



University of
Sheffield



Medical
Research
Council

The problems with systematic reviews

Updates on a living systematic review

Evidence Synthesis Ireland

21st March 2024

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(SCHARR)

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@LesleyUttley

A WORLD
TOP 100
UNIVERSITY

Coming up

- Overview of the project
- Other relevant work and contextual factors
- Unpublished updates!

Funding

- UKRI MRC Career Development Award to Lesley Uttley (MR/T009861/1; 2020-2024): *Investigating human influences in systematic reviews and meta-analyses* which could prove a direct or indirect conflict of interest in the context or content of this presentation.
- Views are my own and not necessarily representative of the MRC/UKRI

Disclosures

- Systematic review advocate
- Not an *ad hominem* researcher

Evidence-based hierarchy



1. Undeclared conflicts

2. Not pre-registering intentions

3. Massaging data with meta-analyses (without statistical expertise)

4. Only including or highlighting positive studies

5. Adding spin in conclusions

Motive? Who is doing this systematic review and why?

**Bad systematic reviews are worse than
non-systematic reviews**

Susceptibility to Fraud in Systematic Reviews

Lessons from the Reuben Case

Emmanuel Marret, M.D.,* Nadia Elia, M.D., M.Sc.,† Jørgen B. Dahl, M.D., D.MSc., M.B.A.,‡
Henry J. McQuay, M.A., D.M., F.R.C.A., F.R.C.P. (Edin.),§ Steen Møiniche, M.D.,||
R. Andrew Moore, M.A., D.Phil., C.Chem., F.R.S.C., F.R.C.A., D.Sc.,# Sebastian Straube, B.M., B.Ch., M.A., D.Phil.,**
Martin R. Tramèr, M.D., D.Phil.††

Healthcare Economics, Policy, and Organization

Section Editor: Nancy Borkowski

Publication Bias and Nonreporting Found in Majority of Systematic Reviews and Meta-analyses in Anesthesiology Journals

Riley J. Hedin, MPH,* Blake A. Umberham,* Byron N. Detweiler,* Lauren Kollmorgen,* and Matt Vassar, PhD†

ORIGINAL ARTICLE

Systematic Reviews in Burns Care: Poor Quality and Getting Worse

Jared M. Campbell, PhD,* Sheila Kavanagh, OAM, RN,†
Rochelle Kurmis, MClInSci,‡ Zachary Munn, PhD*

Créquit et al. BMC Medicine (2014)
DOI 10.1186/s12916-016-0555-0

RESEARCH ARTICLE

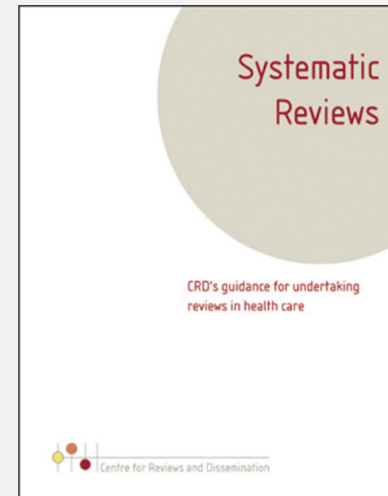
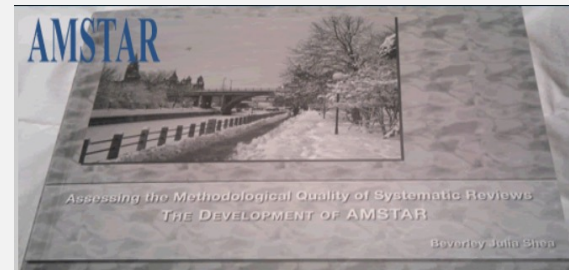
Open Access



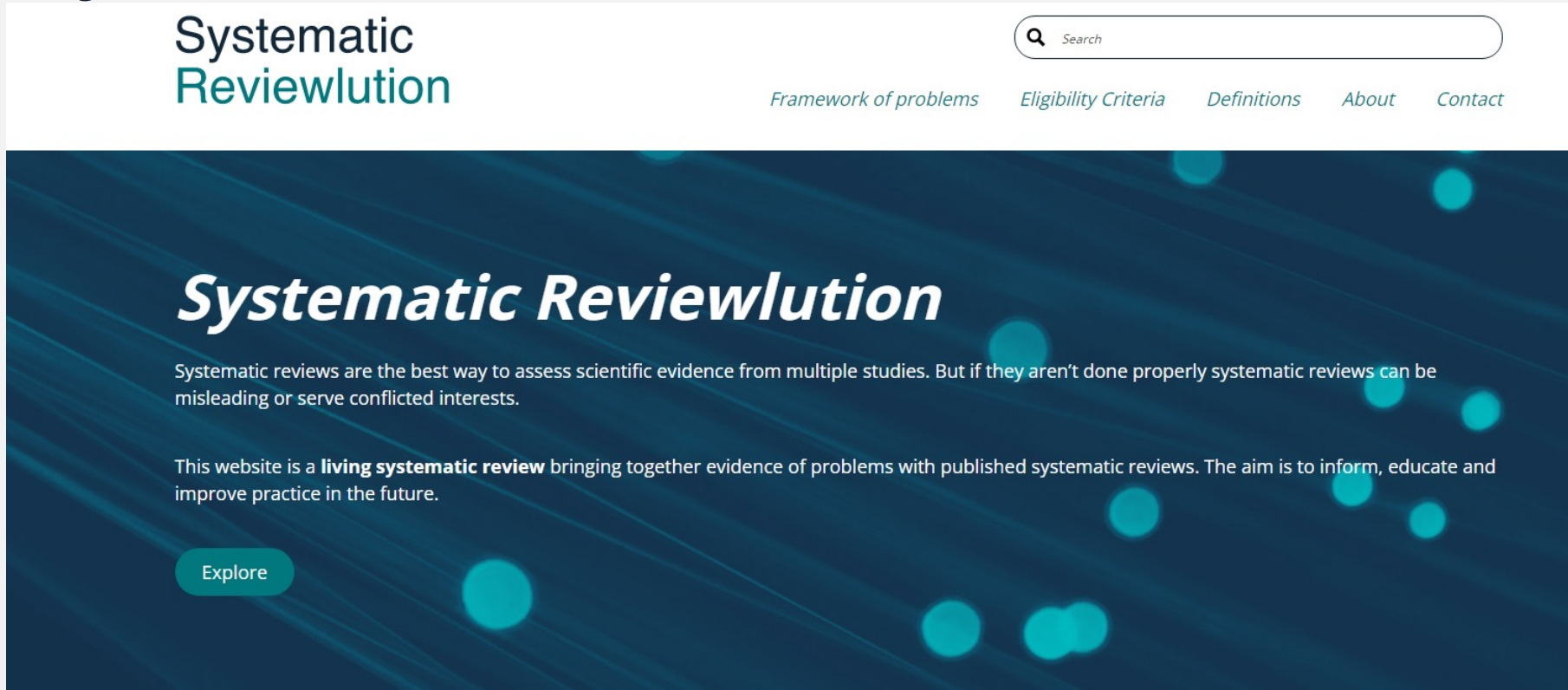
Wasted research when systematic reviews fail to provide a complete and up-to-date evidence synthesis: the example of lung cancer

Perrine Créquit^{1,2†}, Ludovic Trinquart^{1,2,3,4**}, Amélie Yavchitz^{1,2,3} and Philippe Ravaud^{1,2,3,4,5}

Guidelines for good practice



A living systematic review of problems with systematic reviews

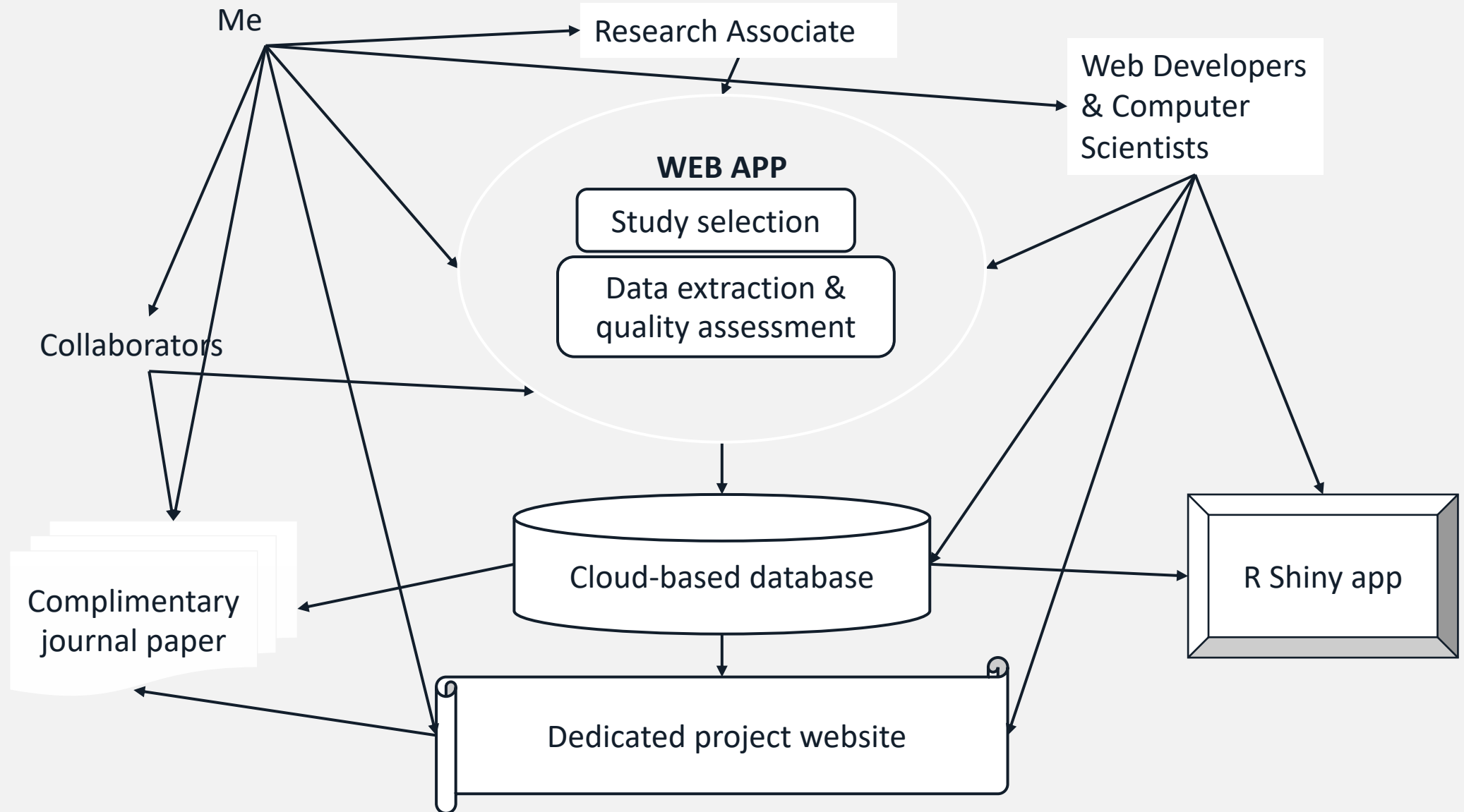


Website: <https://systematicreviewlution.com/>

Published paper: [Uttley, L., Quintana, D. S., Montgomery, P., Carroll, C., Page, M. J., Falzon, L., ... & Moher, D. \(2023\). The problems with systematic reviews: a living systematic review. *Journal of Clinical Epidemiology*.](#)


Why do living research?

My model of living research




The Web App Behind the Database

Systematic Reviewlution

 Home

 Overview

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Overview


Assign Tasks

Add Article

| ID | Title | First Author | Journal | Year of Publishing |
|----|---|------------------|--|--------------------|
| 1 | Incorrect inclusion of individual studies and methodological flaws in systematic review and meta-analysis | R. Aabenhus | BRITISH JOURNAL OF GENERAL PRACTICE | 2014 |
| 2 | Systematic reviews of adverse effects of drug interventions: a survey of their conduct and reporting quality | V. Cornelius | PHARMACOEPIDEMIOLOGY AND DRUG SAFETY | 2009 |
| 5 | Mounting evidence that librarians are essential for comprehensive literature searches for meta-analyses and Cochrane reports | A. C. Weller | JOURNAL OF THE MEDICAL LIBRARY ASSOCIATION | 2004 |
| 6 | Factors predicting completion and time to publication of Cochrane reviews | A. C. Tricco | OPEN MEDICINE | 2009 |
| 7 | Epidemiology and Reporting Characteristics of Systematic Reviews of Biomedical Research: A Cross-Sectional Study | M. J. Page | PLOS MEDICINE | 2016 |
| 8 | Financial Conflicts of Interest and Reporting Bias Regarding the Association between Sugar-Sweetened Beverages and Weight Gain: A Systematic Review of Systematic Reviews | M. Bes-Rastrollo | PLOS MEDICINE | 2014 |

Open Science Framework page

(2020-01-06): <https://osf.io/2hmv9/>

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The range and prevalence of problems with systematic reviews

99.0KB Public 0 ...

Contributors: [Lesley Uttley](#), [Daniel Quintana](#), [Paul Montgomery](#), [Matthew James Page](#), [Christopher Carroll](#), [Sarah Dawson](#)



Date created: 2020-01-06 10:55 AM | Last Updated: 2020-12-03 09:52 AM

Category:  Project

Description: Systematic review of published evidence investigating problems in the conduct or reporting of systematic reviews . These problems, errors, biases or influences may potentially be attributable to stakeholders, sponsors and publishers as well as individuals comprising the project team. They may also affect the reliability or validity of the systematic review conclusions.

This project aims to identify published evidence which examines these issues which could include systematic reviews, primary studies or meta-epidemiological analyses of systematic reviews. In order to avoid publication bias, grey literature from unpublished evidence will also be considered. Comprehensive bibliography searches will be used to search for relevant papers. Literature searches to expand thesaurus and free-text terms related to bias, misconduct or errors will also be complemented with pearl growing searches of relevant papers and contact with experts.

This project is funded through a UK Medical Research Council Career Development Award to Lesley Uttley, University of Sheffield.

| | |
|--|--|
| Wiki  | Citation  |
| If you know of any papers or studies that may be relevant to this review please email l.uttley@sheffield.ac.uk . | Tags |

PROSPERO registration

(March 8th 2020): [CRD42020181371](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020181371)

The problems with systematic reviews: a living methodological systematic review

Lesley Uttley, Daniel Quintana, Paul Montgomery, Christopher Carroll, Matthew Page, Sarah Dawson, David Moher

Citation

Lesley Uttley, Daniel Quintana, Paul Montgomery, Christopher Carroll, Matthew Page, Sarah Dawson, David Moher. The problems with systematic reviews: a living methodological systematic review. PROSPERO 2020 CRD42020181371 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020181371

Review question

What problems are published systematic reviews (either with or without meta-analysis) susceptible to which may compromise their reliability or validity?

This includes:

1. Methodological or reporting quality
2. Adherence to guidelines
3. Author conduct including questionable research practices
4. Presence of conflicts of interest, researcher allegiance and disclosure
4. Methodological limitations

Searches

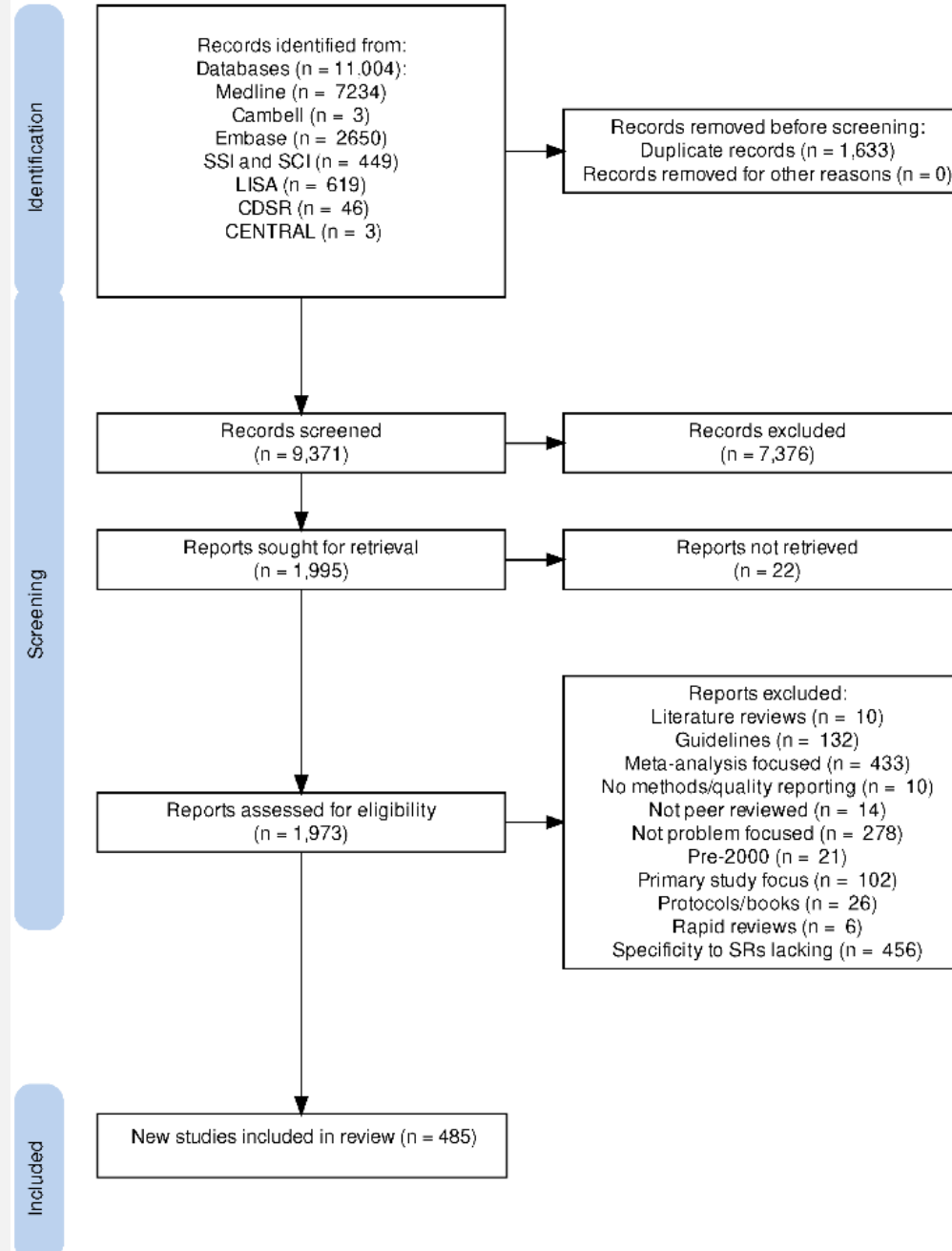
Inclusion criteria

- Academic journal articles highlighting problems with published systematic reviews

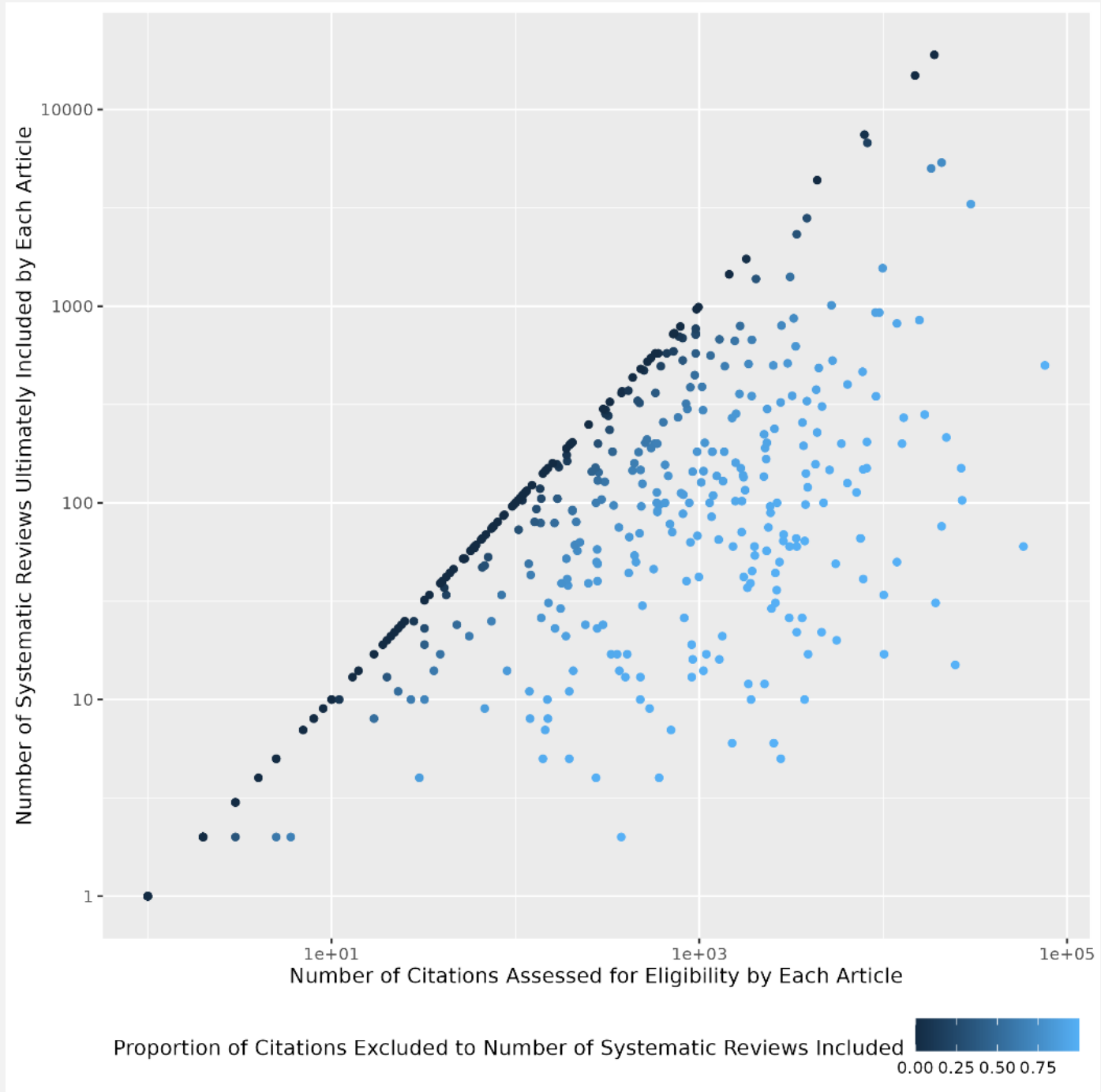
Exclusion criteria

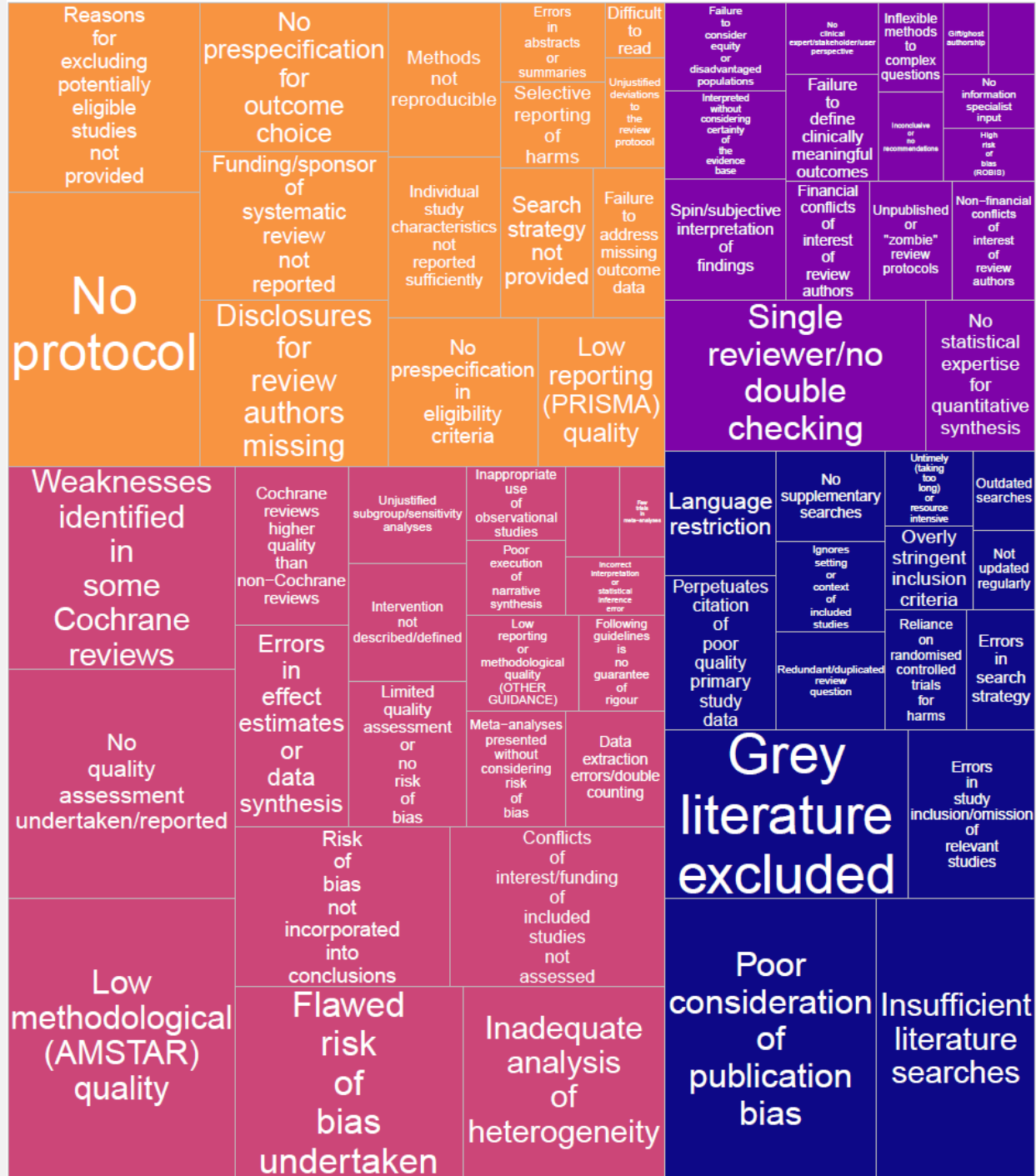
- Articles that discuss theoretical problems in systematic reviews but not in relation to examples in the published literature
- Articles of problems with meta-analyses not conducted in the context of a systematic review

Literature searches from first iteration



Systematic reviews included in the 485 included articles





Domain
 ■ Comprehensive
 ■ Objective
 ■ Rigorous
 ■ Transparent

1. COMPREHENSIVE (does not miss relevant studies)

2. RIGOROUS (uses appropriate methods for data synthesis)

3. TRANSPARENT (reports methods to enable replication)

4. OBJECTIVE (is conducted fairly and without vested interests)

- Overly stringent inclusion criteria affecting external validity
- Insufficient literature searches
- Grey literature excluded
- Language restriction
- Lack of supplementary searches beyond databases
- Errors or omissions in search strategy
- Outdated searches
- Perpetuates citation of poor quality primary study data
- Ignores setting or context of included studies which limits review applicability
- Errors in study inclusion or omission of relevant studies
- Reliance on randomised controlled trials for harms / safety data
- Poor consideration of publication bias
- Redundant / overlapping / duplicated review question; leads to research waste
- Untimely (taking too long) or resource intensive
- Not updated regularly

COMPREHENSIVE

RIGOROUS

- Intervention not described / defined
- Data extraction errors and double counting
- Inclusion of observational / non-randomised studies
- Conflicts of interest or funding of included studies not assessed
- Flawed risk of bias undertaken
- No quality assessment undertaken or reported
- Limited quality assessment or no risk of bias
- Meta-analyses and forest plots presented without considering risk of bias / quality
- Incorrect interpretation or statistical inference error from meta-analysis
- Inadequate analysis of heterogeneity
- Unplanned or unjustified subgroup or sensitivity analyses
- Small number of trials in meta-analyses
- Errors in effect estimate calculations or data synthesis
- Risk of bias not incorporated into conclusions of review
- Poor execution of narrative synthesis
- Low methodological (AMSTAR) quality
- Weaknesses identified in some Cochrane reviews
- Cochrane reviews more rigorous/higher quality than non-Cochrane reviews
- Low reporting or methodological quality (OTHER GUIDANCE)
- Lack of guidance or consistency in systematic overview / umbrella / review of systematic reviews
- Following guidelines is no guarantee of a rigorous systematic review

- No registered or published protocol
- Methods not described to enable replication
- Lack of prespecification in eligibility criteria
- Multiplicity of outcomes and lack of pre-specification for outcome reporting
- Undocumented or unjustified deviations to the review protocol
- Funding or sponsor of systematic review not reported
- Conflict of interest statement or disclosures for review authors missing
- Search strategy not provided
- Reasons for excluding potentially eligible studies not provided
- Individual study characteristics not reported sufficiently
- Selective reporting of harms / safety / adverse events / side effects
- Failure to address missing outcome data in analyses
- Errors in systematic review abstracts or plain language summaries
- Unwieldy/ difficult to read
- Low reporting (PRISMA) quality

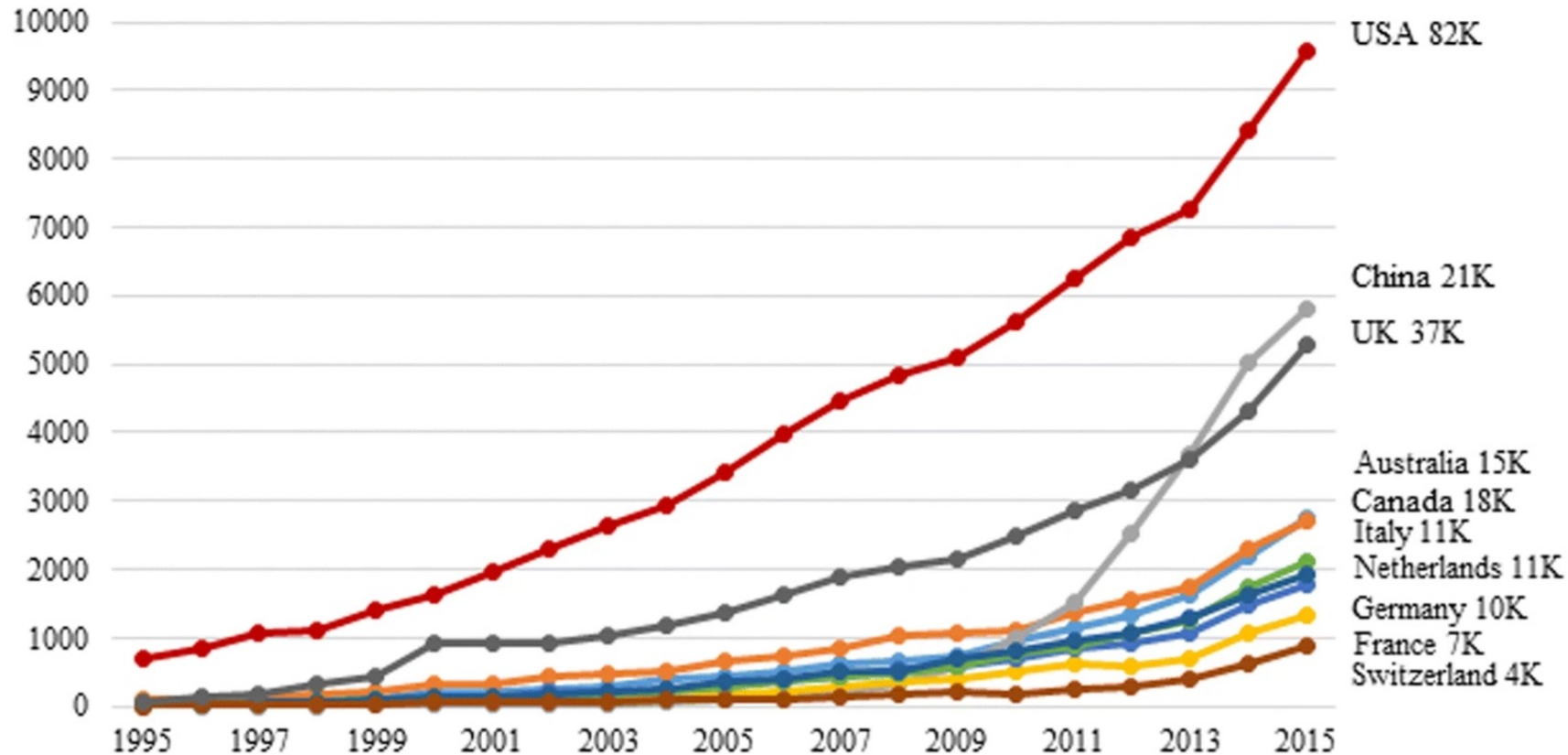
TRANSPARENT

OBJECTIVE

- Lack of clinical expert/ stakeholder/ user perspective
- Review question not justified / important
- Inflexible methods to complex questions
- Failure to consider equity, different socioeconomic groups or disadvantaged populations
- Failure to define clinically meaningful outcomes
- Literature searches not validated by information specialist
- Single reviewer / lack of double checking
- Lack of statistical expertise in handling of quantitative data
- Spin or subjective interpretation of findings
- Unpublished or "zombie" reviews (the file-drawer effect)
- Interpreted without considering certainty or overall quality of the evidence base
- Inconclusive or lack of recommendations
- Guest / gift / ghost authorship
- Non-financial conflicts of interest of review authors
- Financial conflicts of interest of review authors
- High risk of bias (ROBIS)

Secondary research outpacing primary research

Systematic Review Publications, 1995-2015

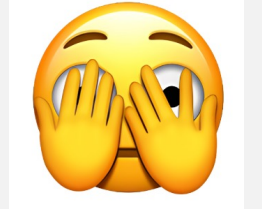
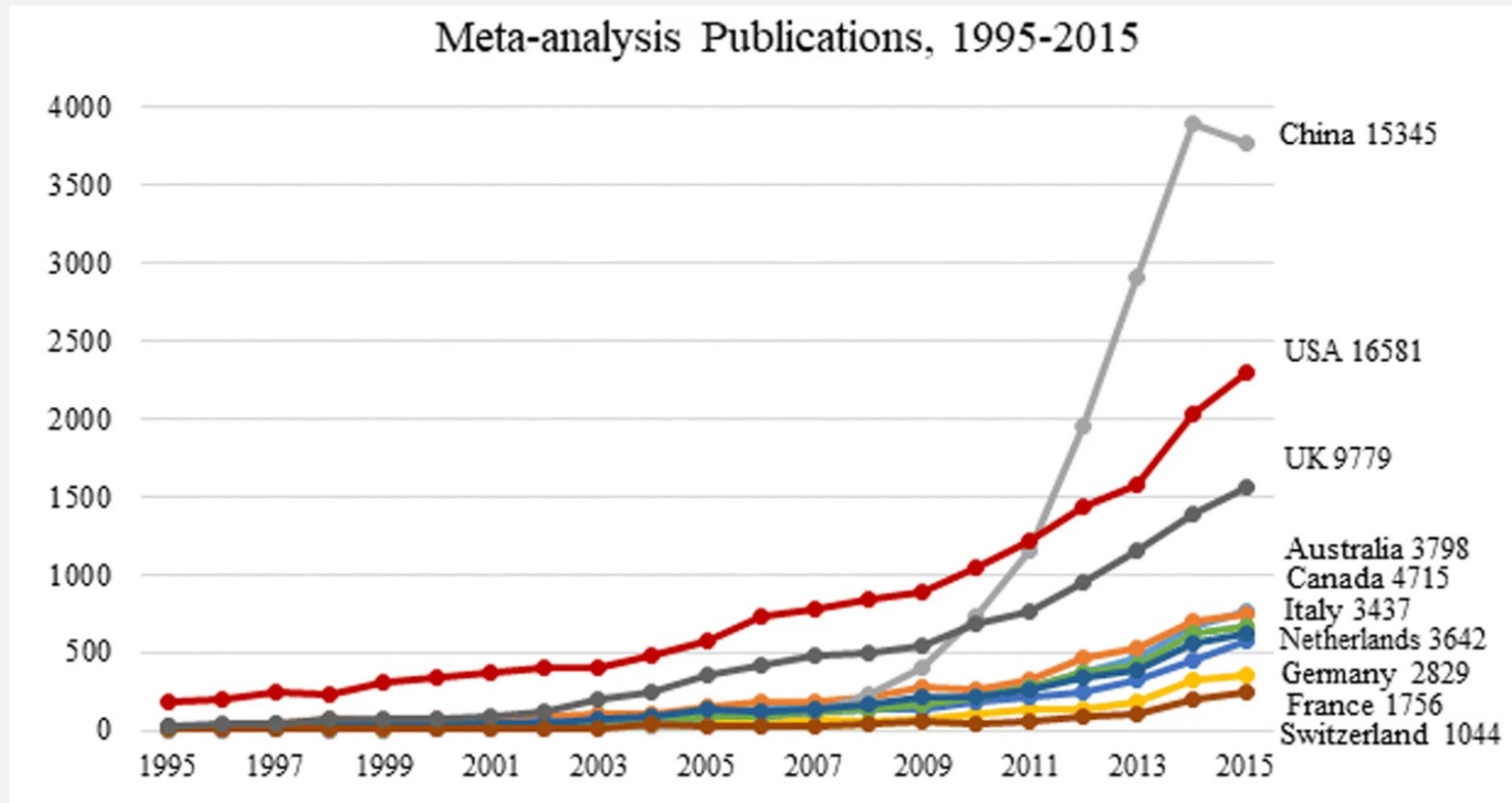


Meta-analysis and systematic reviews all PubMed-indexed publications from 1995 to 2015. Numbers next to the country name indicate 20-year totals

Fontelo, P., & Liu, F. (2018). A review of recent publication trends from top publishing countries. *Systematic reviews*, 7(1), 1-9.

Ioannidis, J. P. (2016). The mass production of redundant, misleading, and conflicted systematic reviews and meta-analyses. *The Milbank Quarterly*, 94(3), 485-514.

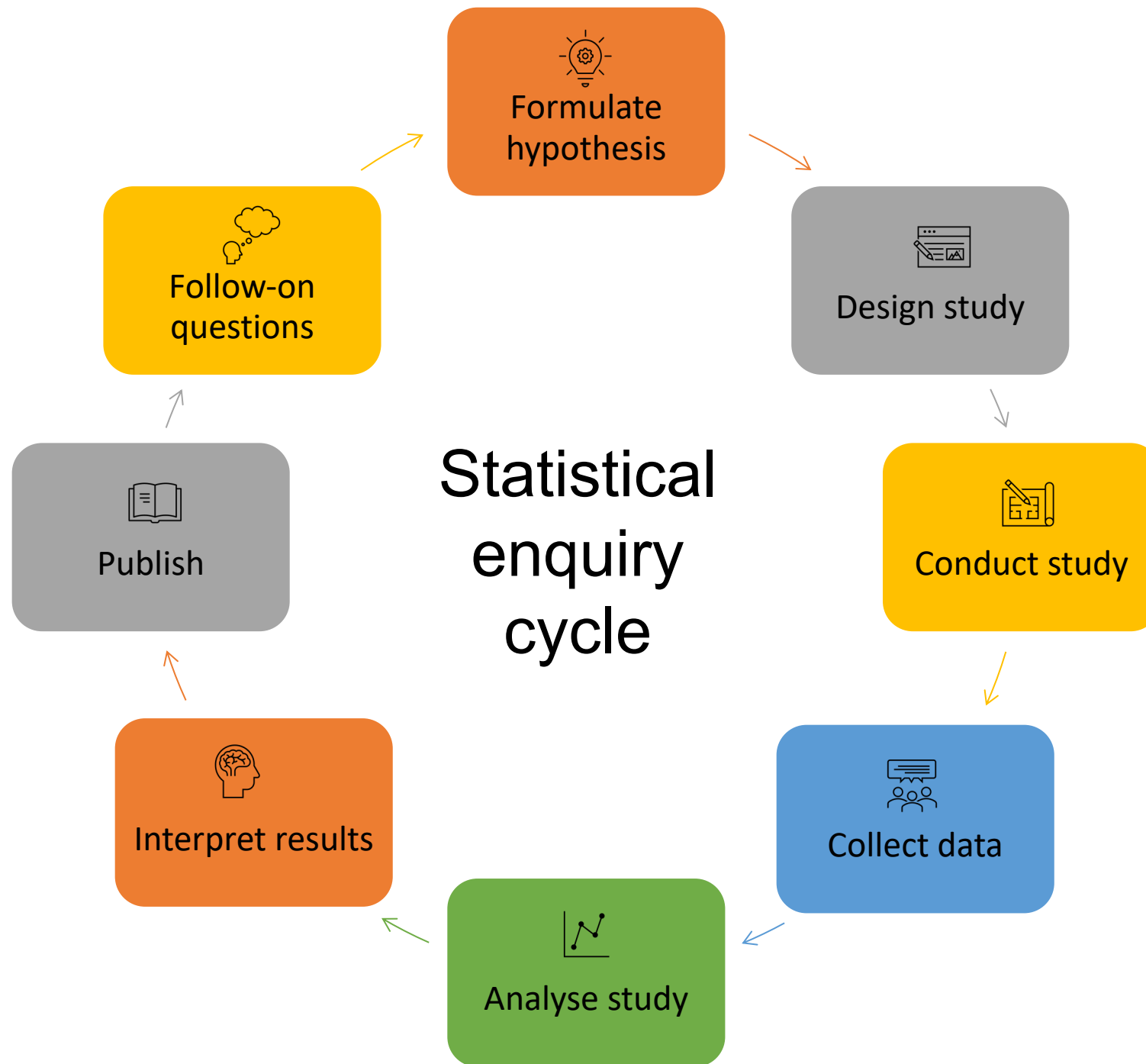
Retrospective meta-analyses: please stop



Fontelo, P., & Liu, F. (2018). A review of recent publication trends from top publishing countries. *Systematic reviews*, 7(1), 1-9.

Niforatos, J. D., Chaitoff, A., Weaver, M., Feinstein, M. M., & Johansen, M. E. (2020). Pediatric literature shift: Growth of meta-analyses was 23 times greater than growth of randomized trials. *Journal of Clinical Epidemiology*, 121, 112-114.

Why so many sub-optimal systematic reviews?

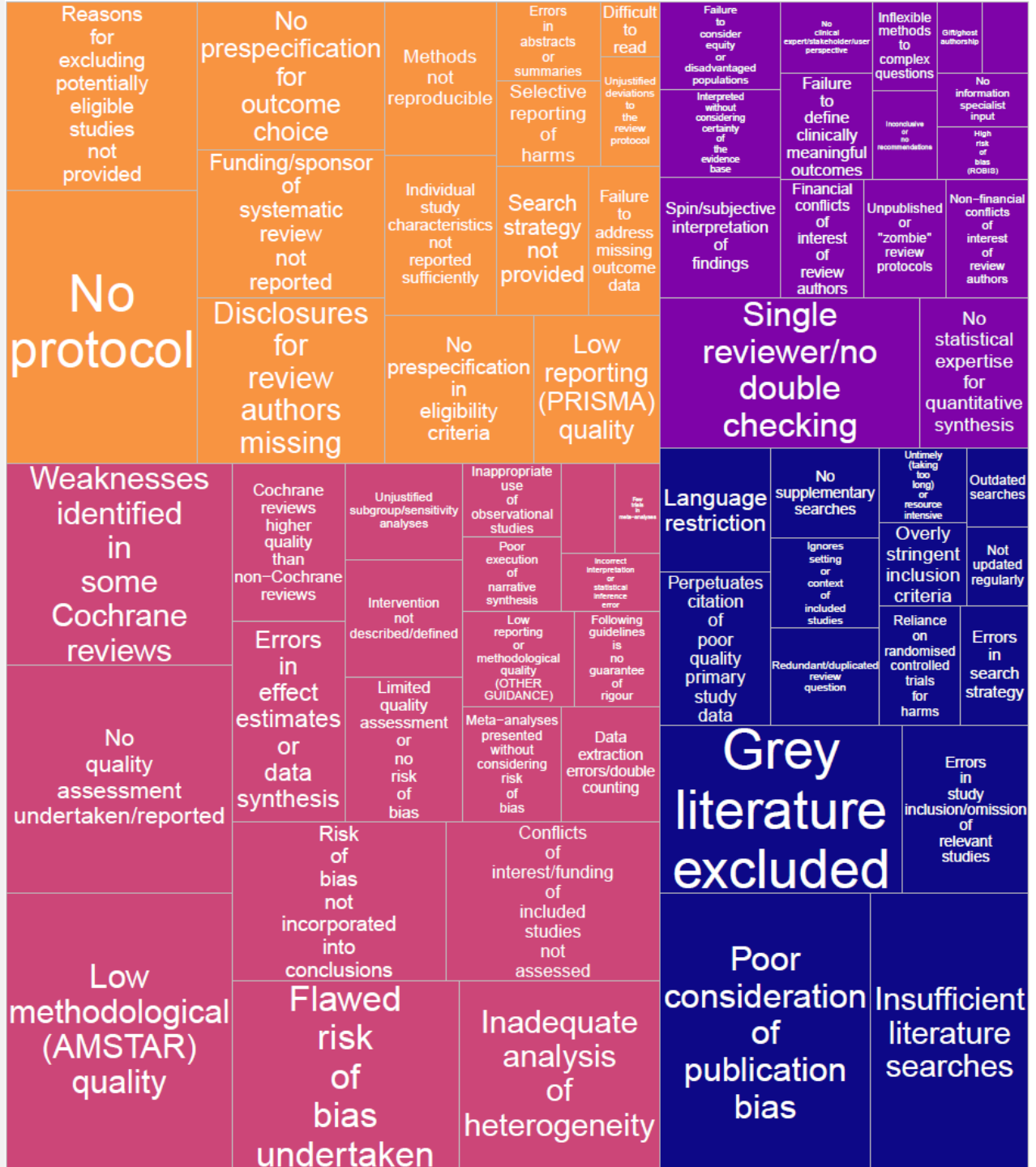




Research waste



Solutions?



Domain

- Comprehensive
- Objective
- Rigorous
- Transparent

Comprehensive

- Team inclusivity
 - Appropriate methodological representation: information specialist/librarian, statistician
 - Public involvement
 - Content/ clinical expertise
- Search reflexivity

Rigour

- Guideline consultation/adherence (e.g. MECIR)
- Planning for heterogeneity in the protocol
- Statistical expertise for quantitative syntheses

Transparency

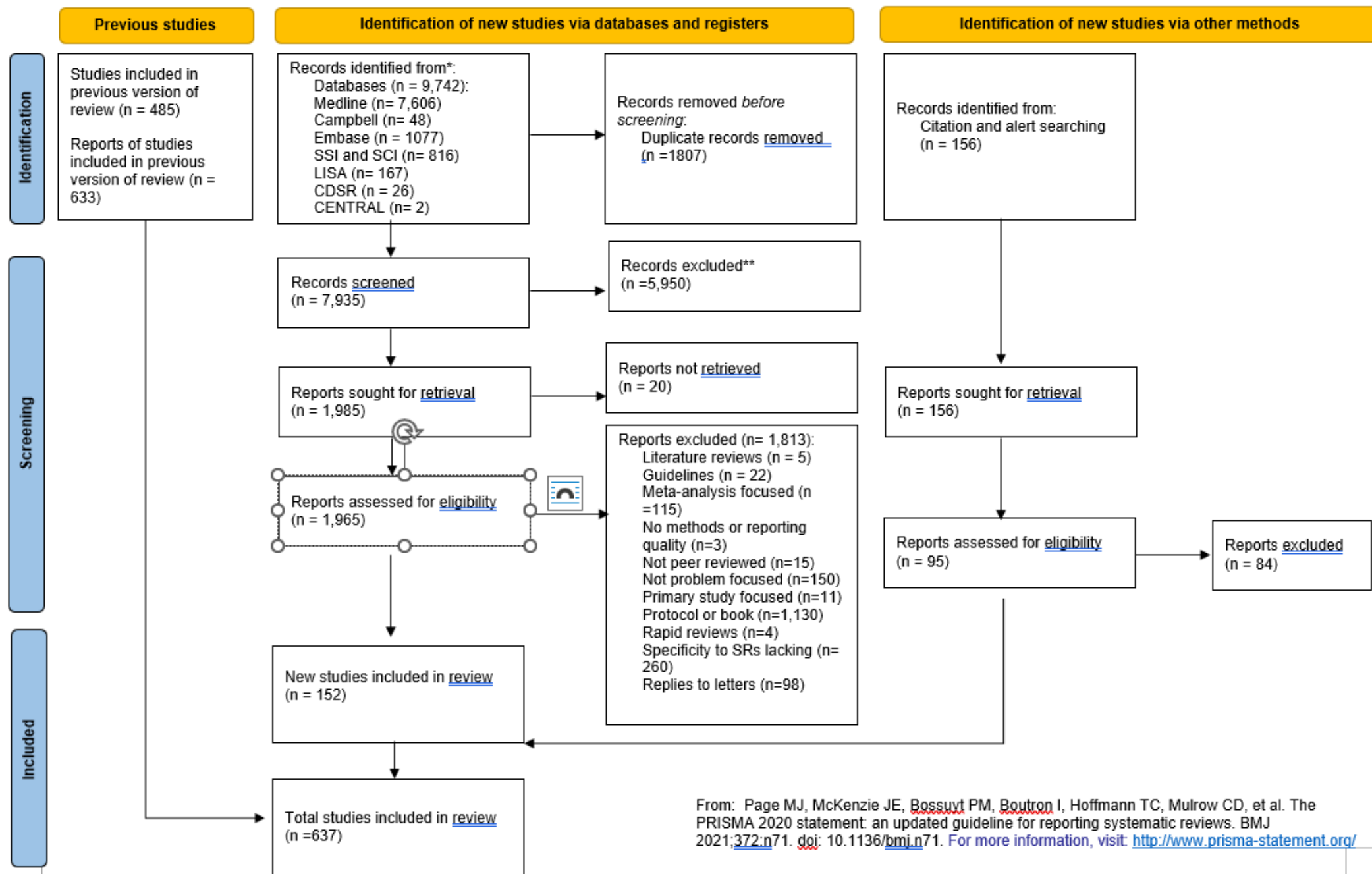
- Pre-specification (e.g. PROSPERO, Open science framework)
- Reporting guidelines (e.g. PRISMA)
- Timely and complete reporting regardless of direction/magnitude of findings; Pre-prints
- Data sharing
- Especially for publicly funded research

Objective

- Diverse research teams for generalizable research
- Engaged representation = clinically meaningful research questions
- Acknowledging own potential conflicts (financial and non-financial)
- Knowing when to step back
- Managing conflicted experts in the team
- Accountability

New developments for this work (1)

- Update performed 2023: now 637 included studies



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>

New developments for this work (2)

- New problem identified: **Lack of diversity in review authorship teams**

OBJECTIVE

New keywords: Immunology, Living, Environment, Haematology

New developments for this work (3)

- Systematic Reviewlution to live a bit longer!
- (MRC Transition Support Award 2025-2026)



Journal of Clinical Epidemiology Special Issue: Methodological Aspects of Research Integrity & Culture

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19 March 2024

Methodological aspects of research
integrity and culture

Submission deadline: **02 September 2024**

24 February 2023

Special Issue: Methodological
Considerations Related to Equity,
Diversity, and Inclusion in Clinical
Epidemiology

Submission deadline: **01 April 2024**

19 March 2024

Methodological aspects of research integrity and culture

This series aims to cover a broad range of methodological issues of relevance to research integrity, scientific misconduct, and questionable research practices.

Guest editors:

- **Gowri Gopalakrishna, PhD**
University of Maastricht, Lead investigator of the Dutch National Survey on Research Integrity, The Netherlands
Research ethics, Research Integrity, Open Science, Responsible Conduct of Research
- **Limbanazo Matandika, PhD**
Interim Steering Committee Member. Africa Research Integrity Network (ARIN)
Research Integrity, Decolonising Global Health, Embedded Ethics Approaches, Informed Consent, Clinical ethics,
Distributive Justice, Authorship, Conflict of Interest
- **David Moher, PhD**
Director of the Centre for Journalology, Senior Scientist in the Clinical Epidemiology Program at Ottawa Hospital
Research Institute, Canada
Reporting guidelines, Open Science, Research Integrity, Publication Science, Systematic Reviews
- **Lesley Uttley, BSc, PhD**
Senior Research Fellow, Sheffield Centre for Health and Related Research (SCHARR), School of Medicine and
Population Health, University of Sheffield, UK
Research Integrity, meta-research, systematic reviews, research culture



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Thank you for listening. Questions?

<https://systematicreviewlution.com/>

[Uttley, L., Quintana, D. S., Montgomery, P., Carroll, C., Page, M. J., Falzon, L., ... & Moher, D. \(2023\). The problems with systematic reviews: a living systematic review. *Journal of Clinical Epidemiology*.](#)

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