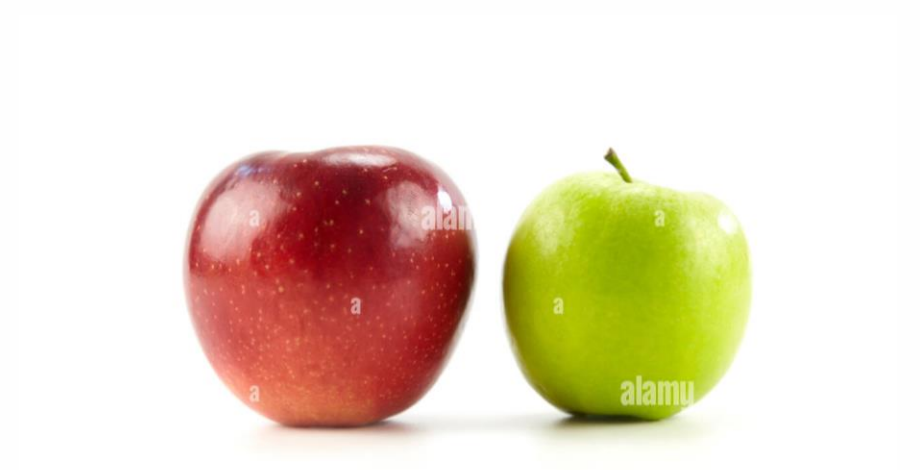
# META-ANALYSIS

## DOES A META-ANALYSIS MAKE SENSE?

Check for comparability in context of:

- Population
- Intervention
- Comparison
- Outcome

... based on qualitative synthesis



# META-ANALYSIS

## INVERSE-VARIANCE APPROACH TO META-ANALYSIS

- Weight given to each study is chosen to be the inverse of the variance of the effect estimate
  - i.e. 1 over the square of its standard error
  - Larger studies (smaller standard errors) are given more weight than smaller studies (larger standard errors)
- Using weighted effect sizes from each study, an overall effect size estimate is computed (weighted average)
- The standard error of the summary intervention effect can be used to derive a confidence interval (Information about precision of result)

# META-ANALYSIS

## FIXED-EFFECTS META-ANALYSIS

### Assumptions:

- Any variation observed between the studies is due to random sampling error, and all other sources of variation are negligible.
- The fixed-effects model is appropriate when the studies being combined are considered to be sampling from the same population and have similar methodologies and characteristics

# META-ANALYSIS

## FIXED-EFFECTS META-ANALYSIS

### Interpretation:

- There is one true effect size that underlies all the studies being analyzed.



# META-ANALYSIS

## RANDOM-EFFECTS META-ANALYSIS

### Assumptions:

- Observed variation between studies is not just due to random sampling error but also includes genuine differences in effect sizes between studies.
- This model is appropriate when the studies being combined are not identical:
  - They are drawn from populations with different effect sizes
  - OR There is heterogeneity among the studies in terms of methodology, participant characteristics, or other factors

# META-ANALYSIS

## RANDOM-EFFECTS META-ANALYSIS – STATISTICALLY SPEAKING

- In the random-effects model, both the within-study variance and the between-study variance are estimated from the data.
- The within-study variance reflects the variability of effect sizes within each individual study – random/sampling error
- The between-study variance quantifies the variability of true effect sizes (genuine differences) across all included studies.

# META-ANALYSIS

## RANDOM-EFFECTS META-ANALYSIS

### Interpretation:

- The result is the best estimate of the average treatment effect.





# META-ANALYSIS

## CONSIDER: HARTUNG-KNAPP METHOD

### Problem:

- The standard (DerSimonian-Laird) random-effects method tends to produce overly narrow confidence intervals
  - This may overstate the precision of the overall effect estimate, especially in small samples

# META-ANALYSIS

## CONSIDER: HARTUNG-KNAPP METHOD

### **Solution:**

- The Hartung-Knapp method adjusts for this bias by penalizing the precision of the estimated variance
  - Gives less weight to studies with overly precise estimates
  - This leads to wider and more conservative confidence intervals.

# META-ANALYSIS

## MEAN DIFFERENCE VERSUS STANDARDIZED MEAN DIFFERENCE

- Meta-analyses with the same outcome measure and scaling
  - Use **mean difference** as measure of effect
- Meta-analyses with different outcome measures and/or scaling
  - Use **standardized mean differences (SMD)** as measure of effect

# META-ANALYSIS

## MEAN DIFFERENCE

- Meta-analyses with the same outcome measure and scaling
  - Interpretation on the scaling of the outcome measure
  - Consider clinical relevance

# META-ANALYSIS

## STANDARDIZED MEAN DIFFERENCE

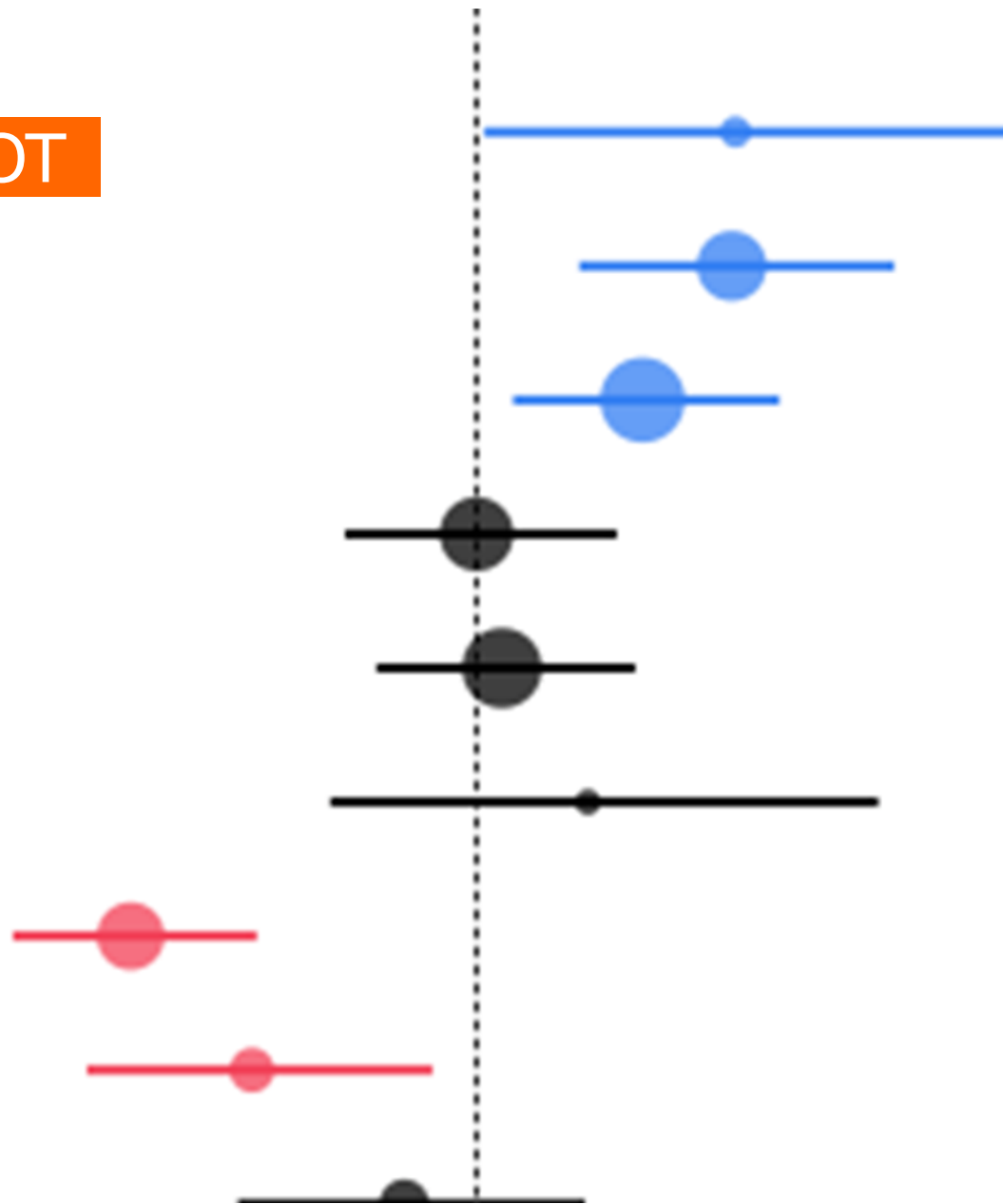
- Meta-analyses with different outcome measures and/or scaling
  - $SMD = (\text{Mean of Group 1} - \text{Mean of Group 2}) / \text{Pooled Standard Deviation}$ 
    - The pooled standard deviation = weighted average of the standard deviations of both groups

# META-ANALYSIS

## STANDARDIZED MEAN DIFFERENCE

- Interpretation of SMD
  - The resulting SMD represents the difference between the means of the two groups  
-> Expressed in standard deviation units.
  - Cohen's d/hedges g are commonly used metrics for interpreting the magnitude of the SMD:
    - Small effect size: SMD 0.2- 0.5
    - Medium effect size: SMD 0.5 – 0.8
    - Large effect size: SMD >0.8

# THE FOREST PLOT



# THE FOREST PLOT

## OVERVIEW

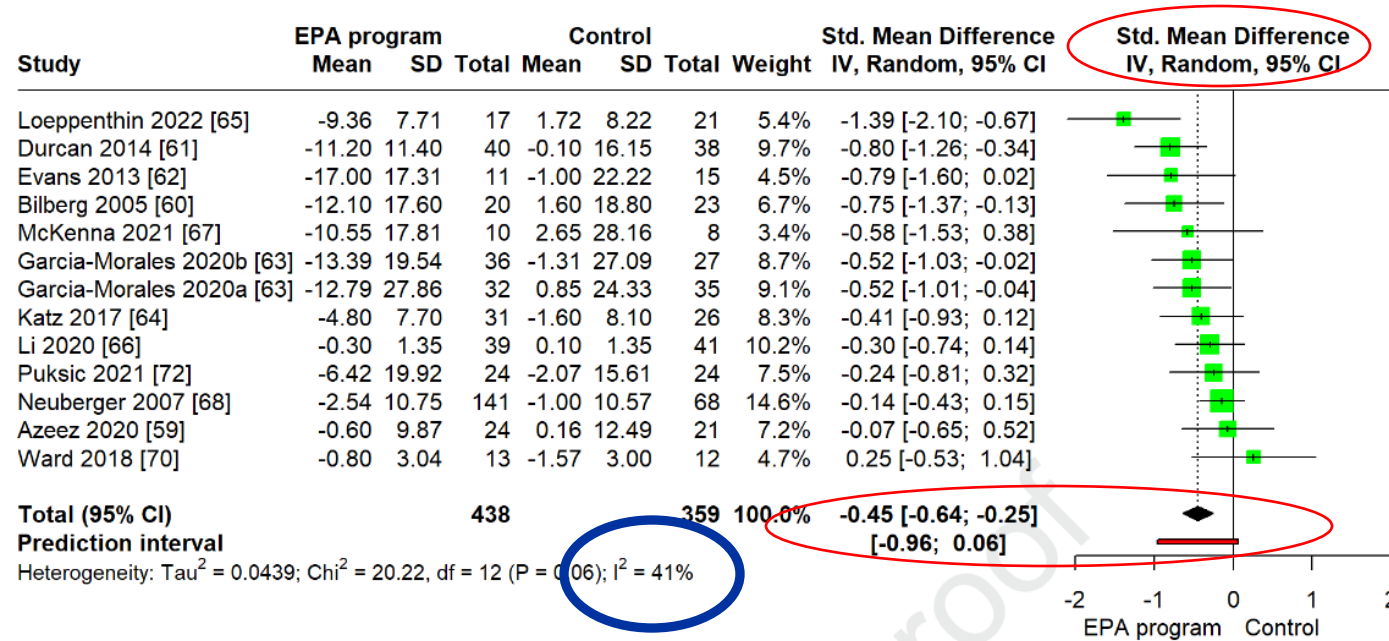


Figure 3: Forest plot showing the results of the meta-analysis on fatigue in the short-term comparing exercise and physical activity programs with inactive control in people with rheumatoid arthritis

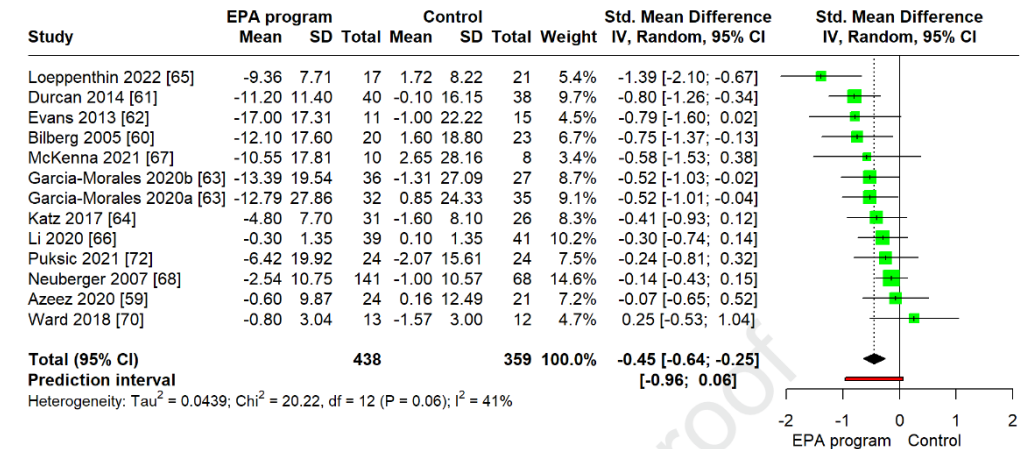
Runge et al. 2023



# THE FOREST PLOT

## INTERPRETATION

- Statistically significant result if Diamond (95%CI) does not cross 0
- Effect size is based on SMD
- Interpretation in paper: "EPA programs may reduce fatigue slightly compared to inactive control in the short-term (SMD -0.45; 95% CI -0.64 to -0.25;  $I^2 = 41\%$ ; Low certainty)"

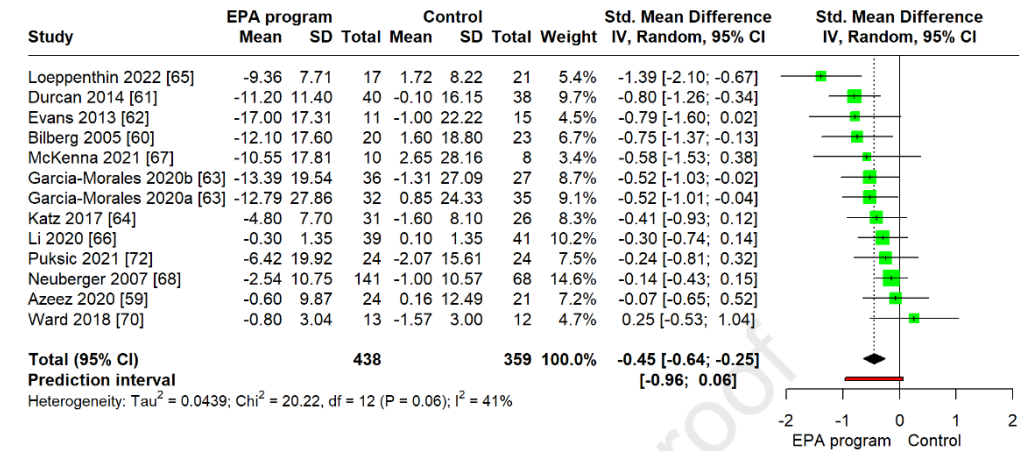


Runge et al. 2023

# THE FOREST PLOT

## HETEROGENEITY

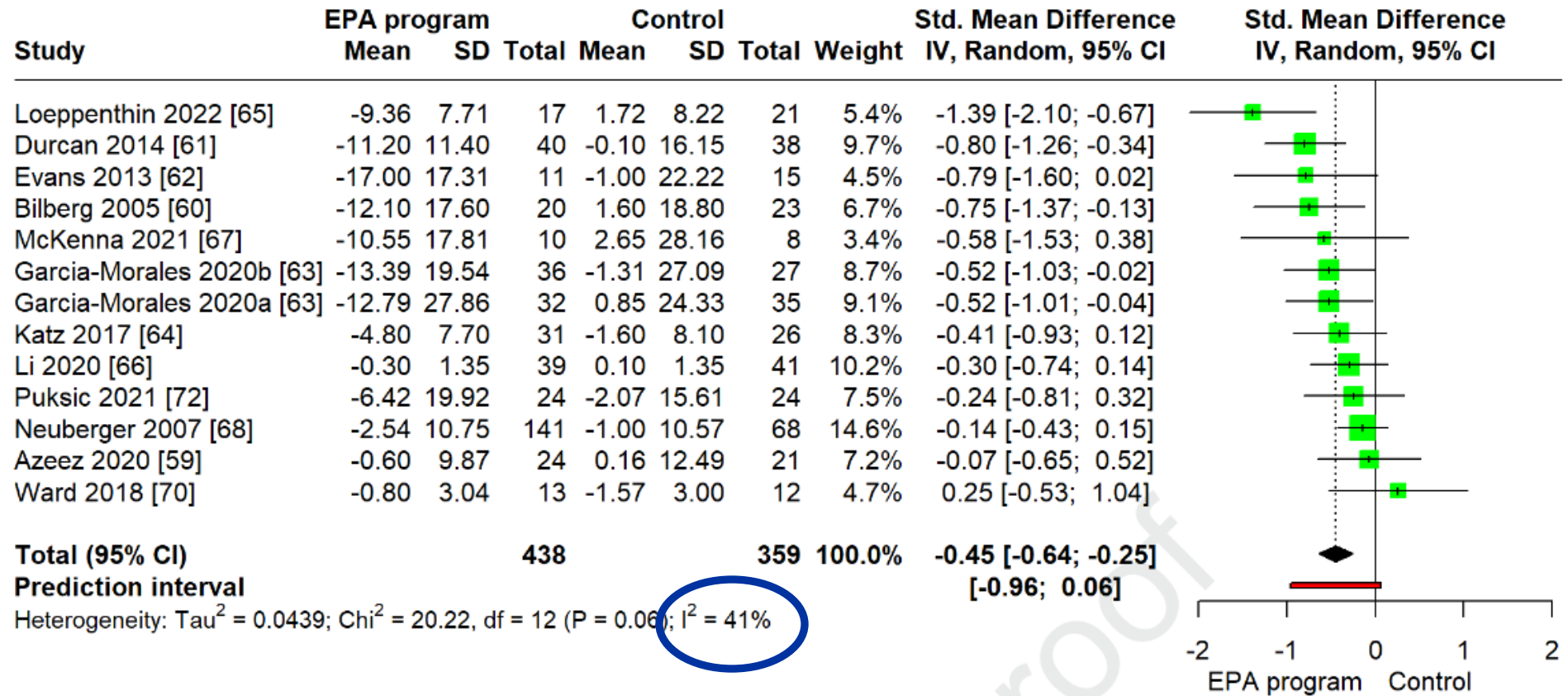
- $I^2$
- Proportion of total variation in effect sizes across studies that is due to heterogeneity rather than chance/measurement error.



Runge et al. 2023

# THE FO HETEROG

- $I^2$
- Prop  
acrc  
rath

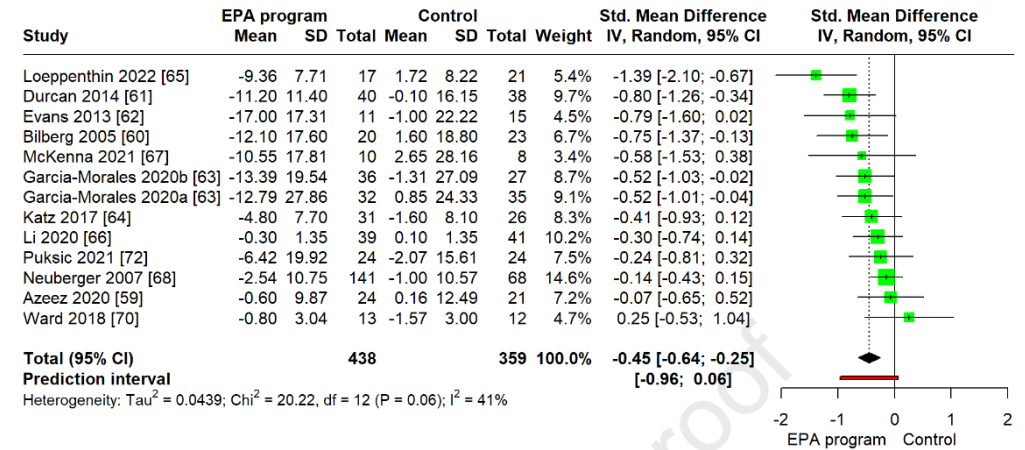


Runge et al. 2023

# THE FOREST PLOT

## HETEROGENEITY

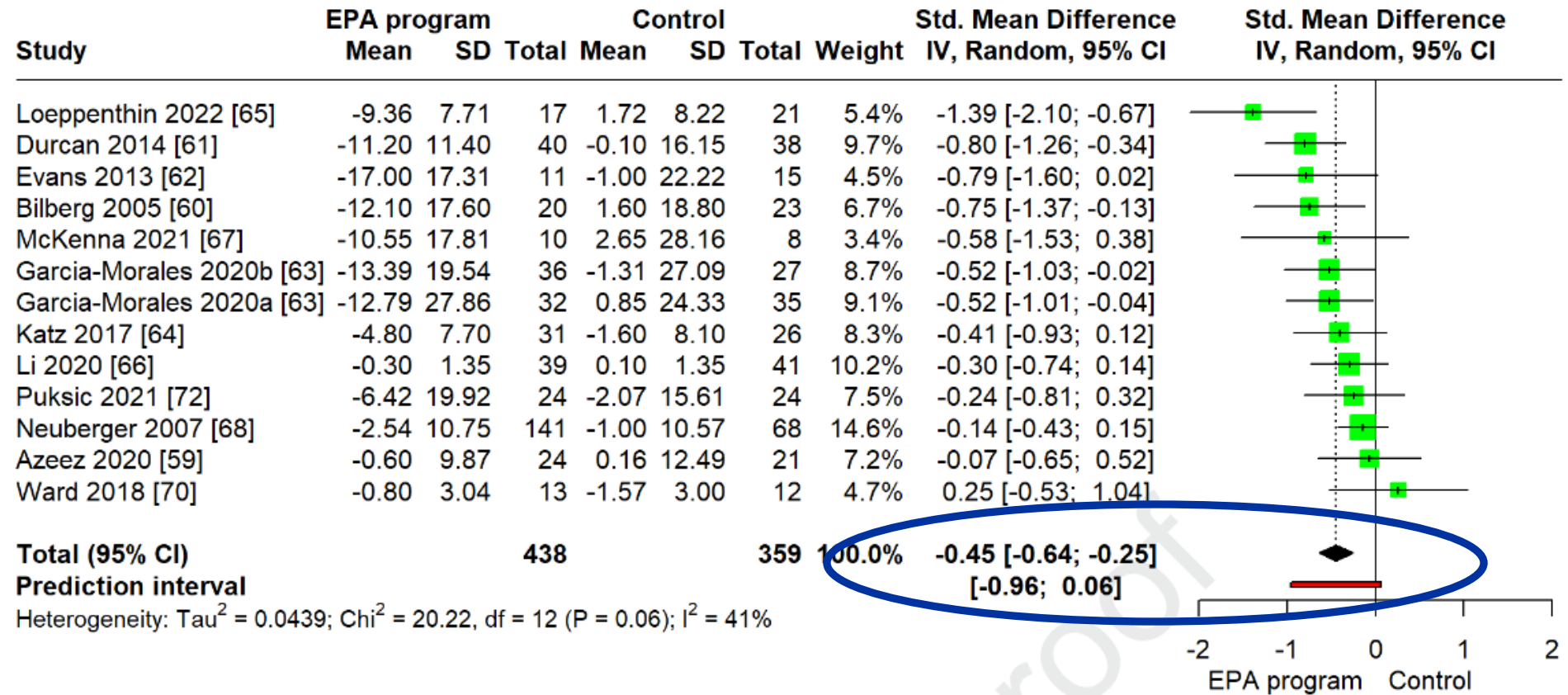
- $I^2$ 
  - Proportion of total variation in effect sizes across studies that is due to heterogeneity rather than chance/measurement error.
- Prediction interval
  - The prediction interval provides a range within which we can expect a future observation (effect size) from a new study to fall.



Runge et al. 2023

# THE FO HETEROG

- $I^2$
- Prop  
acrc  
rath
- Predic
- The  
whic  
(eff



Runge et al. 2023

## THE FOREST PLOT

### SENSITIVITY ANALYSES

- Evaluate robustness of results by examining the effects of excluding certain studies or changing analysis methods.

# THE FOREST PLOT

## SENSITIVITY ANALYSES

Sensitivity analysis (Result main analysis: SMD -0.45; -0.64 to -0.25, I <sup>2</sup> = 41%)	SMD (95%CI)
Exclusion of studies with high RoB	-0.50 (-0.72 to -0.28), I <sup>2</sup> = 46%
Use of intercorrelation coefficient of $r = 0.7$ to estimate change standard deviations where required	-0.52 (-0.73 to -0.31), I <sup>2</sup> = 48%
Exclusion of the study Katz et al.[9]	-0.45 (-0.65 to -0.24), I <sup>2</sup> = 46%
Use of the original standard deviations from Durcan et al.[10]	-0.51 (-0.76 to -0.26), I <sup>2</sup> = 62%
Use of alternative outcome measures of studies that provided data on more than one measure of fatigue	-0.42 (-0.64 to -0.21), I <sup>2</sup> = 53%

Runge et al. 2023

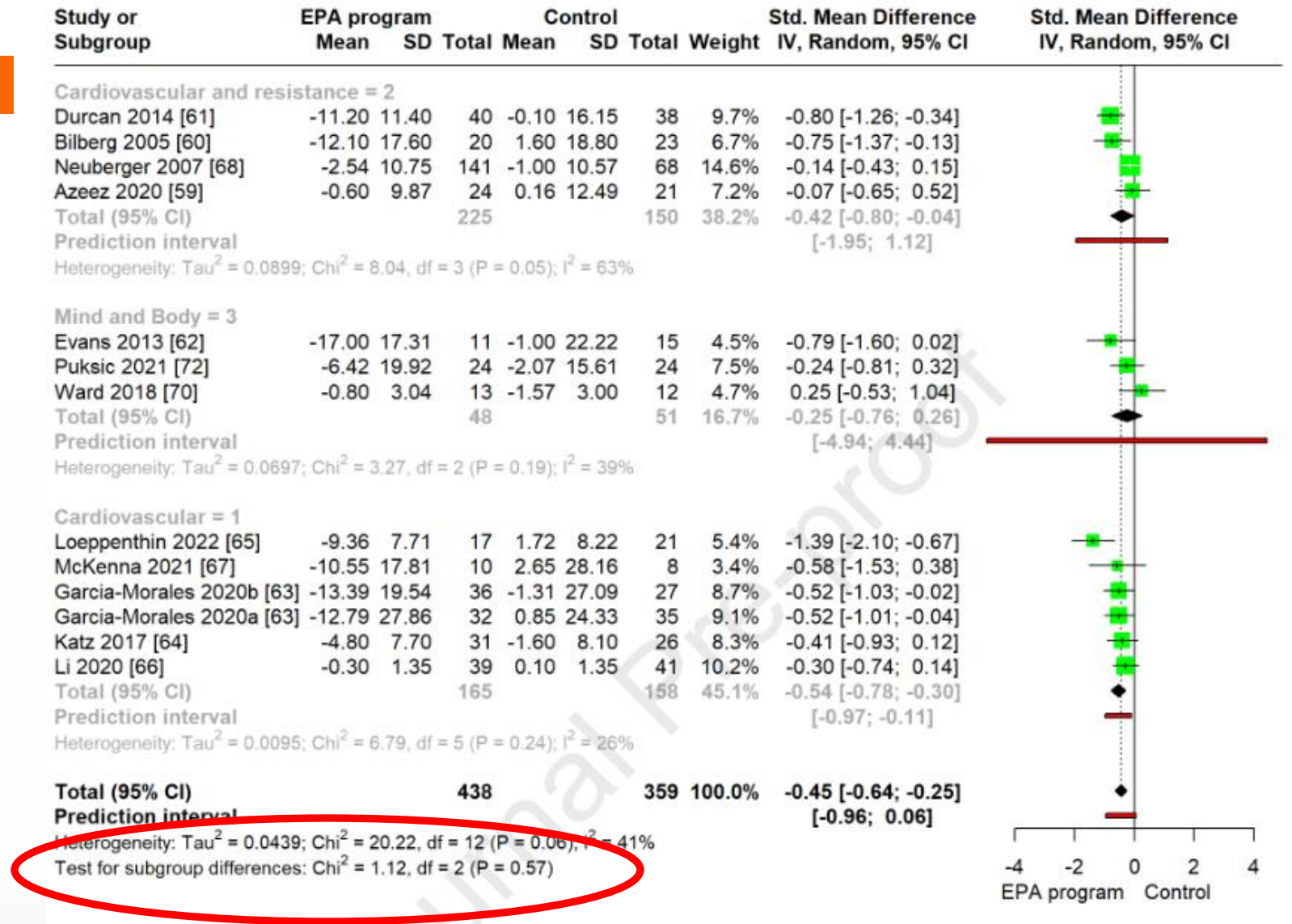
# THE FOREST PLOT

## SUBGROUP ANALYSES

- Investigate whether the effect size varies across different subgroups of studies or participants
- Provide insights into potential sources of heterogeneity.



# THE FOREST PLOT SUBGROUP ANALYSES



Runge et al. 2023

# COMPONENTS OF SYSTEMATIC REVIEWS

## GRADE

“GRADE is a systematic approach to rating the certainty of evidence in systematic reviews and other evidence syntheses”

(Cochrane 2024)

### **Great resource:**

<https://training.cochrane.org/online-learning/cochrane-methodology/grade-approach/jce-series>

# COMPONENTS OF SYSTEMATIC REVIEWS

## GRADE - INTERPRETATION

Certainty level	Current definition
High	We are <b>very confident</b> that the true effect lies close to that of the estimate of the effect
Moderate	We are <b>moderately confident</b> in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is <b>limited</b> : The true effect may be substantially different from the estimate of the effect
Very low	We have <b>very little confidence</b> in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Balshem et al. 2011

# COMPONENTS OF SYSTEMATIC REVIEWS

## GRADE - INTERPRETATION

All outcomes start with high certainty

Downgrade for:

- Study designs
- Risk of Bias (study limitations)
- Imprecision
- Inconsistency
- Indirectness
- Publication bias

# COMPONENTS OF SYSTEMATIC REVIEWS

## GRADE - INTERPRETATION

Effect size	Certainty of evidence	Statement
Small	High	X reduces/increases outcome slightly X results in a slight reduction/increase in outcome
Small	Moderate	X probably reduces/increases outcome slightly X likely reduces/increases outcome slightly
Small	Low	X may reduce/increase outcome slightly The evidence suggests X reduces/increases outcome slightly
Small	Very low	The evidence is very uncertain about the effect of X on outcome X may reduce/increase/have little to no effect on outcome but the evidence is very uncertain

Santesso et al. 2020

## SUMMARY

### SYSTEMATIC REVIEWS WITH META-ANALYSES

#### **If done well:**

- They are an important part of evidence-based medicine
- They can be a comprehensive summary of the current evidence for a specific research question
- They can be used to guide clinical practice, policy and future research

## SUMMARY

### SYSTEMATIC REVIEWS WITH META-ANALYSES

#### **If done poorly or if misinterpreted:**

- They can have negative influence on clinical practice/ future research/ research funding...
- They can create confusion within a field
- They can be used to prove a point
- They can undermine trust in scientific methods