How to Conduct Systematic Reviews to Generate Supportive Evidence for Claims and to Establish Safety

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Conflict of Interest

Author is an academician and declares no conflict of interest.

Generating evidence

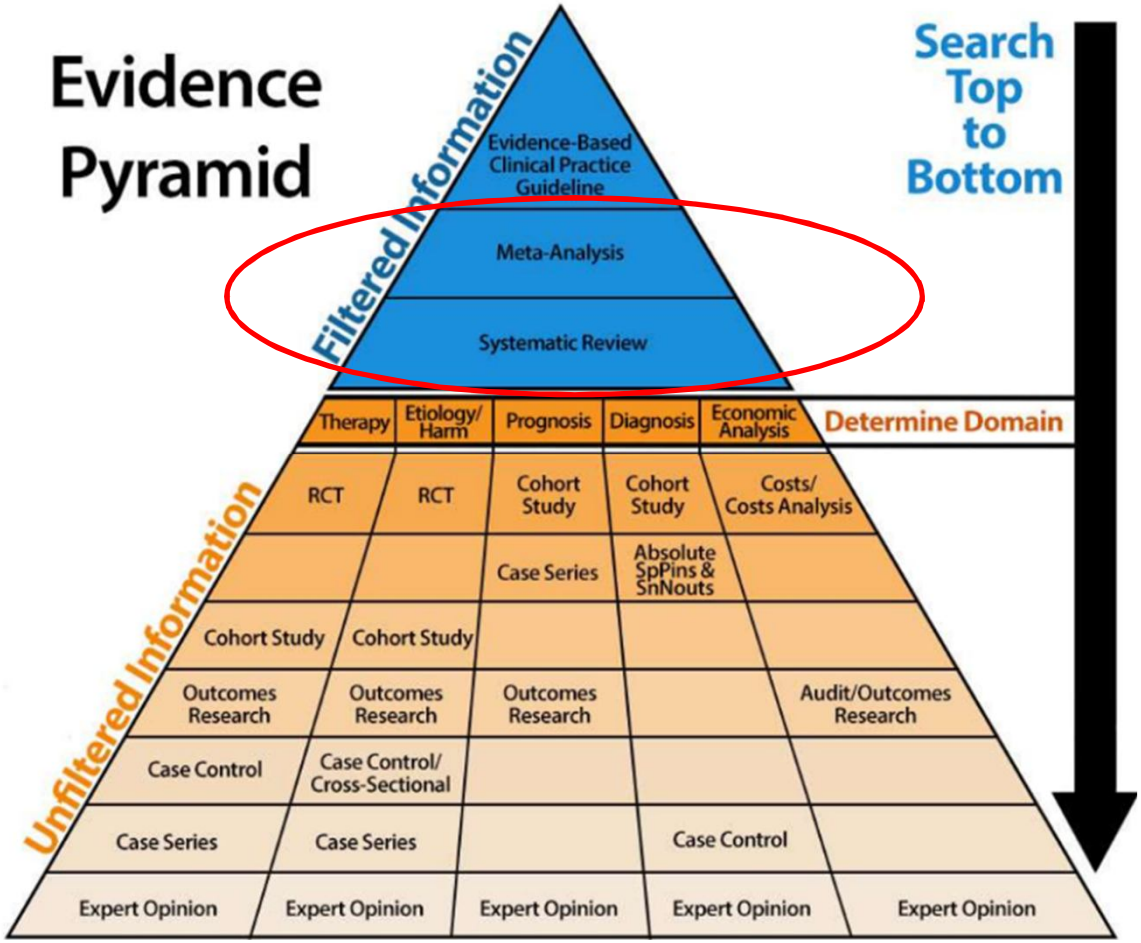
Types of Reviews

- Information specialists should be familiar with review families & types and the associated retrieval methods to enhance their role with the review team.
  - Traditional
  - Systematic
- Given the current overlap of methodologies, there is a need for an internationally agreed set of discrete, coherent and mutually exclusive review types.

Systematic Reviews and Meta-analysis

- Systematic review 'Seeks to systematically search for, appraise and synthesize research evidence, often adhering to guidelines on the conduct of a review' (Grant & Booth, 2009)
- 'Cochrane Reviews are systematic summaries of evidence of the effects of healthcare interventions. They are intended to help people make practical decisions. For a review to be called a 'Cochrane Review' it must be in CDSR (Cochrane Database of Systematic Reviews) or CMR (Cochrane Methodology Register).
- Meta-analysis 'Technique that statistically combines the results of quantitative studies to provide a more precise effect of the results' (Grant & Booth, 2009)

LEVEL OF EVIDENCE



PRISMA is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses.

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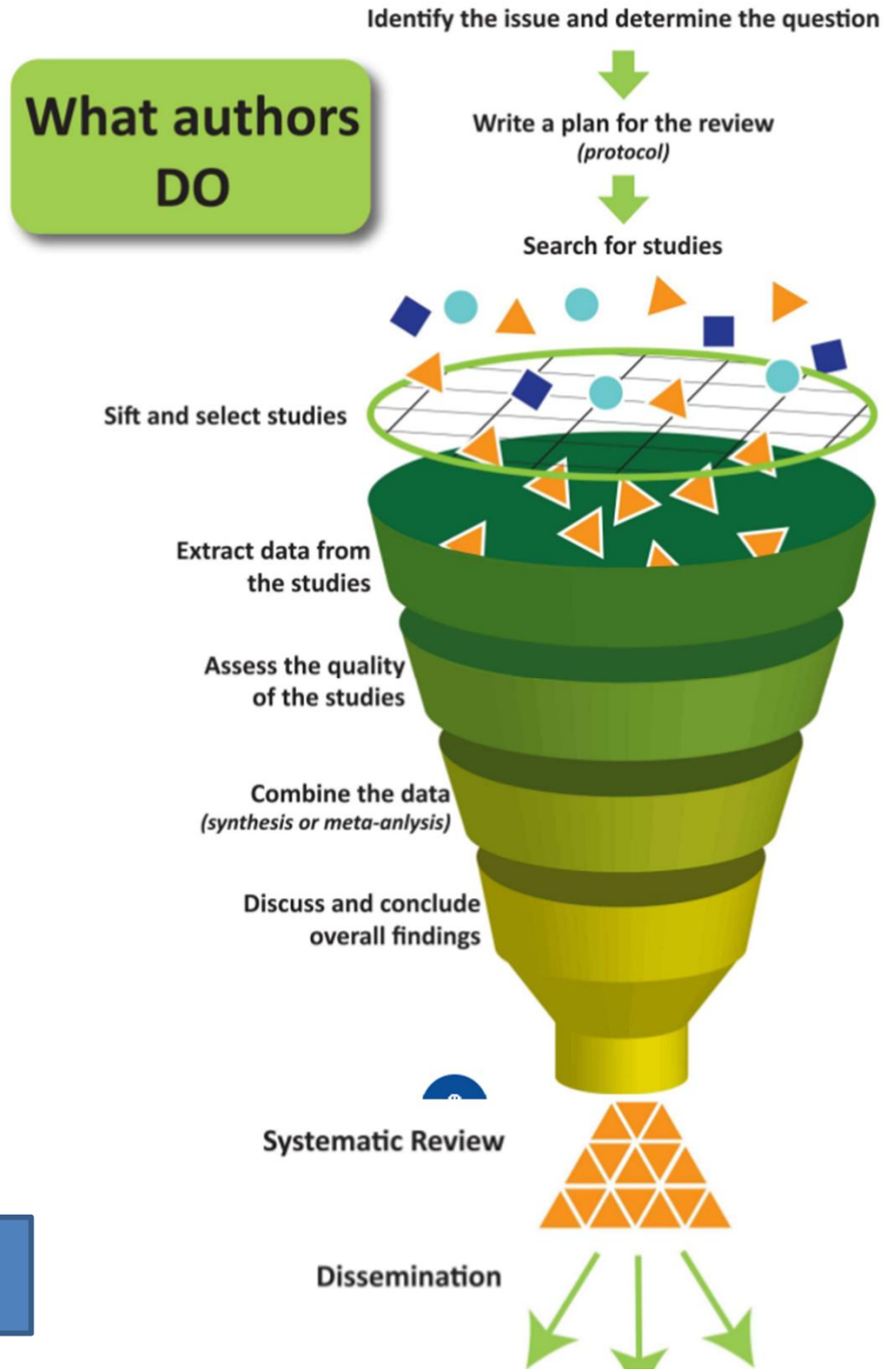
Reference: Level of Evidence, Evidence based practice toolkit- Research Hub at Winona State University

Types of Frameworks and Formats

- PRISMA primarily focuses on the reporting of reviews evaluating the effects of interventions, but can also be used as a basis for reporting systematic reviews with objectives other than evaluating interventions (e.g. evaluating aetiology, prevalence, diagnosis or prognosis).
- The PICO format is commonly used in evidence-based clinical practice. This format creates a "well-built" question that identifies four concepts: (1) the Patient problem or Population, (2) the Intervention, (3) the Comparison (if there is one), and (4) the Outcome(s).
- The PICO tool focuses on the Population, Intervention, Comparison and Outcomes of a (usually quantitative) article. It is commonly used to identify components of clinical evidence for systematic reviews in evidence based medicine and is endorsed by the Cochrane Collaboration
- PEO (Population, Exposure, Outcome) is also used in health research to help identify the key concepts of a topic and structure the literature review.

Cochrane Reviews

- Systematic reviews seek to collate evidence that fits pre-specified eligibility criteria in order to answer a specific research question. They aim to minimize bias by using explicit, systematic methods documented in advance with a protocol.
- Cochrane prepares, maintains and promotes systematic reviews (Cochrane Reviews) to inform decisions about health and social care.
- Cochrane Reviews are published in the Cochrane Database of Systematic Reviews in the Cochrane Library.
- The Cochrane Handbook for Systematic Reviews of Interventions contains methodological guidance for the preparation and maintenance of Cochrane Reviews on the effects of interventions.



Source: Jessica Kaufman

Databases to search

- Google Scholar
- Science Direct
- Scopus
- Ovid Medline,
- Embase
- Cochrane CENTRAL
- Cochrane Database of Syste matic Reviews
- PROSPERO for prospective reviews

Assembling Your Research Team

Reviewers – You may need at least two reviewers working independently to screen abstracts, with a potential third as a tie-breaker

Subject matter experts – Subject matter experts can clarify issues related to the topic,

Statistician – A statistician can help with data analysis

Project leader – A project leader can coordinate and write the final report

Librarians – Librarian(s) can develop comprehensive search strategies and identify appropriate databases

Formulate Your Research Question

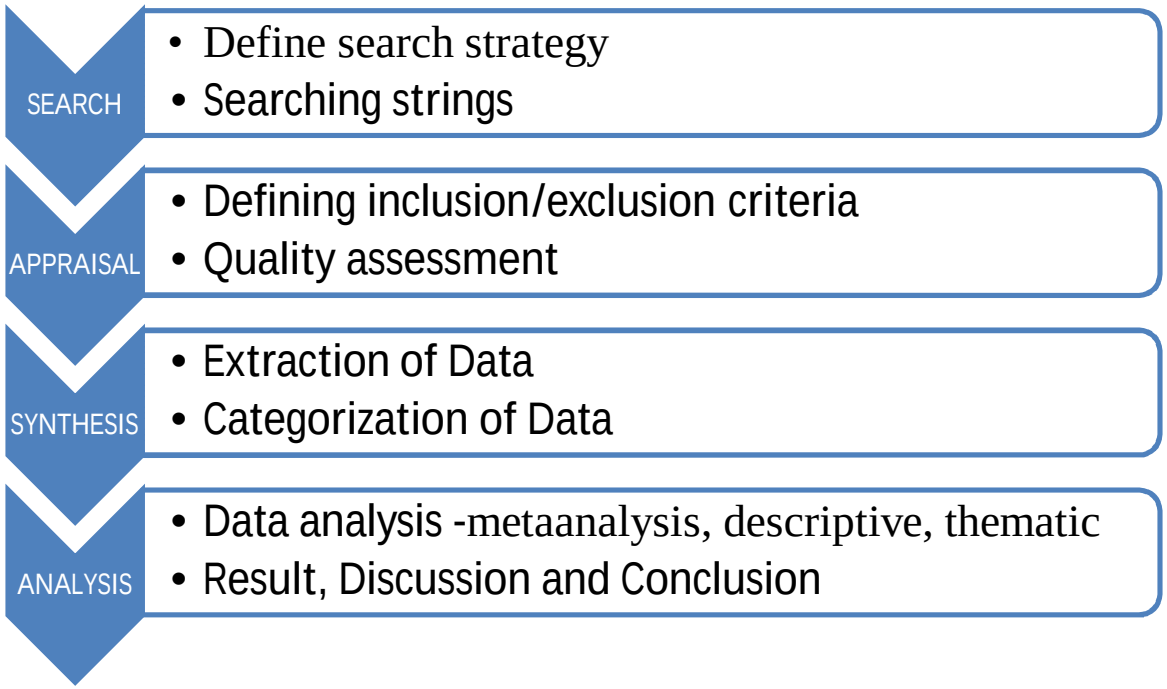
- Do artificial sweeteners increase insulin resistance?
- How much of vitamin C should be present in food to help improve the immunity?

Create a Review Protocol

- Reviews like a systematic review require a **protocol**, which is essentially a planning document that indicates how your review will be carried out.
- You may wish to register your protocol to avoid the duplication of work and to reduce the potential for bias by enabling a comparison between what was stated in the protocol to the completed review.
- It is also a way to share your current research interests with the research community at large and help build your research profile.

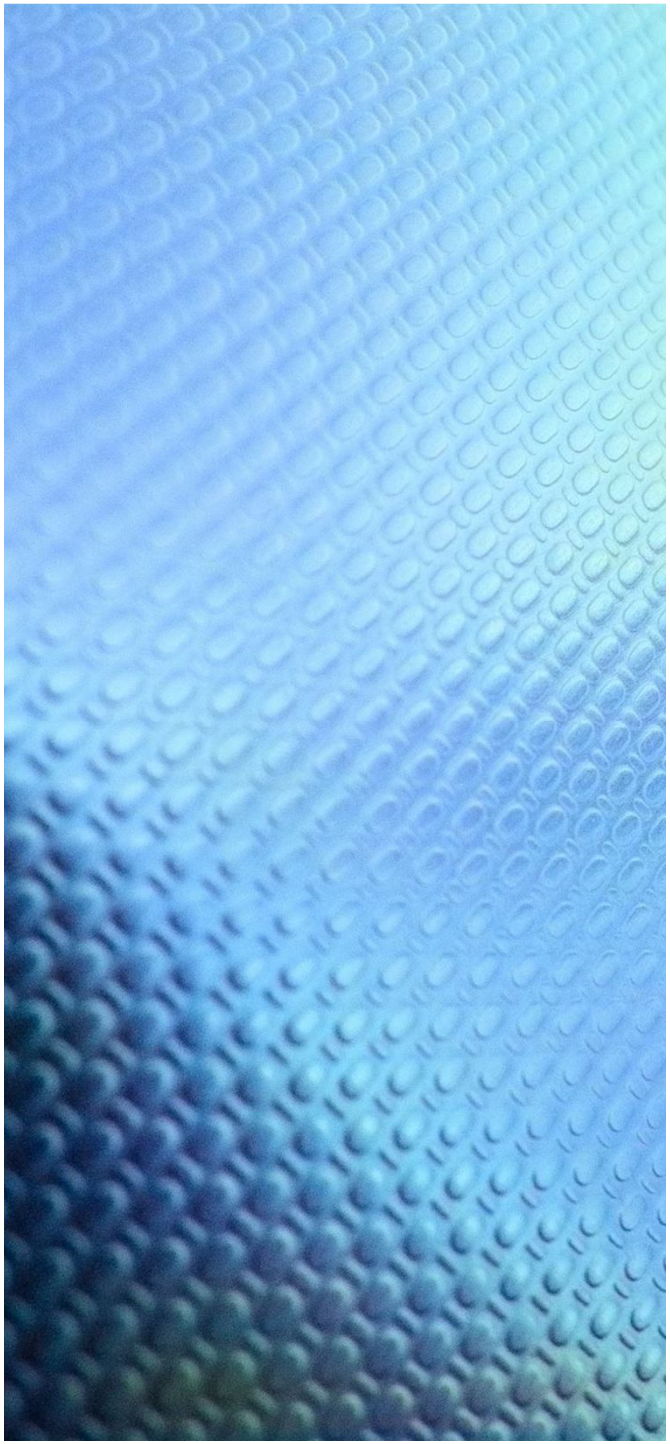
Conducting Your Review Using the SALSA Framework

- Once you have a research question, there are four stages you can follow when conducting your chosen review. These are known as the SALSA Framework: **s**earch, **a**ppraisa**l**, **s**ynthesis and **a**nalysis.



How to GRADE the quality of the evidence

- The GRADE system rates the quality or certainty of the evidence
- Summary of findings (SoF) tables presents the results (together with the GRADE rating) for the most important outcomes in the review.
- Need to be reported at protocol stage
- You will need to decide which outcomes you will include in the table at the outset.
- GRADE starts with a baseline rating of HIGH for RCTs, and LOW for non-RCTs.
- This baseline rating can then be adjusted (downgraded or, less commonly, upgraded) after considering 8 assessment criteria and making a judgement about quality based on these.



Grading process

At least two review authors should work independently to assess the quality of evidence and resolve disagreements.

The process for reaching consensus where there are disagreements in ratings should be outlined in your Protocol.

Preparing Summary of Findings (SoF) Tables

- A Summary of Findings (SoF) table provides a summary of the main results of a review together with an assessment of the quality or certainty of the evidence (assessed using the GRADE tool) upon which these results are based.
- Assessing the quality of the evidence using the GRADE criteria is an essential step in preparing a SoF table.
- There are four main steps in creating a SoF:

1. Choose **one main comparison** from the review for the main SoF
2. Choose **up to 7 outcomes** to include in the SoF
3. Assess the quality of evidence for each outcome
4. Present the effects or impact of the intervention (relative and absolute)

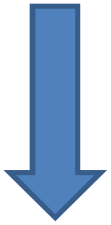
- **Steps 1 and 2 should ideally be completed at protocol stage; while steps 3 and 4 occur at review stage.**

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines

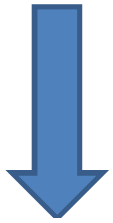
The 2020 PRISMA statement consists of a 27-item checklist and a 4-phase flow diagram.

PRISMA 2020 CHECKLIST

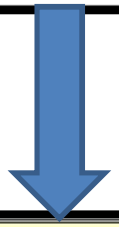
Section and Topic	Item #	Checklist item
TITLE		
Title	1	Identify the report as a systematic review.
ABSTRACT		
Abstract	2	See the PRISMA 2020 for Abstracts checklist.
INTRODUCTION		
Rationale	3	Describe the rationale for the review in the context of existing knowledge.
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.



METHODS		
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.

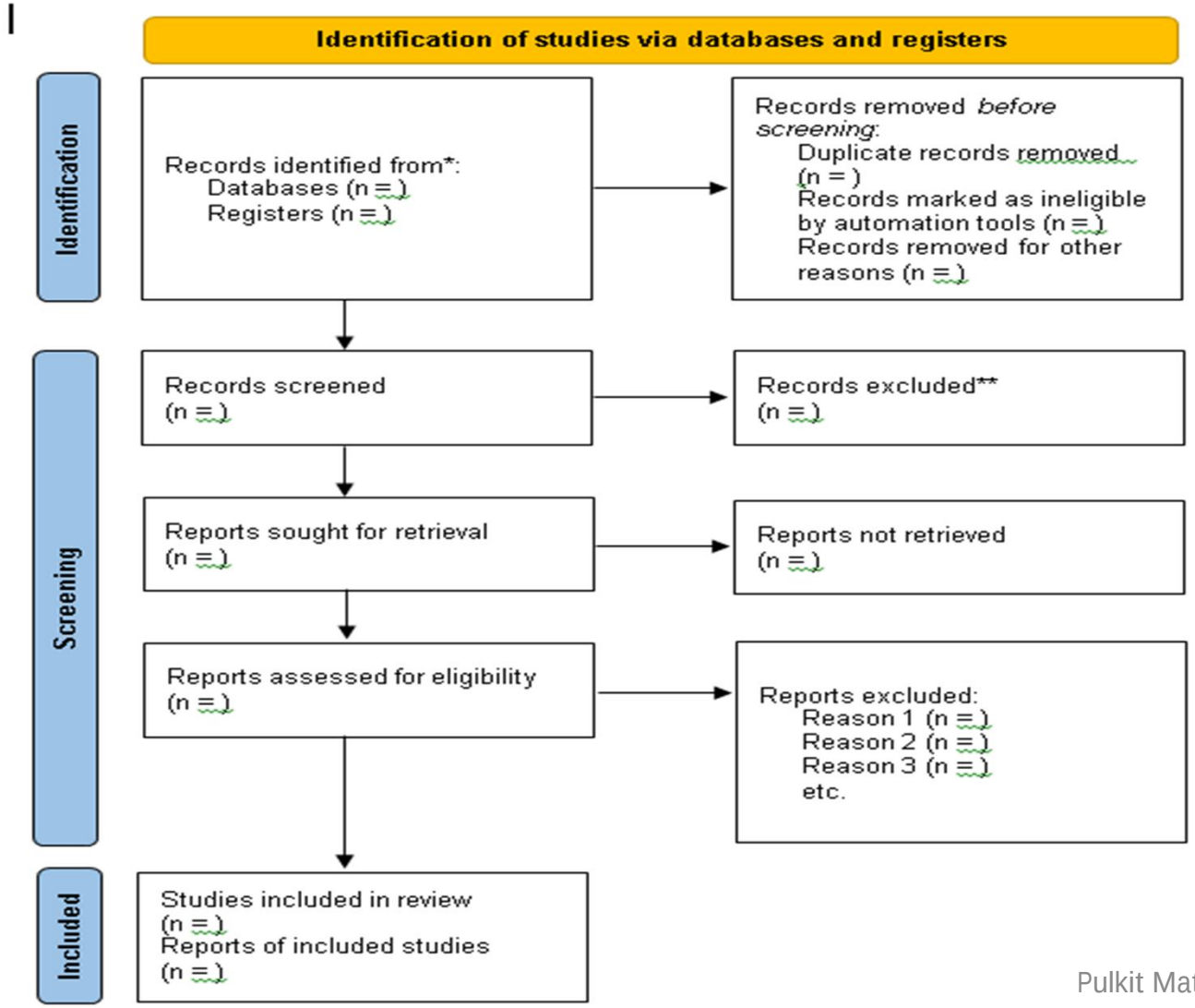


RESULTS		
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.
Study characteristics	17	Cite each included study and present its characteristics.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.
	20c	Present results of all investigations of possible causes of heterogeneity among study results.
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.



DISCUSSION		
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.
	23b	Discuss any limitations of the evidence included in the review.
	23c	Discuss any limitations of the review processes used.
	23d	Discuss implications of the results for practice, policy, and future research.
OTHER INFORMATION		
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.
	24c	Describe and explain any amendments to information provided at registration or in the protocol.
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.
Competing interests	26	Declare any competing interests of review authors.
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.

PRISMA 2020 FLOW DIAGRAM FOR NEW SYSTEMATIC REVIEWS



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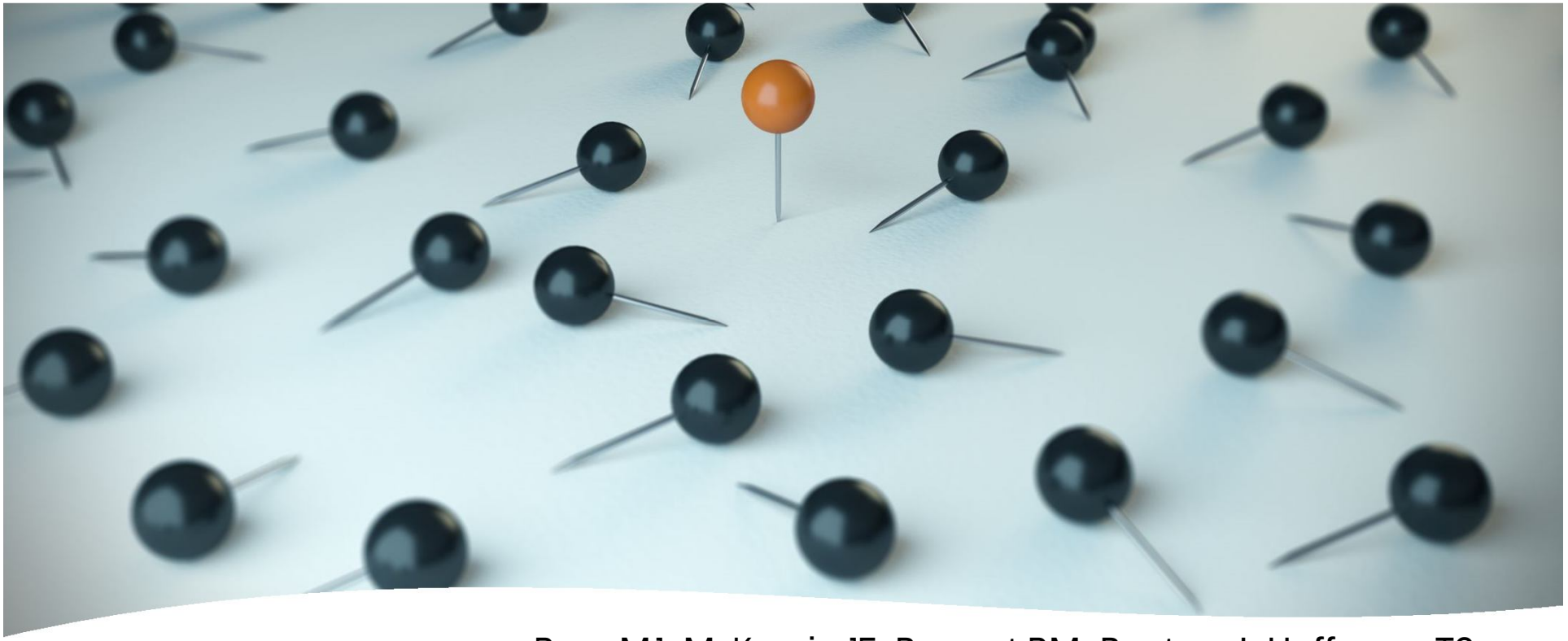

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Useful websites

- https://scientific-publishing.webshop.elsevier.com/research-process/levels-of-evidence-in-research/
- http://www.prisma-statement.org/
- https://training.cochrane.org/handbook/current

Thank you for your attention!